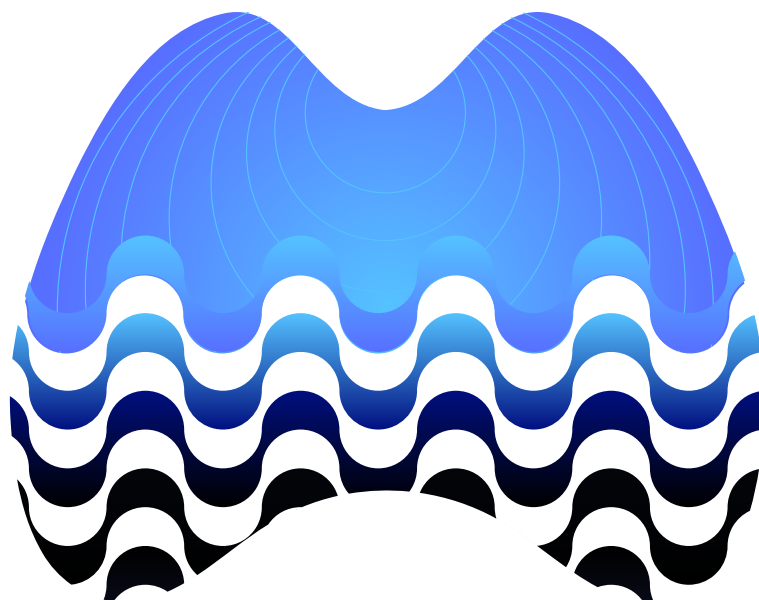


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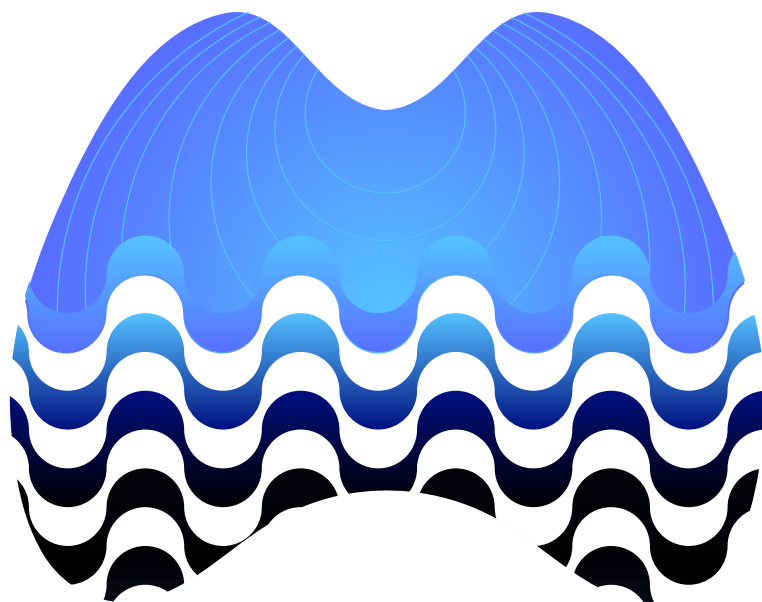
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17th

International **Thyroid** Congress

18 – 22 **June 2025**

Rio de Janeiro Brazil

17th International Thyroid Congress Welcome Message

Dear Attendees,

On behalf of the Latin American Thyroid Society (LATS) it is with great pleasure that we welcome you to the 17th International Thyroid Congress (ITC), which is held from June 18th to 22nd, 2025, at the Centro de Convenções Windsor Oceânico, in the city of Rio de Janeiro, Brazil.

The ITC meetings, held every five years, are co-sponsored by the **LATS**, European Thyroid Association (**ETA**), the American Thyroid Association (**ATA**), and the Asia & Oceania Thyroid Association (**AOTA**). Each edition of the ITC is hosted by one of these sister societies on a rotational basis. This unique alliance underscores our shared commitment to promoting excellence in thyroid research and care worldwide.

The ITC 2025 event marks the third occasion in Latin America, following the successful gatherings in São Paulo (9th edition) and Buenos Aires (13th edition).

The scientific program is the result of four years of dedicated work by the Program Organizing Committee (POC), with representatives from all four sister societies: AOTA, ATA, ETA, and LATS. This collaborative and synergistic group concentrated their efforts to shape an outstanding program featuring a rich and diverse agenda, including 4 plenary sessions and 4 prize lectures – one from each participating society – as well as an impressive lineup of 24 symposia and 30 Meet-the-Professor sessions or debates. These sessions explore a wide spectrum of cutting-edge topics, spanning both basic and clinical aspects of thyroid diseases. Scientific meetings should serve as a catalyst for advancing science. Indeed, the ITC proudly features nearly 700 original research abstracts from 59 countries across 6 continents: Africa, Asia, Europe, North America, South America, and Oceania. Of these, 52 will be presented as Oral Presentations, 86 as Short Oral Communications, and 524 as Posters. Needless to say, the Congress showcases the most distinguished researchers and professors from around the world, presenting the latest advancements in the field. Such remarkable global engagement and scientific excellence underscore the resounding success of the 17th International Thyroid Congress, firmly establishing it as a premier forum for advancing thyroid research and clinical practice worldwide.

Kind regards,



Janete Cerutti
LATS President



Ines Califano
LATS Secretary

Ana Luiza Maia
POC President

Claudia Gabriella Pelizzas
POC Secretary

Denise Pires de Carvalho
LOC President

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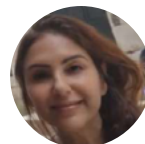

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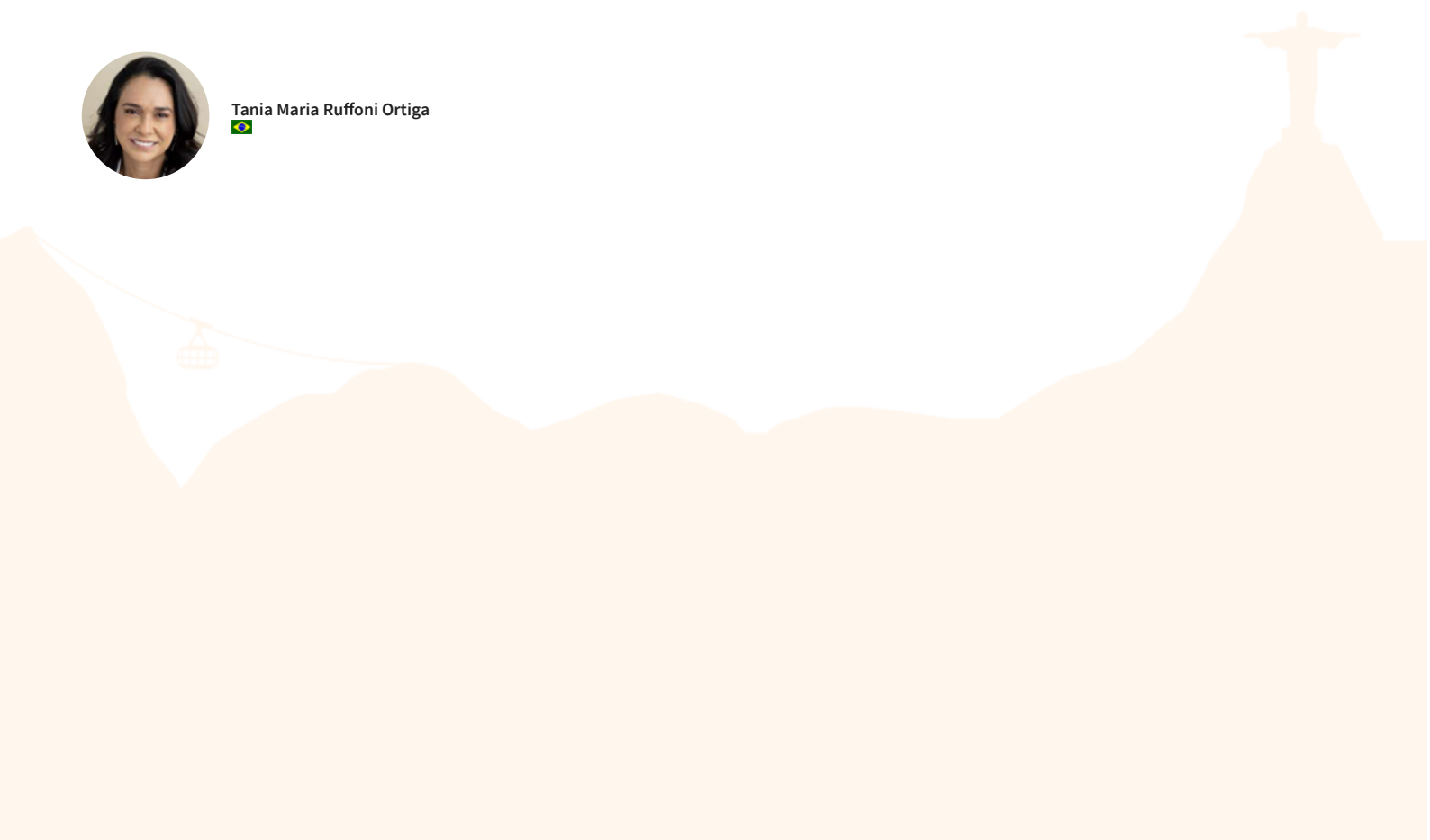

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17th International Thyroid Congress Travel Grants Award

The following societies generously provided travel grant funding for their respective members:

LATS: \$15,500 USD in travel grants for LATS members

ETA: \$15,000 USD in travel grants for ETA members

AOTA: \$20,000 USD in travel grants for AOTA members

ATA: \$15,000 USD in travel grants for ATA members

Award Criteria

Travel grant awards were given to young investigator members who are first authors of accepted oral or poster presentations at the 17th International Thyroid Congress. Age eligibility was determined according to the rules of each society. Awards were granted based on scientific merit, specifically the average review score of the submitted abstract.

Eligibility Criteria

Applicants must be current members in good standing of the ATA, AOTA, ETA, or LATS.

Support for African Delegates

In addition, each of the LATS, ETA, AOTA, and ATA societies awarded one travel grant to support a delegate from an African country not currently affiliated with any of the participating societies – reflecting a shared commitment to global inclusion and scientific exchange.



17th International Thyroid Congress Travel Grant Honorees

LATS Grant Recipients

1. Adriano Francisco De Marchi Junior (Brazil)
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4. Antonella Blanco (Argentina)
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12. Guilherme Henrique (Brazil)
13. Gustavo Felisola Caso
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15. Gustavo Maresi Rodrigues (Brazil)
16. Isabela Nogueira Nunes (Brazil)
17. Izabela Fernanda Dal' Bó Cruz (Brazil)
18. Javier Ignacio Jaramillo Medina (Chile)
19. Júlia Helena Tezzei (Brazil)
20. Júlia Isabel Richter Cicogna (Brazil)
21. Lara Bessa Campelo Pinheiro Cavalcante (Brazil)
22. Laura Marmitt (Brazil)
23. Leonardo Barbi Walter (Brazil)
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27. Mariana Pires Cavalcanti Teixeira (Argentina)
28. Natália Schara Nascimento (Brazil)
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30. Nicole Lustig Franco (Chile)
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32. Thacila de Oliveira Marques (Brazil)
33. Thamires Siqueira de Oliveira (Brazil)
34. Vinicius Gonçalves Rodrigues (Brazil)
35. Welbert Gomes Rocha (Brazil)

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1. Anna Lopez Marti (Netherlands)
2. Benái Paponette (Ireland)
3. Camilo Ignacio Fuentes Pena (Belgium)
4. Chiara Mur (Italy)
5. Elisa Minaldi (Italy)
6. Elisabete Teixeira (Portugal)
7. Giulia Lanzolla (Italy)
8. Karine Aleksanyan (Armenia)
9. Laurine Mebarki (France)
10. Maciej Bulwa (Poland)
11. Matteo Trevisan (Italy)
12. Nguyen Van Bang (Vietnam)
13. Prashant Changoer (Netherlands)
14. Tim Brandenburg (Germany)
15. Victor Valcarcel Hernandez (France)
16. Yindi Liu (Netherlands)

ATA Grant Recipients

1. Sarah Hamidi (United States)
2. Jennifer Rui Wang (United States)
3. Thomas Szabo Yamashita (United States)
4. Sonam Kumari (United States)
5. Xiao Zhao (United States)
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11. Steven Xie (United States)
12. Sahar Alizada
13. Annunziata Cicatiello



Past Meetings of the International Thyroid Congress (ITC)

1st International Conference on Goitre

Berne, Switzerland – August 24–26, 1927

2nd International Conference on Goitre

Berne, Switzerland – August 1933

3rd International Goitre Conference & American Association for the Study of Goiter

Mayflower Hotel, Washington, DC – September 12–14, 1938

4th International Goitre Conference

London, UK – July 5–8, 1960

5th International Thyroid Conference

Rome, Italy – May 23–27, 1965

6th International Thyroid Conference

Vienna, Austria – June 22–25, 1970

7th International Thyroid Conference

Boston, Massachusetts, USA – June 9–13, 1975

8th International Thyroid Congress & 55th Annual Meeting of the ATA

Sydney, Australia – February 3–8, 1980

9th International Thyroid Congress

São Paulo, Brazil – September 1–6, 1985

10th International Thyroid Conference

Netherlands Conference Centre, The Hague, The Netherlands – February 3–8, 1991

11th International Thyroid Congress

The Sheraton Centre, Toronto, Ontario, Canada – September 10–15, 1995

12th International Thyroid Conference

Kyoto International Conference Hall, Kyoto, Japan – October 22–27, 2000

13th International Thyroid Congress

Buenos Aires, Argentina – October 30–November 4, 2005

14th International Thyroid Congress

Palais des Congrès, Paris, France – September 11–16, 2010

15th International Thyroid Congress & 85th Annual Meeting of the ATA

Walt Disney World Swan and Dolphin Resort, Lake Buena Vista, Florida, USA – October 18–23, 2015

16th International Thyroid Congress (Virtual Edition)

December 16–20, 2020

17th International Thyroid Congress

Rio de Janeiro, Brazil – June 18–22, 2025





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Dr. Carla Moran, Ireland
Prof. Robert Opitz, Germany
Dr. Cristina Romei, Italy

European Thyroid Association (ETA) – Anno 1965

Mission & Activities

The European Thyroid Association (ETA) is a leading scientific organization dedicated to advancing research, education, and clinical practice in the field of thyroidology. Established in 1965, the ETA fosters collaboration among clinicians, researchers, and healthcare professionals across Europe and beyond.

The ETA's primary mission is to promote both basic and clinical research in thyroidology, enhance understanding of thyroid diseases, and improve patient care.

Key activities include:

- Organizing annual scientific meetings, attracting around 1000 participants and more than 350 abstract submissions.
- Developing and publishing clinical guidelines to standardize and improve thyroid disease management.
- Offering research grants and awards to support innovative studies in thyroidology.
- Offering several prizes for outstanding work and presentations, both for Jr and Sr members.
- Publishing the European Thyroid Journal (ETJ), a peer-reviewed journal disseminating cutting-edge research.
- Maintaining specialized boards and working groups focusing on areas such as cancer, public health, education, and research.

Communication with the member happens through the annual meeting, a general assembly, the website, social media, mails and the bi-annual magazine "Thyroidologist".

Organizational Structure

The ETA operates through various specialized boards and committees, each focusing on specific aspects of thyroidology and comprising experts in the field to ensure dynamic and effective governance

- Archives Board: Preserves the history and legacy of the ETA.
- Educational Board: Oversees educational initiatives and training programs.
- Guidelines and Publications Board: Develops clinical guidelines and oversees publications.
- Public Health Board: Addresses thyroid-related public health issues.
- Website and Social Media Board: Manages the ETA's digital presence.
- Research Grants Board: Administers research funding and supports scientific studies.
- Nominations Committee: Handles nominations for awards and leadership positions.

Our main working group is the cancer group (ETA-CG), designed to address all aspect on cancer with specific objectives and defined time base.

Contact & Further Information

Website: eurothyroid.com

ETA Standing Office: Susanne Rothe rothe@endoscience.de



American Thyroid Association (ATA)

The American Thyroid Association® (ATA) is dedicated to transforming thyroid care through clinical excellence, education, scientific discovery and advocacy in a collaborative community. ATA® is a global professional medical society with more than 1,700 members from 70 countries around the world. Our vision is a world in which there is “Optimal Thyroid Health for All”.

Our members and staff are dedicated to making the world a better place for patients suffering with thyroid disease and thyroid cancer. The philanthropic support of our members, the public, and grateful patients helps ATA to support research that advances clinical care and improves patient outcomes. We hold ourselves to the highest standards of nonprofit and charitable organizations.

Our core values set a foundation for our organizational culture and are essential elements of our strategic foundation. As an organization we believe in:

- Scientific inquiry
- Clinical excellence
- Patient advocacy
- Education
- Public service
- Diversity, equity and inclusion
- Ethical conduct,
- Worldwide collaboration and collegiality

ATA provides researchers and clinicians with networking opportunities and resources that will help them grow their careers and stay current on leading-edge research and advances in clinical care. Additionally, ATA is committed to providing patients and their families with reliable information and tools to help them learn more about and manage their thyroid disease and thyroid cancer.

2024-2025 ATA Board of Directors

President

Jacqueline Jonklaas, MD, PhD
Washington, DC

Secretary

Christopher McCabe, PhD
Birmingham, UK

Treasurer

Anthony Hollenberg, MD
Boston, MA

Treasurer-Elect

Mark Zafereo, MD
Houston, TX

Past-President

Michael McDermott, MD
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President-Elect

M. Regina Castro, MD
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Directors

Peter Angelos, MD (2024-2025)
Chicago, IL
Zubair Baloch, MD, PhD (2023-2026)
Philadelphia, PA
Maria Cabanillas, MD (2023-2026)
Houston, TX
Elizabeth Grubbs, MD (2024-2027)
Houston, TX
Cari Kitahara, PhD (2024-2027)
Bethesda, MD
Maya Lodish, MD (2024-2027)
San Francisco, CA
Jennifer Sipos, MD (2022-2025)
Columbus, OH
David Steward, MD (2023-2026)
Cincinnati, OH

Executive Director

Pamela Mechler, CAE



ASIA & OCEANIA THYROID ASSOCIATION

Asia and Oceania Thyroid Association (AOTA)

AOTA is composed of 11 member countries from across Asian and Oceania region (Australia, Bangladesh, China, India, Indonesia, Iran, Japan, Philippines, Singapore, South Korea, Taiwan, and Thailand, alphabetical order). Several other countries are trying to join AOTA.

AOTA had been established since 1975 when the 7th International Thyroid Congress (ITC) was held in Boston. The association set the term of office for its Office Bearers for every five years. It also had elected officers and other members of the AOTA Council in the Delegates Assembly during the ITC's which have been held every 5 years. First president of AOTA was Ian Hales (Australia, 1975~1980), followed by Nabuo Ui (Japan, 1980~1985), Shigenobu Nagataki (1985~2000), Bo Youn Cho (South Korea, 2000~2005), Junji Konish (Japan, 2005~2010), Yoshiharu Murata (Japan, 2010~2015) and Takashi Akamizu (Japan, 20015~2020). Dr. Won Bae Kim from south Korea is current president and is to serve until June 2025.

Regular academic meetings of AOTA had been held every four years, first one in 1978 (Singapore), followed by 1982 (Tokyo, Japan), 1986 (Bangkok, Thailand), 1989 (Seoul, South Korea), 1993 (Leura, New South Wales, Australia), 1997 (Osaka, Japan), 2003 (Singapore), 2007 (Manilla, Philippines). Thereafter, the congresses have been held more frequently; in 2009 (Nagoya, Japan), in 2012 (Bali, Indonesia), in 2014 (Kochi, India), in 2017 (Busan, South Korea), in 2019 (Sydney, Australia) and in 2024 (Bali, Indonesia).

AOTA had successfully organized International Thyroid Congresses (ITC) three times so far. First ITC organized by AOTA was 8th ITC (1980, Sydney, Australia), and has been followed by 12th ITC (2000, Kyoto, Japan), and 16th ITC (2020, Xian, China which was held online due to the COVID-19 pandemic).

AOTA presents an Academic Prize, now named as Nagataki Prize, to an outstanding AOTA researchers at every AOTA congress and ITC. The congresses feature the AOTA Prize Lecture. In addition, AOTA awards Young Investigator Travel Grants regularly during AOTA Congresses and ITC's.

The current officers of AOTA are the President (Won Bae Kim from South Korea), Vice-president (R.V. Jayakumar from India and Weiping Teng from China), Secretary General (Byeong-Cheol Ahn from South Korea), Treasurer (Noriyuki Koibuchi from Japan) and POC chairman (Iwao Sugitani from Japan). AOTA Council members representing each member country are responsible for important decisions on society's affairs.

Website for AOTA is www.aota.kr and it can be contacted to secretary general at aotasecretary@gmail.com.



2023-2025 LATS Executive Committee

President

Janete Maria Cerutti
São Paulo, Brazil

Vice-president

Célia Regina Nogueira
Botucatu, Brazil

Secretary

Ines Califano
Buenos Aires, Argentina

Treasurer

Maria Tereza Nunes
São Paulo, Brazil

Directors

Ana Ines Voogd
Buenos Aires, Argentina
Anabela Zunino
Buenos Aires, Argentina
Caroline Serrano do Nascimento
São Paulo, Brazil
Erika Laurini de Souza Meyer
Porto Alegre, Brazil
Erika Abelleira
Buenos Aires, Argentina
Fernanda Vaisman
Rio de Janeiro, Brazil
Gisah de Carvalho
Curitiba, Brazil
Luiz Paulo Kowalski
São Paulo, Brazil
Rosana Teresita Sklate
Buenos Aires, Argentina
Suemi Marui
São Paulo, Brazil

LATS Committees

Fiscal Council

Lenara Golbert
Lucas Leite Cunha
Luiz Roberto Medina dos Santos

Clinical Affairs Committee

Fabian Pitoia (Chair)
Ana Luiza Maia
José Sgarbi
José Miguel Dora
Gabriela Brenta
Veronica Ilera
Alejandro Román-González

Basic and Translational Affairs Committee

Maria Tereza Nunes (Chair)
Guillermo Juvenal
Maria del Mar Montesinos
Caroline Serrano-Nascimento
Laura Fozzatti
Leandro Alves
Miriam Ribeiro

Surgical Affairs Committee

Luiz Kowalski (Chair)
Alvaro Sanabria
Juan Pablo Dueñas
José Luis Novelli
Santiago Zund
Erivelto Volpi
Ana Voogd

Internet and Social Media Committee

Janete Cerutti (Chair)
Lucas Leite Cunha
Laila Bielski

Staff

Cristiane Yoshizato

LATS Memories

Founders Members (1974)

According to the 1st General Assembly minute, on October 30th, 1974, during the Panamerican Congress of Endocrinology held at the Sheraton Hotel in Buenos Aires, Argentina, a pivotal moment in Latin American thyroidology took place. During the event, Geraldo Medeiros Neto (Brazil) shared with a group of attending thyroidologists a conversation he had previously had with David Solomon (California, USA), then a member of the Board of Directors of the American Thyroid Association. In that conversation, Solomon had suggested that it would be both valuable and timely for Latin American endocrinologists with a focus on thyroid diseases to establish a dedicated organization. Motivated by this vision, an official founding meeting was organized, during which Geraldo Medeiros Neto proposed the establishment of a new scientific organization: the Sociedad Latino Americana de Tiroides (Latin American Thyroid Society – LATS). The motion was seconded and unanimously approved by all thyroidologists present. It was also agreed that a provisional Executive Committee would be appointed to take the initial steps toward consolidating the Society. Walter Bloise proposed that Geraldo Medeiros Neto be elected as the first President of LATS, with Hugo Niepomniszcze as General Secretary and Eduardo Pretell as Vice-president. Additionally, other thyroidologists present at the meeting were designated as national delegates, including:

President: Geraldo Medeiros Neto, Brazil

Vice-president: Eduardo Pretell, Peru

Secretary: Hugo Niepomniszcze, Argentina

Directors

Jose Varea Terán, Ecuador

Luis Carlos Fernandes Reis, Brazil

Mario Alberto Pisarev, Argentina

Victor Sporn, Argentina

Eduardo Gaitan, Colombia

Jorge Maisterrena, Mexico

Noe Altschuler, Argentina

Manfredo Weinstein, Argentina

Walter Bloise, Brazil

Osvaldo J. Degrossi, Argentina

Pablo Fletcher, Panama

Carlos Valverde, Mexico

Legal Foundation (1975)

In 1975, Hugo Niepomniszcze drafted the provisional Bylaws, which were subsequently approved by the LATS membership. These Bylaws were later revised to comply with the Brazilian Civil Code and formally registered at a notarial office in São Paulo in 1976. One year later, LATS was officially chartered and registered with the Ministry of Justice in Brazil, thereby gaining full legal rights to begin its activities as a scientific society.

International Recognition of LATS (1975)

At the International Thyroid Congress in Boston, USA, from June 9-13 (1975), LATS was formally recognized and accepted as a new “sister” organization alongside established societies such as the American Thyroid Association (ATA) and the European Thyroid Association (ETA). In the following years, the Asia and Oceania Thyroid Association (AOTA) also joined this international alliance.

During this meeting (June 12, 1975), the delegates elected the first Board of Directors of LATS, establishing the Society's official leadership. This founding board served a four-year term from 1975 to 1978.

President: Geraldo Medeiros Neto, Brazil

Vice-president: Eduardo Pretell, Peru

Secretary: Hugo Niepomniszcze, Argentina

Directors

Eduardo Gaitan, Colombia
Jorge Maisterrana, Mexico
Pablo Fletcher, Panama
Doris Rosenthal, Brazil
Gustavo Pineda, Chile
Rodrigo F. Benitez, Ecuador
Jose Luis Ceralillos, Venezuela
Enrique Alvarez Martins, Cuba

International Thyroid Congress (ITC) Representation (1976)

During the 3rd General Assembly held in Guarujá on October 2, 1976, Dr. Geraldo Medeiros Neto announced that LATS would participate for the first time in the 8th International Thyroid Congress (ITC), to be held in Australia in 1980. He mentioned that an important meeting of the Program Committee for the upcoming ITC, which is scheduled to take place in Singapore in 1978, on the next Congress of Endocrinology of Asia, is being organized. He emphasized that participation in the Program Committee meetings required each local association to independently fund the travel expenses of its representatives. He also highlighted that nominees must possess exceptional scientific and academic credentials, ensuring that the society would be represented at the highest international level. The Executive Committee unanimously approved the nomination of Drs. Geraldo Medeiros-Neto and Eduardo Gaitán as LATS representatives

International Thyroid Congress in Latin American Countries

At the 8th ITC, held in Sydney, Australia, in 1980, LATS proposed that future congresses rotate among the major thyroid societies, allowing one congress every 20 years to each. Based on this proposal, it was agreed that:

The 9th ITC (1985) would take place in São Paulo, Brazil

The 13th ITC (2005) would be hosted in Buenos Aires, Argentina

This rotation system was officially approved by the International Committee of Thyroid Societies in Sydney.

LATS Presidents

During this foundational period, LATS Presidents were elected for four-year terms. The individuals who held the presidency during this initial phase were:

Geraldo Medeiros Neto (1974-1978)

Eduardo Pretell, Peru (1978-1982)

Eduardo Gaitán, Colombia (1982-1986)

Jorge Maisterrena, Mexico (1986-1990)

In 1990, it was decided that future mandates would last two years. The subsequent Presidents were:

Mario Pisarev, Argentina (1991-1993)

João H. Romaldini, Brazil (1993-1995)

Gustavo Pineda, Chile (1995-1997)

Hugo Niepomniszcz, Argentina (1997-1999)

Rui M. B. Maciel, Brazil (1999-2001)

Aldo H. Coleoni, Argentina (2001-2003)

Doris Rosenthal, Brazil (2003-2005)

Nelson Wolhk, Chile (2005-2007)

Guillermo Juvenal, Argentina (2007-2009)

Hans Graf, Brazil (2009-2011)

Marcos S. Abalovich, Argentina (2011-2013)

Ana Maria Masini-Repiso, Argentina (2013-2015)

Denise Pires de Carvalho, Brazil (2015-2017)

Gabriela Brenta, Argentina (2017-2019)

Ana Luiza S. Maia, Brazil (2019-2021)

Fabian Pitoia, Argentina (2021-2023)

Janete M. Cerutti, Brazil (2023-2025)

LATS Secretaries

Ines Califano, Argentina (2023-2027)
Claudia Gabriella Pellizas, Argentina (2019-2023)
Ana Maria Orlandi, Argentina (2015-2019)
Eduardo Kyoshi Tomimori, Brazil (2011-2015)
Ana Maria Masini-Repiso, Argentina (2007-2011)
Hans Graf, Brazil (2001-2007)
Antonio C. Bianco, Brazil (1997-2001)
Rui MB Maciel, Brazil (1993-1997)
João H. Romaldini, Brazil (1986-1993)
Hugo Niepomniszcz, Argentina (1974-1986)

LATS Congresses

The first official LATS Congress was held in 1981, organized by Hugo Niepomniszcz in Mar del Plata, Argentina, and was attended by a significant number of endocrinologists from across South America. This event played a key role in consolidating the Society. A proceeding of the first Latin American Thyroid Congress was organized by Hugo Niepomniszcz and Mario Pisarev and published 1982.

In 1983, Eduardo Pretell organized the second LATS Congress in Lima, Peru.

In 1985, São Paulo hosted the 3rd LATS meeting together with the 9th International Thyroid Congress with Geraldo Medeiros Neto as Congress President. The event welcomed more than 1,100 delegates from numerous countries and was widely recognized as a major scientific and social success.

In 1986, the Fourth LATS Congress was held in Caracas, Venezuela, under the leadership of María Cristina Blanco.

In 1989, plans to host the next congress in Quito, Ecuador, were hindered due to lack of local support.

The 5th meeting was successfully held in São Paulo, Brazil, in 1991, under the leadership of Rui Maciel.

Two years later, in 1993, Mario Pisarev organized the 6th meeting in Buenos Aires, Argentina.

The following LATS Congresses were:

7th LATS: May 21-24, 1997, Viña del Mar, Chile
8th LATS: May 27-30, 1999, Foz do Iguaçu, Brazil
9th LATS: April 28 – May 1, 2001, Rio de Janeiro, Brazil
10th LATS: May 1-4, 2003, Córdoba, Argentina
11th LATS and 13th ITC: October 30 – November 4, 2005, Buenos Aires, Argentina
12th LATS: April 27-30, 2007, Santiago, Chile
13th LATS: April 30 – May 3, 2009, Gramado, Brazil
14th LATS: August 4-7, 2011, Lima, Peru
15th LATS: March 20-23, 2013, Florianópolis, Brazil
16th LATS: June 15-18, 2017, Rio de Janeiro, Brazil
17th LATS: June 20-23, 2019, Buenos Aires, Argentina
18th LATS: November 18-20, 2021, Online, Brazil
19th LATS: April 20-23, 2023, Curitiba, Brazil

LATS Senior Investigator Award

The LATS Senior Investigator Award is presented at each LATS Congress or during years when the International Thyroid Congress (ITC) is held. This prestigious award recognizes an outstanding senior member of the Society for their significant and sustained contributions to thyroid research and/or clinical practice in Latin America. The recipient is chosen by the LATS Scientific Committee and is honored with an invitation to deliver a keynote lecture at the Congress

LATS Senior Investigator Past Winners

2023, Claudia Pellizas, Argentina
2021, Maria Tereza Nunes, Brazil and Carmen C. Pazos de Moura, Brazil
2019, Guillermo Juvenal, Argentina
2017, Ana Maria Masini-Repiso, Argentina
2015 (ITC), Janete Maria Cerutti, Brazil
2013, Ana Luiza Maia, Brazil
2011, Laura S. Ward, Brazil
2010 (ITC), Denise Pires de Carvalho, Brazil
2009, Edna Kimura, Brazil
2007, Mario Vaisman, Brazil
2005 (ITC), Hector Ruben Harach, Argentina
2003, João H. Romaldini, Brazil
2001, Gregorio Chazenbalk, Argentina
2000 (ITC), Antonio C. Bianco, Brazil
1999, Eduardo A. Pretell, Peru
1997, Doris Rosenthal, Brazil
1995 (ITC), J. Enrique Silva, Chile
1993, Hugo Niepomniszcz, Argentina
1991, Rui M. B. Maciel, Brazil
1990 (ITC), Mario Pisarev, Argentina
1985 (ITC), Eduardo A. Gaitan, Colombia
1983, Aldo Coleoni, Argentina
1980 (ITC), Geraldo A. Medeiros-Neto, Brazil

LATS Young Investigator Award

The LATS Prize for Young Investigators is awarded at each LATS Congress to two young members of the Society (under 40 years of age) who present an accepted paper at the Congress. Awards are given in two categories: (1) Clinical Research and (2) Basic Research. To be eligible, applicants must be the first author of the presented work, must attend the Congress in person, and the research must have been conducted entirely in a Latin American country.

LATS Young Investigator Past Winners

2023

Diego Claro de Mello
Priscilla Moreira

2021

Fernando Jerkovich
Rafael Marschener

2019

Iuri Martin Goemann
Mariano Martín

2017

Gisele Oler
Lais S. Moraes

2015

Cesar Seigi Fuziwara
Denise Momesso

2013

Aline Neves Araujo
Juliana Cazarin
Thalita G. Alves
Vanina Alaminio

2011

André Uchimura Bastos
Magali Nazar
Mirian Romitti
Paula Bargi de Souza

2010

Alex Shimura Yamashita
Letícia Aragão Santiago

2009

Juan Pablo Nicola
Monalisa Ferreira Azevedo

2007

Flavia Roche Moreira Latini
Helton Estrela Ramos

2005

Maria Izabel Chiamolera
Cléber P. Camacho

2003

Alejandra Dagrosa
Marcia Khaled Pufiales

2001

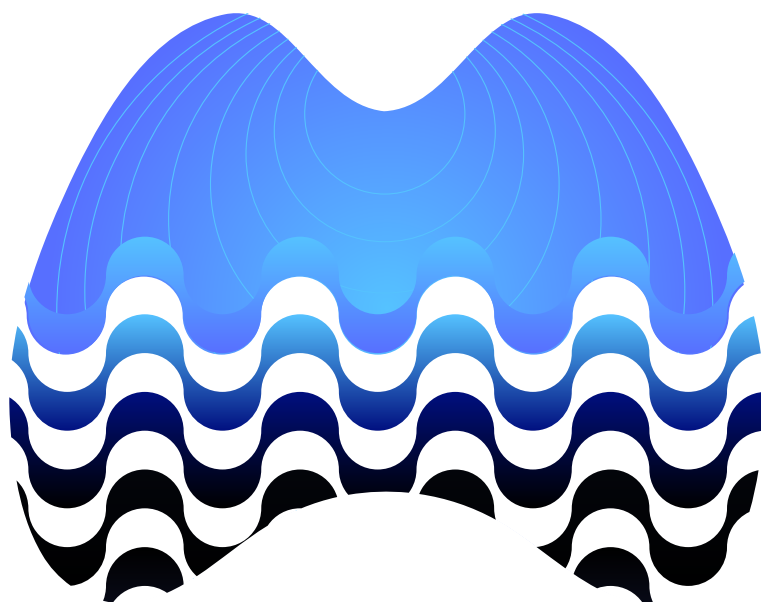
Janete Maria Cerutti
Gisele Giannocco
Leonardo Gabriel Bazzara

1999

Magnus R. Dias da Silva
Tania M. Ortiga Carvalho

1998

Claudia G. Pellizas
Marcelo Branco



17th

International **Thyroid** Congress

18 – 22 **June 2025**

Rio de Janeiro Brazil

SCIENTIFIC PROGRAM

2025-06-18 (Wednesday)	
Room 2 – Eduardo Gaitán (LATS President 1982–85; Colombia)	
13:00 - 14:30	IODINE GLOBAL NETWORK / IODINE GLOBAL NETWORK Session I
13:00 - 13:10	Introduction
	Presenter: JANETE MARIA CERUTTI - BRAZIL
	Presenter: RODRIGO MORENO REYES - BELGIUM
	Chair: OMAR DARY - UNITED STATES
13:10 - 13:30	Chair: MARIA DEL CARMEN SILVA CROOME - ARGENTINA
	Despite major progress, iodine deficiency remains a global health problem in 2025
13:30 - 13:45	Speaker: RODRIGO MORENO REYES - BELGIUM
13:45 - 14:00	The history of the elimination of iodine deficiency disorders in the Americas
	Speaker: EDUARDO PRETELL - PERU
14:00 - 14:15	Awareness and capacity building to sustain optimal iodine nutrition in Latin America
	Speaker: ANA MARÍA HIGA YAMASHIRO - PERU
14:15 - 14:30	Effects of iodine intake on thyroid autoimmunity
	Speaker: ELIZABETH PEARCE - UNITED STATES
14:30 - 16:30	Iodotyrosines as novel biomarkers for iodine deficiency
	Speaker: JOSÉ MORENO - SPAIN
16:30 - 18:00	IODINE GLOBAL NETWORK / IODINE GLOBAL NETWORK Break
	Session II
16:30 - 16:45	Chair: ELIZABETH PEARCE - UNITED STATES
	Chair: EVELYN L. JARA FERNÁNDEZ - CHILE
16:45 - 17:00	Strengthening design and surveillance of salt iodization to support safe and effective programs on thyroid function
	Speaker: OMAR DARY - UNITED STATES
17:00 - 17:15	Not too little, not too much: the Chilean iodine fortification experience
	Speaker: LORENA MOSSO - CHILE
17:15 - 17:30	Iodine nutritional status in Brazil
	Speaker: HELTON ESTRELA RAMOS - BRAZIL
17:30 - 17:45	Iodine supplementation in pregnancy in Brazil
	Speaker: ROSALIA PADRO PADOVANI COLETTE - BRAZIL
17:45 - 18:00	The Danish investigation on iodine intake and thyroid disease (DanThyr): history and implications
	Speaker: LENA BJERGVED SIGURD - DENMARK
	Iodine status in Colombia and its possible association with thyroid autoimmunity
	Speaker: IVÁN DARÍO ESCOBAR DUQUE - COLOMBIA
2025-06-19 (Thursday)	
Room 6 – Hugo Niepomniszcze (LATS President 1997–99; Argentina)	
08:00 - 08:10	KOCHER CONFERENCE / KOCHER CONFERENCE
	Opening
	Presenter: LUIZ PAULO KOWALSKI - BRAZIL
	Presenter: GREGORY RANDOLPH - UNITED STATES
08:10 - 09:30	Presenter: ERIVELTO VOLPI - BRAZIL
	KOCHER CONFERENCE / KOCHER CONFERENCE
	First Session
	Chair: ANA INES VOOGD - ARGENTINA
08:30 - 08:45	Chair: JOSÉ HIGINO STECK - BRAZIL
	Navigating uncertainty: advancements in managing indeterminate thyroid nodules
08:45 - 09:00	Speaker: DENISE MOMESSO - BRAZIL
	RFA x MW – Nuances of indications and techniques
09:00 - 09:15	Speaker: LEONARDO RANGEL - BRAZIL
	Is thermal ablation safe for malignancies?
09:15 - 09:30	Speaker: RAFAEL DE CICCIO - BRAZIL
	Expanding the indications for thermal ablations
09:30 - 10:30	Speaker: ERIVELTO VOLPI - BRAZIL
	Q&A
	KOCHER CONFERENCE / KOCHER CONFERENCE
	Second Session
	Chair: JOSÉ GUILHERME VARTANIAN - BRAZIL
	Chair: JOSE LUIS NOVELLI - ARGENTINA

09:30 - 09:50	Effective surveillance strategies for micropapillary thyroid cancer: integrating surgical insight Speaker: MICHAEL TUTTLE - UNITED STATES
09:50 - 10:05	Total thyroidectomy x Lobectomy (indications and follow-up) Speaker: SANTIAGO ZUND - ARGENTINA
10:05 - 10:20	Defining the best preoperative approach for thyroid cancer Speaker: MARIKA RUSSELL - UNITED STATES
10:20 - 10:30	Q&A
10:30 - 10:45	KOCHER CONFERENCE / KOCHER CONFERENCE Break
10:45 - 11:30	KOCHER CONFERENCE / KOCHER CONFERENCE Third Session Chair: ALVARO SANABRIA - COLOMBIA Chair: FELIPE CAPDEVILLE - CHILE
10:45 - 11:00	Medical management of GD: When is the time for RAI? Speaker: ADRIANO NAMO CURY - BRAZIL
11:00 - 11:15	Way and when Surgery for GD Speaker: EVANDRO VASCONCELOS - BRAZIL
11:15 - 11:30	Q&A
11:30 - 12:15	KOCHER CONFERENCE / KOCHER CONFERENCE Fourth Session Chair: RENAN B. LIRA - BRAZIL Chair: MARCO AURÉLIO VAMONDES KULCSAR - BRAZIL
11:30 - 11:45	Autofluorescence and Parathyroid Vascular Assessment Speaker: MARCO DEMARCHI - SWITZERLAND
11:45 - 12:00	Remote thyroid access: breakthroughs and future directions in surgical innovation Speaker: RENAN B. LIRA - BRAZIL
12:15 - 12:30	KOCHER CONFERENCE / KOCHER CONFERENCE Presentation of the New Book "Carcinoma Diferenciado de Tiroides de Bajo Riesgo" Editor: LUIZ PAULO KOWALSKI - BRAZIL Editor: JOSE LUIS NOVELLI - ARGENTINA Editor: STELLA MARIS BATALLÉS - ARGENTINA Editor: FABIAN PITOIA - ARGENTINA
12:30 - 13:00	KOCHER CONFERENCE / KOCHER CONFERENCE Keynote lecture: Prognostic factors of papillary and follicular carcinomas based on pre-, intra-, and poto-operartive findings Speaker: YASUHIRO ITO - JAPAN
13:00 - 14:00	KOCHER CONFERENCE / KOCHER CONFERENCE Fifth Session Chair: ANTONIO BERTELLI - BRAZIL Chair: JOSE CARLOS LAZARTE GUTIÉRREZ - PERU
13:00 - 13:15	Poorly Differentiated Thyroid Cancer – Contemporary Definitions and Management Speaker: MARK ZAFEREO - UNITED STATES
13:15 - 13:30	Neoadjuvant Therapy for Advanced Disease Speaker: ANA HOFF - BRAZIL
13:30 - 13:45	Disparities in Access to Thyroid Care Speaker: LUIZ PAULO KOWALSKI - BRAZIL
13:45 - 14:00	Q&A
14:00 - 15:45	KOCHER CONFERENCE / KOCHER CONFERENCE Interdisciplinary tumor board: collaborative strategies for thyroid cancer management Moderator: FERNANDA VAISMAN - BRAZIL Moderator: GREGORY RANDOLPH - UNITED STATES Panelist: JUAN PABLO DUENAS - COLOMBIA Panelist: RAFAEL DE CICCIO - BRAZIL Panelist: THIAGO BUENO DE OLIVEIRA - BRAZIL Panelist: PEDRO DE MARCHI - BRAZIL Panelist: FATIMA CRISTINA MENDES DE MATOS - BRAZIL Panelist: MATHEUS GERHARD ROSENFELD - BRAZIL
15:45 - 16:00	KOCHER CONFERENCE / KOCHER CONFERENCE Closing remarks Presenter: LUIZ PAULO KOWALSKI - BRAZIL Presenter: GREGORY RANDOLPH - UNITED STATES Presenter: ERIVELTO VOLPI - BRAZIL

16:20 - 17:20	HOT ABSTRACTS / ABSTRACTS
	Hot Abstracts - Basic
	Chair: MARIA TEREZA NUNES - BRAZIL
	Chair: BALÁZS GERESEN - HUNGARY
16:20 - 16:35	1112267 - CHARACTERIZATION OF PATIENT DERIVED XENOGRAPHS (PDX) MOUSE MODELS AND THEIR RESPECTIVE CELL LINES FROM ANAPLASTIC THYROID CANCER (ATC) PRESENTER : MIRA SALEH
16:35 - 16:50	1112491 - ENDOCRINE DISRUPTORS MIXTURE IMPAIRS THYROID DIFFERENTIATION THROUGH EPIGENETIC MECHANISMS AND DYSREGULATED PKA AND AKT SIGNALING PATHWAYS PRESENTER: GUILHERME HENRIQUE
16:50 - 17:05	1112483 - IMPACT OF MICROBIOTA-NLRP3 INFLAMMASOME INTERACTIONS ON PROGRESSION OF AUTOIMMUNE THYROIDITIS PRESENTER: BOSHEN GONG
17:05 - 17:20	1112666 - REGULATION OF ADULT NEUROGENESIS BY DIO2 IN MOUSE BRAIN: A TALE OF TWO WAVES PRESENTER: VICTOR VALCARCEL HERNÁNDEZ
Room 7 – Aldo H. Coleoni (LATS President 2001-2003; Argentina)	
08:00 - 10:00	ULTRASOUND COURSE / ULTRASOUND COURSE
	Session 1
08:00 - 08:10	Introduction
	Presenter: SUSAN MANDEL - UNITED STATES Presenter: EDUARDO TOMIMORI - BRAZIL
08:10 - 08:40	Basic Principles of Thyroid Ultrasound and Device Settings to Optimize Imaging Speaker: SARA AHMADI - UNITED STATES
08:40 - 09:10	Ultrasound of Diffuse Thyroid Disorders Speaker: RUDOLF PFEILSTICKER - BRAZIL
09:10 - 09:40	Challenges in Thyroid Nodule Imaging Speaker: SUSAN MANDEL - UNITED STATES
09:40 - 10:00	Assessment of Cervical Lymph Nodes Speaker: DEBORA DANILOVIC - BRAZIL
10:00 - 10:30	ULTRASOUND COURSE / ULTRASOUND COURSE
	Break
10:30 - 11:50	ULTRASOUND COURSE / ULTRASOUND COURSE
	Session 2
10:30 - 10:50	Artificial Intelligence for Evaluation of Thyroid Nodules Speaker: NAYKKY SINGH OSPINA - UNITED STATES
10:50 - 11:10	Parathyroid Imaging Speaker: MAISIE SHINDO - UNITED STATES
11:10 - 11:30	Nonthyroid neck pathology Speaker: LEONARDO RANGEL - BRAZIL
11:30 - 11:50	Techniques to Optimize Fine Needle Aspiration Biopsy Speaker: MARIO ARAUJO JUNIOR - BRAZIL
11:50 - 13:00	ULTRASOUND COURSE / ULTRASOUND COURSE
	Break
13:00 - 16:00	ULTRASOUND COURSE / ULTRASOUND COURSE
	Session 3
13:00 - 13:20	Correlation between ultrasound and thyroid cytology Speaker: FERNANDA FARO - BRAZIL
13:20 - 13:40	Patient demos - Examining physician Speaker: BERNARDO LOPES CANÇADO FONSECA - MG
13:40 - 16:00	Presentation of clinical cases
	Moderator: LEONARDO RANGEL - BRAZIL
	Panelist: SUSAN MANDEL - UNITED STATES
	Panelist: MAISIE SHINDO - UNITED STATES
16:20 - 17:20	HOT ABSTRACTS / ABSTRACTS
	Hot Abstracts - Translational
	Chair: LUCA PERSANI - ITALY
	Chair: TANIA MARIA RUFFONI ORTIGA - BRAZIL
16:20 - 16:35	1112615 - MECHANISMS IN THYROID EYE DISEASE (TED) - TSH RECEPTOR ANTIBODIES ENHANCE THE EXPRESSION OF BOTH TSH RECEPTORS AND IGF-1 RECEPTORS IN FIBROBLASTS. PRESENTER: TERRY FRANCIS DAVIES
16:35 - 16:50	1112290- PD-L1 ACTIVATES INTRINSIC CELLULAR FUNCTIONS IN THYROID CELLS: IMPLICATIONS FOR IMMUNE CHECKPOINT INHIBITOR INDUCED THYROIDITIS PRESENTER: MIHAELA STEFAN LIFSHITZ
16:50 - 17:05	1112488 - ROLE OF T3 IN DENDRITIC CELL ACTIVATION: INSIGHTS INTO THE METABOLIC REPROGRAMMING AND ITS FUNCTIONAL IMPACT PRESENTER: ANTONELLA BLANCO
17:05 - 17:20	1112247 - THE ROLE OF TYPE 3 DEIODINASE IN A HUMAN MODEL FOR EARLY BRAIN DEVELOPMENT PRESENTER: ANNA LOPEZ MARTI

Room 1 - Geraldo A. Medeiros Neto (LATS President 1974–78; Brazil)

15:00 - 16:10	TUMOR BOARD / THYROID CANCER
	Tumor Board in the context of the new guidelines
	Moderator: TREVOR ANGELL - UNITED STATES
	Panelist: ANTHONY GLOVER - AUSTRALIA
	Panelist: IWAO SUGITANI - JAPAN
	Panelist: JOSE M DOMINGUEZ - CHILE
	Panelist: KEPAL PATEL - UNITED STATES
16:20 - 17:20	HOT ABSTRACTS / ABSTRACTS
	Hot Abstracts - Clinical
	Chair: SIMON PEARCE - UNITED KINGDOM
	Chair: JENNIFER SIPOS - UNITED STATES
16:20 - 16:35	1112237 - REAL-WORLD EXPERIENCE WITH LENVATINIB PLUS PEMBROLIZUMAB IN METASTATIC BRAF WILD-TYPE ANAPLASTIC THYROID CARCINOMA (BRAFWT-ATC) Presenter: SARAH HAMIDI
16:35 - 16:50	1112402 - REDIFFERENTIATION OF REFRACTORY THYROID CANCER OF FOLLICULAR ORIGIN: NATIONAL FRENCH REAL LIFE EXPERIENCE Presenter: LAMARTINA
16:50 - 17:05	1112371 - T3 ANALOGUE TRIIODOTHYROACETIC ACID (TRIAC) TREATMENT AND SURVIVAL IN MCT8 DEFICIENCY: AN INTERNATIONAL REAL-WORLD COHORT STUDY Presenter: FLOOR VAN DER MOST
17:05 - 17:20	1112577 - TOTAL TRIIODOTHYRONINE AND TOTAL THYROXINE LEVELS ARE POSITIVELY ASSOCIATED WITH PREGNANCY LOSS OF CHROMOSOME NORMAL (EUPLOID) FETUSES Presenter: SOFIE BLIDDAL
17:30 - 19:50	OPENING CEREMONY / OPENING CEREMONY
	ITC Opening Ceremony - 17th International Thyroid Congress
17:30 - 17:40	Speech - LATS President
	Presenter: JANETE MARIA CERUTTI - BRAZIL
17:40 - 17:45	Speech - Presidents of ETA, AOTA, and ATA
17:45 - 17:50	Speech - Thyroid Federation International
17:50 - 18:00	Speech - LOC President
	Presenter: DENISE PIRES DE CARVALHO - BRAZIL
18:00 - 18:10	Speech - POC President
	Presenter: ANA LUIZA MAIA - BRAZIL
18:10 - 18:35	Advances in thyroid cancer management (LATS)
	Speaker: ANA HOFF - BRAZIL
18:35 - 19:00	What has changed in Thyroid Eye Disease? (ETA)
	Speaker: MARIO SALVI - ITALY
19:00 - 19:25	Surgical approach changes in thyroid cancer over the years (ATA)
	Speaker: JULIE SOSA - UNITED STATES
19:25 - 19:50	Progress in Basic thyroid research: a 5 year overview (AOTA)
	Speaker: NORIYUKI KOIBUCHI - JAPAN

Room 2 - Eduardo Gaitán (LATS President 1982–85; Colombia)

11:00 - 13:00	LEGACY LUNCH
	Insights, Challenges, and Reflections from Leaders of Thyroid Research (Activity restricted to invited guests only)
	Presenter: JANETE MARIA CERUTTI - BRAZIL
	Presenter: ANA LUIZA MAIA - BRAZIL
	Invited Legend: PETER KOPP - SWITZERLAND
	Invited Legend: LUCA PERSANI - ITALY
	Invited Legend: ROSSELLA ELISEI - ITALY
	Invited Legend: AKIRA MIYAUCHI - JAPAN
	Invited Legend: TERRY FRANCIS DAVIES - UNITED STATES
	Invited Legend: MICHAEL TUTTLE - UNITED STATES
	Invited Legend: RUI MACIEL - BRAZIL
15:00 - 16:20	SYMPOSIUM / PEDIATRICS & GENETIC DISEASES
	Updates on neonatal CH screening
15:00 - 15:20	Chair: PETER KOPP - SWITZERLAND
	Metabolomics can be of help?
15:20 - 15:45	Speaker: ANITA BOELEN - NETHERLANDS
	Is neonatal diagnosis of Central Hypothyroidism worthy to be implemented?
15:45 - 16:00	Speaker: HELTON ESTRELA RAMOS - BRAZIL
	The changing spectrum of CH after the lowering of TSH thresholds
16:00 - 16:20	Speaker: MARIA CRISTINA VIGONE - ITALY
	Discussion

Room 3 – Marcos S. Abalovich (LATS President 2011-2013; Argentina)	
15:00 - 15:50	MEET THE PROFESSOR / GOITER, IODINE AND OTHER ENVIRONMENTAL FACTORS
	Environmental endocrine disruptors
	Chair: FRANCESCA COPERCHINI - ITALY
	Chair: DENISE PIRES DE CARVALHO - BRAZIL
15:00 - 15:30	Animal Models
	Speaker: JOSEF KÖHRLE - GERMANY
15:30 - 15:50	Discussion
Room 4 – Jorge Maisterrena (LATS President 1986–90; Mexico)	
15:00 - 16:20	SYMPOSIUM / AUTOIMMUNITY
	Advances in role of TSHR
	Chair: JUAN PABLO NICOLA - ARGENTINA
	Chair: TAKASHI AKAMIZU - JAPAN
15:00 - 15:20	Advances in structural biology
	Speaker: JANE SANDERS - UNITED KINGDOM
15:20 - 15:40	TSHR-IGF1R crosstalk
	Speaker: TERRY FRANCIS DAVIES - UNITED STATES
15:40 - 16:00	Utility of TSHR antibodies in clinical practice-Graves'
	Speaker: GEORGE KAHALY - GERMANY
16:00 - 16:20	Discussion
Room 5 – Gustavo Pineda (LATS President 1995–97; Chile)	
15:00 - 16:20	SYMPOSIUM / REGULATION OF TH M&S
	Thyroid hormone action in health and disease
	Chair: MONICA DENTICE - ITALY
	Chair: CLAUDIA GABRIELA PELLIZAS - ARGENTINA
15:00 - 15:20	Structure and function of type 2 and type 3 deiodinase enzymes
	Speaker: ULRICH SCHWEIZER - GERMANY
15:20 - 15:40	Thyroid hormone in non-alcoholic liver diseases
	Speaker: PAUL YEN - SINGAPORE
15:40 - 16:00	Thyroid hormone and muscle differentiation
	Speaker: FLAVIA FONSECA BLOISE - BRAZIL
16:00 - 16:20	Discussion
2025-06-20 (Friday)	
Room 1 - Geraldo A. Medeiros Neto (LATS President 1974–78; Brazil)	
07:00 - 08:25	EARLY RISER SYMPOSIA / THYROID CANCER
	Thyroid cancer management: Difficult clinical cases
	Chair: MICHAEL TUTTLE - UNITED STATES
	Chair: GIORGIO GRANI - ITALY
07:00 - 08:25	Representative for ATA
	Panelist: LAURA BOUCAI - UNITED STATES
07:00 - 08:25	Representative for AOTA
	Panelist: KENICHI-ITO - JAPAN
07:00 - 08:25	Representative for ETA
	Panelist: SIMONE DE LEO - ITALY
07:00 - 08:25	Representative for LATS
	Panelist: FERNANDA VAISMAN - RJ
08:30 - 09:00	PLENARY / PLENARY SESSION
	30 years of active surveillance for low risk thyroid cancer, lessons learned and future directions
	Chair: FABIAN PITOIA - ARGENTINA
	Chair: IWAO SUGITANI - JAPAN
	Speaker: AKIRA MIYAUCHI - JAPAN
09:00 - 09:30	PLENARY / PLENARY SESSION
	Thyroid hormone analogues and potential applications
	Chair: MARIA TEREZA NUNES - BRAZIL
	Chair: MIN JI JEON - SOUTH KOREA
	Speaker: THOMAS SCANLAN - UNITED STATES
09:30 - 09:45	POSTER / Break
	POSTER / EXHIBIT HALL BREAK
09:45 - 10:30	LATS PRIZE LECTURE
	Chair: CARMEN C PAZOS-MOURA - BRAZIL
09:45 - 10:30	My Journey in Thyroid Research
	Speaker: TANIA MARIA RUFFONI ORTIGA - BRAZIL

10:35 - 12:00	DEBATE / THYROID & PREGNANCY
	TSH threshold for replacement thyroid hormone in pregnancy
	Moderator: KRIS POPPE - BELGIUM Moderator: MARIA DEL CARMEN SILVA CROOME - ARGENTINA
10:35 - 10:55	For the proposal
	Speaker: SOFIE BLIDDAL - DENMARK
10:55 - 11:15	Against for the proposal
	Speaker: SPYRIDOULA MARAKA - UNITED STATES
11:15 - 12:00	Discussion
12:00 - 13:00	POSTER / Break
	POSTER / EXHIBIT HALL BREAK
13:00 - 14:00	SHORT ORAL COMMUNICATIONS / ABSTRACTS
	SHORT ORAL COMMUNICATIONS - Clinical and Translational Thyroid Cancer
	Chair: LENARA GOLBERT - BRAZIL
	Chair: SARAH HAMIDI - UNITED STATES
13:00 - 13:05	1112409 - PREDICTIVE FACTORS OF RADIOACTIVE IODINE-REFRACTORY EVOLUTION OF THYROID CANCER IN A PROSPECTIVE COHORT Presenter: LAURINE MEBARKI
13:05 - 13:10	1112342 - IMPACT OF PHYSICAL ACTIVITY AND ITS MAINTENANCE IN THE EFFICACY AND SAFETY OF TYROSINE KINASE INHIBITORS IN ADVANCED THYROID CARCINOMA PATIENTS Presenter: CARLA COLOMBO
13:10 - 13:15	1112385 - LESIONAL DOSIMETRY IN 131I REFRACTORY METASTATIC DIFFERENTIATED THYROID CANCER WITH BRAFPV600E OR RAS MUTATION TREATED WITH TRAMETINIB +/- DABRAFENIB FOLLOWED BY HIGH ACTIVITY OF RADIOACTIVE IODINE Presenter: SOPHIE LEBoulleux
13:15 - 13:20	1112183 - LONG-TERM OUTCOME FOR PAPILLARY THYROID CARCINOMA WITH LUNG METASTASIS Presenter: IWAO SUGITANI
13:20 - 13:25	1112956 - Exposomic Analysis of Thyroid Cancer: Correlating histopathological characteristics with persistent environmental organic pollutants Presenter: THOMAS SZABO YAMASHITA
13:25 - 13:30	1112631 - ANALYTICAL VALIDATION OF A CUSTOMIZED TARGETED RNA NGS PANEL FOR DETECTING GENETIC ALTERATIONS IN 57 RECURRENT MUTATED GENES FOR DIAGNOSIS AND PROGNOSIS OF INDETERMINATE THYROID NODULES AND THYROID CANCER Presenter: ISABELA NOGUEIRA NUNES
13:30 - 13:35	1112329 - ASSESSMENT OF INTERNATIONAL MEDULLARY THYROID CARCINOMA GRADING SYSTEM PROGNOSIS IN PATIENTS WITH DISTANT METASTASES. Presenter: TOMMASO PORCELLI
13:35 - 13:40	1112623 - CHALLENGES IN DETERMINING THE OPTIMAL TIMING FOR THYROID REMOVAL IN YOUNG MEN2A PATIENTS: INSIGHTS FROM TWO BRAZILIAN REFERRAL CENTERS Presenter: LAURA MARMITT
13:40 - 13:45	1112460 - CIRCULATING MICRORNAs IN THE FOLLOW-UP OF PATIENTS WITH PAPILLARY THYROID CARCINOMA Presenter: NATHÁLIA DA CRUZ DE SOUSA MURAD
13:45 - 13:50	1113636 - ALK Inhibition Prolongs Survival in a Mouse Model of ALK-positive Anaplastic Thyroid Cancer Presenter: YARA MARIA MACHLAH
13:50 - 13:55	1112228 - IMMUNOMODULATORY EFFECTS OF LENVATINIB IN ADVANCED THYROID CARCINOMA Presenter: PRASHANT CHANGOER
14:00 - 14:45	ETA PRIZE LECTURE
	Chair: LAURA FUGAZZOLA - ITALY
	Chair: KRIS POPPE - BELGIUM
	Awardees: BARBARA JARZAB - POLAND
14:45 - 15:45	ORAL ABSTRACTS / ABSTRACTS
	ORAL SESSION - CLINICAL THYROID CANCER 1
	Chair: FABIAN PITOIA - ARGENTINA
	Chair: MAISIE SHINDO - UNITED STATES
14:45 - 15:00	1112369 - CLINICAL AND PATHOLOGICAL CHARACTERISTICS OF DIFFERENTIATED THYROID CANCER ACCORDING TO DISTANT METASTASIS STATUS Presenter: Kamille Guidolin
15:00 - 15:15	1112243 - REAL WORLD RESULTS OF IMMUNE CHECKPOINT BLOCKERS IN ANAPLASTIC THYROID CARCINOMA PATIENTS: INSIGHT FROM THE COMEDIMS COMPASSIONATE PROGRAM AT GUSTAVE ROUSSY Presenter: JULIEN HADOUX
15:15 - 15:30	1112439 - SURGERY FOR THYROID CANCER WITH OR WITHOUT AUTOFLUORESCENCE TO PREVENT HYPOPARATHYROIDISM IN A RANDOMIZED, CONTROLLED TRIAL Presenter: JACOB LILJA-FISCHER
15:30 - 15:45	1112557 - THE ROLE OF ADJUVANT VOLUMETRIC MODULATED ARC RADIOTHERAPY (VMAT) IN THE TREATMENT OF LOCALLY ADVANCED DIFFERENTIATED THYROID CANCER: A SINGLE INSTITUTION EXPERIENCE Presenter: CHIARA MURA
15:45 - 16:00	POSTER / GENERAL
	POSTER SESSION/BREAK IN THE EXHIBIT HALL
16:00 - 17:30	SYMPOSIUM / THYROID CANCER
	Treatment decisions in low risk thyroid cancer
	Chair: ERIKA ABELLEIRA - ARGENTINA
	Chair: KENICHI-ITO - JAPAN
16:00 - 16:25	Indications for Active surveillance
	Speaker: YASUHIRO ITO - JAPAN
16:25 - 16:50	Less than total thyroidectomy: indications for hemithyroidectomy or RFA
	Speaker: JUAN PABLO DUENAS - COLOMBIA
16:50 - 17:15	Dynamic risk stratification, indications for completion thyroidectomy & RAI
	Speaker: ELIZABETH GRUBBS - UNITED STATES

17:15 - 17:30	Discussion
18:00 - 20:00	GENERAL ASSEMBLY
	LATS General Assembly
Room 2 – Eduardo Gaitán (LATS President 1982–85; Colombia)	
	DEBATE / AUTOIMMUNITY
10:35 - 12:00	Is Surgical Treatment Still an Option for Thyroid Eye Disease?
	Moderator: ILARIA MULLER - ITALY
	Moderator: MARIUS STAN - UNITED STATES
10:35 - 10:55	For the proposal
	Speaker: ANABELA ZUNINO - ARGENTINA
10:55 - 11:15	Against the proposal
	Speaker: ROBERTO MIRASOL - PHILIPPINES
11:15 - 12:00	Discussion
	SHORT ORAL COMMUNICATIONS / ABSTRACTS
13:00 - 14:00	SHORT ORAL COMMUNICATIONS - Thyroid Nodules and Surgery
	Chair: ALVARO SANABRIA - COLOMBIA
	Chair: MICHAEL YEH - UNITED STATES
13:00 - 13:05	1112644 - DEFINING A CUTOFF FOR CALCITONIN LEVELS IN FINE-NEEDLE ASPIRATION WASHOUT FLUID TO EXCLUDE MEDULLARY THYROID CARCINOMA DIAGNOSIS Presenter: GUSTAVO IVANI DE PAULA
13:05 - 13:10	1112476 - REVOLUTIONIZING BENIGN NODULE TREATMENT: THE IMPACT OF RADIOFREQUENCY ABLATION Presenter: Gerardo Russier
13:10 - 13:15	1112527 - TRANSFORMING PARATHYROID SURGERY: THE ROLE OF RADIOFREQUENCY ABLATION IN TREATING ADENOMAS Presenter: ANA INES VOOGD
13:15 - 13:20	1112390 - ENHANCED ALGORITHM FOR THYROID NODULE CLASSIFICATION: PERFORMANCE COMPARISON OF MIR-THYPE V1 AND V2 Presenter: MARCOS TADEU DOS SANTOS
13:20 - 13:25	1112275 - RADIOFREQUENCY ABLATION VERSUS ETHANOL ABLATION FOR BENIGN THYROID NODULES TREATMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS Presenter: ALINE LEVY SITNOVETER
13:25 - 13:30	1112455 - REDEFINING BETHESDA III: THE VALUE OF BINARY STRATIFICATION IN PREDICTING THYROID MALIGNANCY Presenter: VERONICA ILERA
13:30 - 13:35	1112599 - ULTRASONOGRAPHIC-HISTOLOGICAL CORRELATION OF THYROID NODULES IN A CHILEAN CENTER AND PERFORMANCE OF ACR-TIRADS VARIABLES Presenter: NICOLE LUSTIG FRANCO
13:35 - 13:40	1112186 - IDENTIFYING PREDICTORS OF PERMANENT HYPOPARATHYROIDISM AFTER THYROID CANCER SURGERY: A COMPREHENSIVE REAL-LIFE RETROSPECTIVE ANALYSIS Presenter: ROSSELLA MELCARNE
13:40 - 13:45	1112242 - INTRAOPERATIVE USE OF FLUORESCENCE WITH INDOCYANINE GREEN TO PREDICT POSTOPERATIVE HYPOPARATHYROIDISM Presenter: RASMUS REINKE
13:45 - 13:50	1112305 - LARYNGEAL ULTRASOUND PERFORMANCE FOR THE DIAGNOSIS OF VOCAL CORD PARALYSIS POST-THYROIDECTOMY: A MULTICENTER DIAGNOSTIC TEST STUDY IN MEDELLIN, COLOMBIA. Presenter: DAVID MAURICIO FIGUEROA BOHORQUEZ
13:50 - 13:55	1112391 - PREOPERATIVE MIR-146B EXPRESSION AS A PREDICTOR OF AGGRESSIVE OUTCOMES IN DIFFERENTIATED THYROID CARCINOMAS Presenter: MARCOS TADEU DOS SANTOS
	ORAL ABSTRACTS / ABSTRACTS
14:45 - 15:45	ORAL SESSION - CLINICAL THYROIDOLOGY 2
	Chair: KEPAL PATEL - UNITED STATES
	Chair: PATRÍCIA DE FÁTIMA TEIXEIRA - BRAZIL
14:45 - 15:00	1113894 - Efficacy and Safety of Veligrotag (VRDN-001), a Full Antagonist Humanized Monoclonal Antibody to IGF-1 Receptor, in Chronic Thyroid Eye Disease (TED): THRIVE-2 Phase 3 Results at 15 Weeks PRESENTER: PATRICE RODIEN
15:00 - 15:15	1114060 - Predicting Reoperation Outcomes in Papillary Thyroid Carcinoma Using Interpretable Machine Learning PRESENTER: ZIMEI TANG
15:15 - 15:30	1114099 - TREATMENT OF CHRONIC HYPOPARATHYROIDISM POST THYROID CANCER SURGERY THROUGH INTER VIVO PARATHYROID TRANSPLANTATION PRESENTER: LEONARDO KRUSCHEWSKY
15:30 - 15:45	1112357 - TRAB DYNAMICS AND SURGICAL OUTCOMES IN GRAVES' ORBITOPATHY: A RETROSPECTIVE ANALYSIS PRESENTER: LAURA DELFINO
	SYMPOSIUM / REGULATION OF TH M&S
16:00 - 17:30	Developmental functions of thyroid hormone
	Chair: VICTOR VALCARCEL HERNÁNDEZ - FRANCE
	Chair: RUI MACIEL - BRAZIL
16:00 - 16:25	Thyroid hormone and brain development
	Speaker: ANA GUADANO-FERRAZ - SPAIN
16:25 - 16:50	Thyroid hormone transporters and deiodinases in development
	Speaker: FEDERICO SALAS-LUCIA - UNITED STATES
16:50 - 17:15	Thyroid hormone and neuronal differentiation in organoids
	Speaker: ROBERT OPITZ - GERMANY
17:15 - 17:30	Discussion
18:00 - 20:00	GENERAL ASSEMBLY / GENERAL ASSEMBLY
	AOTA General Assembly

Room 3 – Marcos S. Abalovich (LATS President 2011-2013; Argentina)	
10:35 - 11:30	MEET THE PROFESSOR / GOITER, IODINE AND OTHER ENVIRONMENTAL FACTORS
	Iodine and nutrition: Global Trends
	Chair: OMAR DARY - UNITED STATES
	Chair: HELTON ESTRELA RAMOS - BRAZIL
10:35 - 10:55	Global iodine nutrition and thyroid diseases: Where do we stand in 2025?
	Speaker: RODRIGO MORENO REYES - BELGIUM
10:55 - 11:15	State-of-the-Art Guidelines for Monitoring Iodine Nutrition in Populations
	Speaker: SUN Y LEE - UNITED STATES
11:15 - 11:30	Discussion
18:00 - 20:00	GENERAL ASSEMBLY / GENERAL ASSEMBLY
Room 4 – Jorge Maisterrena (LATS President 1986–90; Mexico)	
10:35 - 11:30	MEET THE PROFESSOR / REGULATION OF TH M&S
	Thyroid hormone and disease mechanisms
	Chair: DOMENICO SALVATORE - ITALY
	Chair: Antonio C. Bianco - UNITED STATES
10:35 - 10:55	MCT8 thyroid hormone transporter and disease
	Speaker: EDWARD VISSER - NETHERLANDS
10:55 - 11:15	The Leptin-D2 axis controls the energy balance in Skeletal muscle
	Speaker: MONICA DENTICE - ITALY
11:15 - 11:30	Discussion
11:30 - 14:45	POSTER / Break
	POSTER / EXHIBIT HALL BREAK
14:45 - 15:45	ORAL ABSTRACTS / ABSTRACTS
	ORAL SESSION - BASIC THYROIDOLOGY 1
	Moderator: SABINE COSTAGLIOLA - BELGIUM
	Moderator: CARMELO NUCERA - UNITED STATES
14:45 - 15:00	1112250 - PATIENT-DERIVED HIPSC MODEL OF HUMAN BRAIN REVEAL MOLECULAR MECHANISMS OF CLINICAL CONSEQUENCES OF CEREBRAL SBP2 DEFICIENCY PRESENTER: ULGU ARSLAN-VAN BERGEN
15:00 - 15:15	1112513 - PHENYLBUTYRATE INCREASES THYROXINE UPTAKE IN PRIMARY ASTROCYTES FROM MICE CARRYING A MCT8 MISSENSE MUTATION PRESENTER: DOREEN BRAUN
15:15 - 15:30	1112197 - RHGH PARTIALLY IMPROVES CORTICAL AND HIPPOCAMPAL DEVELOPMENTAL IMPAIRMENTS IN TRA1 MUTANT MICE BY RESTORING THE GH/IGF-1 AXIS PRESENTER: YANG LI
15:30 - 15:45	1112314 - THE RELEVANCE OF CO-REPRESSOR BINDING FOR THE RESISTANCE TO THYROID HORMONE ALPHA PHENOTYPE AS REVEALED BY A FAMILY CARRYING AN H175R VARIANT IN THE THYROID HORMONE RECEPTOR ALPHA PRESENTER: MARCEL MEIMA
16:00 - 16:50	MEET THE PROFESSOR / THYROID DYSFUNCTION
	Obesity following treatment for thyroid dysfunction
	Chair: KRISTIEN BOELAERT - UNITED KINGDOM
	Chair: IURI GOEMANN - BRAZIL
	Speaker: FERRUCCIO SANTINI - ITALY
16:30 - 16:50	Discussion
Room 5 – Gustavo Pineda (LATS President 1995–97; Chile)	
10:35 - 11:30	MEET THE PROFESSOR / PEDIATRICS & GENETIC DISEASES
	Pediatric thyroid cancer: Recent advances
	Chair: MARIA ISABEL CUNHA VIEIRA CORDIOLI - BRAZIL
	Chair: HANNEKE VAN SANTEN - NETHERLANDS
	Speaker: STEVEN WAGUESPACK - UNITED STATES
11:15 - 11:30	Discussion
11:30 - 13:00	POSTER / Break
	POSTER / EXHIBIT HALL BREAK
13:00 - 14:00	SHORT ORAL COMMUNICATIONS / ABSTRACTS
	SHORT ORAL COMMUNICATIONS - Thyroid Cancer Basic
	Chair: IURI GOEMANN - BRAZIL
	Chair: JULIEN HADOUX - FRANCE
13:00 - 13:05	1112395 - DELIVERY OF MIR-485-5P AND MIR-495-3P VIA EXTRACELLULAR VESICLES IMPAIRS CELL MIGRATION AND INVASION IN THYROID CANCER CELLS Presenter: MURILO VIEIRA GERALDO
13:05 - 13:10	1112387 - IN VIVO DETECTION OF THE MOLECULAR MECHANISMS OF CELL DEATH INDUCED BY CARBON ION THERAPY IN ANAPLASTIC THYROID CANCER Presenter: PIETRO DI FAZIO
13:10 - 13:15	1112367 - METFOMIN REDUCES JAK/STAT PATHWAY ACTIVATION IN ANAPLASTIC THYROID CANCER IN MONOLAYER AND SPHEROID CELLS MODELS PRESENTER: PALOMA RAMOS DE OLIVEIRA

13:15 - 13:20	1112399 - NIFUROXAZIDE ACTIVITY IN ANAPLASTIC THYROID CANCER: MODULATION OF CANCER STEM-LIKE CELL PROPERTIES AND THE INVOLVEMENT OF JAK/STAT3 PATHWAY PRESENTER: GUSTAVO FELISOLA CASO
13:20 - 13:25	1112561 - SERUM MICRORNA ANALYSIS FACILITATES THE DECISION BETWEEN ACTIVE SURVEILLANCE AND IMMEDIATE SURGERY OF THYROID MICROCARCINOMA PRESENTER:FERNANDA FARO
13:25 - 13:30	1112284 - STUDY ON THE ROLE AND MECHANISM OF MIOX IN REGULATING FERROPTOSIS IN PAPILLARY THYROID CARCINOMA PRESENTER:SONGBO
13:30 - 13:35	1112306 - TARGETING PI3K/AKT/MTOR SIGNALING AND INHIBITION OF BCR/ABL TYROSINE KINASE AND GLUCOSE UPTAKE OVERCOMES RESISTANCE TO LENVATINIB IN THYROID CANCER PRESENTER:SONAM KUMARI
13:35 - 13:40	1112572 - THE PHENOTYPE CORRELATED WITH NON CYSTEINE RET GERMLINE MUTATION IS CHARACTERIZED BY THE PRESENCE OF MEDULLARY THYROID CANCER ALONE PRESENTER: Cristina Romei
13:40 - 13:45	1112601 - TRACING THE MOLECULAR ROUTE TO PROGRESSION IN DEFECTIVE MIRNA BIOGENESIS THYROID LESIONS PRESENTER:BARBARA RIVERA POLO
13:45 - 13:50	1112265 - HETEROGENEITY OF MYELOID CELLS IN ANAPLASTIC THYROID CANCER: WHEN "NICHE" MATTER PRESENTER: CORNUOT CLÉMENTINE
16:00 - 16:50	MEET THE PROFESSOR / PEDIATRICS & GENETIC DISEASES
	Management of Graves's disease in children
	Chair: MICHELE MARINO - ITALY Speaker: PAUL VAN TROTSBURG - NETHERLANDS
16:30 - 16:50	Discussion
Room 6 – Hugo Niepomniszcze (LATS President 1997–99; Argentina)	
10:35 - 11:30	MEET THE PROFESSOR / THYROID CANCER
	Role of calcitonin measurement in the surgical decision making
	Chair: KIYOMI HORIUCHI - JAPAN
	Chair: ANDREA CAMILA CAVALLO - ARGENTINA Speaker: ANTONIO MATRONE - ITALY
11:15 - 11:30	Discussion
14:45 - 15:45	ORAL ABSTRACTS / ABSTRACTS
	ORAL SESSION - THYROID CANCER BASIC
	Chair: CHRIS MCCABE - UNITED KINGDOM Chair: PRIYA DEDHIA - UNITED STATES
14:45 - 15:00	1112461 - ANAPLASTIC THYROID CANCER CELL-SECRETED TGFB1 UPREGULATES THE EXPRESSION OF THE IMMUNE CHECKPOINT TIM3 IN HUMAN MONOCYTES PRESENTER: AGUSTINA JAROSZEWSKI
15:00 - 15:15	1113747 - BISPHENOL-A EXPOSURE MAY BE RELATED TO THE GROWING INCIDENCE OF THYROID TUMORS AND THE OCCURRENCE OF MORE AGGRESSIVE CANCER TYPES PRESENTER: ELISANGELA DE SOUZA TEIXEIRA
15:15 - 15:30	1113896 - CELL INTRINSIC IFN-I SIGNATURE CORRELATES WITH DEDIFFERENTIATION OF THYROID CANCER AND DETERMINES ITS IMMUNOLOGICAL FATE PRESENTER: TIM BRANDENBURG
15:30 - 15:45	1112581 - UNRAVELING THYROID CANCER ORIGINS: A CUTTING-EDGE HUMAN THYROID ORGANOID MODEL PRESENTER: EDUARDO ANDRÉS RIOS MORRIS
16:00 - 17:30	SYMPOSIUM / THYROID NODULES
	Emerging Trends in Thyroid Nodule Imaging
	Chair: EDUARDO TOMIMORI - BRAZIL Chair: ANA MARIA ORLANDI - ARGENTINA
16:00 - 16:25	Performance of different US classification systems Speaker: TREVOR ANGELL - UNITED STATES
16:25 - 16:50	Application of AI in thyroid nodule imaging Speaker: JIN YOUNG KWAK - SOUTH KOREA
16:50 - 17:15	Contrast enhance imaging /elastography Speaker: RICARDO MIGUEL COSTA DE FREITAS - SP
17:15 - 17:30	Discussion
18:00 - 20:00	GENERAL ASSEMBLY / GENERAL ASSEMBLY ETA General Assembly
10:35 - 11:30	MEET THE PROFESSOR / THYROID NODULES
	The ATA approach of molecular testing for thyroid nodules
	Chair: ROSALIA PADRO PADOVANI COLETTE - BRAZIL
	Chair: DAGMAR FUEHRER - GERMANY Speaker: MICHAEL YEY - UNITED STATES
11:15 - 11:30	Discussion
13:00 - 14:00	SHORT ORAL COMMUNICATIONS / ABSTRACTS
	SHORT ORAL COMMUNICATIONS - Hyperthyroidism and Thyroid Eye Disease
	Chair: LAURA DELFINO -BRAZIL Chair: KYEONG JIN KIM - SOUTH KOREA

13:00 - 13:05	1112436 - INFILTRATED MACROPHAGES CONTRIBUTE TO CARDIAC HYPERTROPHY ASSOCIATED WITH HYPERTHYROIDISM PRESENTER: NATHALIA SENDER
13:05 - 13:10	1112560 - NEUTROPENIA IN CHILDREN WITH GRAVES' DISEASE TREATED WITH METHIMAZOLE: A CHINESE CHILDREN COHORT (3C) STUDY PRESENTER: SHI TANG
13:10 - 13:15	1112530 - RESTING CARDIAC SYMPTOMS CAN PERSIST IN PATIENTS WITH GRAVES' DISEASE TREATED TO STABLE EUTHYROIDISM PRESENTER: ANOUK VAN HALL
13:15 - 13:20	1112364 - TIME-DEPENDENT CHANGES OF THE RISK OF ATRIAL FIBRILLATION IN PATIENTS WITH HYPERTHYROIDISM RECEIVING RADIOACTIVE IODINE TREATMENT COMPARING TO ANTI-THYROID DRUG: A NATIONWIDE COHORT STUDY PRESENTER: KYEONG JIN KIM
13:20 - 13:25	1112282 - RELATIONSHIP BETWEEN SERUM LEVELS OF SIROLIMUS (RAPAMYCIN) AND OUTCOME OF MODERATE-TO-SEVERE, ACTIVE GRAVES' ORBITOPATHY SIMONE COMI
13:25 - 13:30	1112533 - SPECIFIC INTRA-ORBITAL FAT AND MUSCLE LYMPHOCYTE INFILTRATES ARE ASSOCIATED WITH DIFFERENT CLINICAL MANIFESTATIONS OF THYROID EYE DISEASE PRESENTER: ILARIA MULLER
13:30 - 13:35	1112239 - COMPARATIVE ANALYSIS OF ORBITAL TISSUE MICROENVIRONMENTS IN ACTIVE VERSUS INACTIVE THYROID EYE DISEASE: A SINGLE-CELL TRANSCRIPTOMICS APPROACH PRESENTER: YUANPING HAI
13:35 - 13:40	1112238 - HIGH-THROUGHPUT PROTEOMICS COMBINED WITH IMMUNOHISTOCHEMISTRY OF ORBITAL CONNECTIVE TISSUE IN THYROID EYE DISEASE PRESENTER: YUANPING HAI
13:40 - 13:45	1112503 - TWENTY-YEAR SECULAR TREND OF THYROTOXICOSIS AND THYROTOXIC PERIODIC PARALYSIS IN HONG KONG PRESENTER: GLORIA HOI-YEE LI
13:45 - 13:50	1112363 - THERMOGRAPHIC ASSESSMENT OF THYROID EYE DISEASE IN RESPONSE TO STEROID THERAPY PRESENTER: IVANA LOPES ROMERO KUSABARA
13:50 - 13:55	1112664 - MOLECULAR AND CLINICAL UPDATE IN THYROTOXIC PERIODIC PARALYSIS: A COMPREHENSIVE 30-YEAR STUDY OF A LARGE BRAZILIAN COHORT PRESENTER: SUSAN CHOW LINDSEY
14:45 - 15:45	ORAL ABSTRACTS / ABSTRACTS
	ORAL SESSION - CLINICAL THYROIDOLOGY 1
	Chair: GRACIELA ALCARAZ - ARGENTINA
	Chair: LEONIDAS DUNTAS - GREECE
14:45 - 15:00	1112344 - ASSOCIATION OF PERCHLORATE, THIOCYANATE, AND NITRATE WITH GESTATIONAL THYROID FUNCTION AND CHILD NEURODEVELOPMENT PRESENTER: YINDI LIU
15:00 - 15:15	1112606 - CHARACTERIZATION AND IMPACT OF THE GESTATIONAL HYPOTHYROXINEMIC ENVIRONMENT ON MACROPHAGE POLARIZATION AND FUNCTION. PRESENTER: EVELYN L. JARA FERNÁNDEZ
15:15 - 15:30	1112316 - THE FCRN INHIBITOR, BATOCLIMAB, RAPIDLY NORMALIZES THYROID FUNCTION IN GRAVES' HYPERTHYROIDISM: A PROOF-OF-CONCEPT STUDY PRESENTER: GEORGE KAHALY
15:30 - 15:45	1112518 - THE IMPACT OF TRAB ON GUT MICROBIOTA AND NON-TARGET METABOLITES IN HUMAN AND MURINE MODEL WITH THYROID EYE DISEASE PRESENTER: YANAN WANG
16:00 - 17:30	SYMPOSIUM / THYROID & PREGNANCY
	Update on Hyperthyroidism in Pregnancy
	Chair: PATRÍCIA DE FÁTIMA TEIXEIRA - BRAZIL
	Chair: BIJAY VAIDYA - UNITED KINGDOM
16:00 - 16:25	Thyroid storm in pregnancy
	Speaker: ULLA FELDT-RASMUSSEN - DENMARK
16:25 - 16:50	Iodide for the management of hyperthyroidism in pregnancy
	Speaker: AI YOSHIHARA - JAPAN
16:50 - 17:15	Management in the post-partum
	Speaker: ELIZABETH PEARCE - UNITED STATES
17:15 - 17:30	Discussion
2025-06-21 (Saturday)	
Room 1 - Geraldo A. Medeiros Neto (LATS President 1974–78; Brazil)	
07:00 - 08:25	EARLY RISER SYMPOSIA / THYROID NODULES
	Challenging clinical cases of Thyroid Nodules
	Chair: SARA AHMADI - UNITED STATES
	Chair: SINA JASIM - UNITED STATES
07:00 - 08:25	Representative for ATA
	Panelist: MARIA REGINA CASTRO - UNITED STATES
07:00 - 08:25	Representative for ETA
	Panelist: COSIMO DURANTE - ITALY
07:00 - 08:25	Representative for AOTA
	Panelist: HARUHIKO YAMAZAKI - JAPAN
07:00 - 08:25	Representative for LATS
	Panelist: RAFAEL SELBACH SCHEFFEL - BRAZIL
08:30 - 09:00	PLENARY / PLENARY SESSION
	Opportunities and challenges of artificial intelligence in healthcare
	Chair: SIMON PEARCE - UNITED KINGDOM
	Chair: JENNIFER SIPOS - UNITED STATES
	Speaker: JOHNSON THOMAS - UNITED STATES

09:00 - 09:30	PLENARY / PLENARY SESSION
	Modeling human thyroid development and diseases using stem cell-derived organoids
	Chair: ANA LUIZA MAIA - BRAZIL
	Chair: LUCA PERSANI - ITALY
09:30 - 09:45	Speaker: SABINE COSTAGLIOLA - BELGIUM
	POSTER / Break
	POSTER / EXHIBIT HALL BREAK
	SYMPOSIUM / THYROID CANCER
09:45 - 11:10	Novel therapeutic perspectives for advanced thyroid cancer
	Chair: MARK ZAFEREO - UNITED STATES
	Chair: ANTHONY GLOVER - AUSTRALIA
	Advances in Medullary Thyroid Cancer
09:45 - 10:10	Speaker: MIMI HU - UNITED STATES
	Redifferentiation therapy
	Speaker: SOPHIE LEBoulLEUX - FRANCE
	Neoadjuvant therapy
10:10 - 10:35	Speaker: INES CALIFANO - ARGENTINA
	Discussion
10:35 - 11:00	MEET THE PROFESSOR / THYROID CANCER
	Outcomes in ATC: Is It Evolving into a Treatable Disease?
	Chair: ALEJANDRO ROMAN GONZALEZ - COLOMBIA
	Chair: SOPHIE LEBoulLEUX - FRANCE
11:00 - 11:10	Speaker: MARIA CABANILLAS - UNITED STATES
	Discussion
11:15 - 12:00	SHORT ORAL COMMUNICATIONS / ABSTRACTS
	SHORT ORAL COMMUNICATIONS - Thyroid Nodule and Cancer
	Chair: COSIMO DURANTE - ITALY
	Chair: CAROLINA FERRAZ - BRAZIL
11:45 to 12:00	1112394 - PROGNOSTIC VALUE OF RET STATUS IN PATIENTS WITH UNRESECTABLE MEDULLARY THYROID CANCER TREATED BY VANDETANIB: THE PRONOMED STUDY Presenter: NOÉMIE SIMON-TILLAUX
	1112624 - MOLECULAR CHARACTERIZATION OF A LARGE SERIES OF SUBCENTIMETRIC PAPILLARY THYROID CARCINOMAS Presenter: ELISABETE OLIVEIRA TEIXEIRA
	1114103 - The Genomic Landscape of 250,000+ Thyroid Nodules Undergoing Exome-enriched RNA Sequencing Presenter: Sarah Hamidi
	1112612 - SAFETY AND EFFICACY OF SELPERCATINIB TREATMENT IN ADVANCED MEDULLARY THYROID CANCER PATIENTS: A REAL-LIFE STUDY Presenter: ANTONIO MATRONE
13:00 - 14:00	1112424 - ULTRASOUND-GUIDED CRYOABLATION, LASER OR RADIOFREQUENCY ABLATION OF CERVICAL METASTASES FROM THYROID CARCINOMA: A PROSPECTIVE CLINICAL TRIAL Presenter: RICARDO MIGUEL COSTA DE FREITAS
	1112312 - VALIDATION OF THE INTERNATIONAL MEDULLARY THYROID CANCER GRADING SYSTEM AND IDENTIFICATION OF EZH2 AS A PROGNOSTIC AND POTENTIAL THERAPEUTIC MARKER IN MEDULLARY THYROID CANCER PATIENTS Presenter: ELINE CESILIE JAGER
	1112193 - VASCULAR INVASION AS A PREDICTOR OF DISTANT RECURRENCE IN FOLLICULAR CARCINOMAS: ARE THE DEFINITIONS OF 'WIDELY INVASIVE FOLLICULAR CARCINOMA' AND 'ENCAPSULATED ANGIOINVASIVE FOLLICULAR CARCINOMA' APPROPRIATE? Presenter: YASHURO ITO
	1114005 - Lenvatinib treatment as a neoadjuvant option in locally advanced thyroid cancer Presenter: ALEJANDRO ROMAN GONZALEZ
13:00 - 13:05	1113739 - Unstimulated Postoperative Thyroglobulin Is Highly Accurate In Predicting Treatment Response In High-Risk Differentiated Thyroid Cancer Patients - A Retrospective Cohort Study Presenter: JULIA ISABEL RICHTER CICOGNA
	1112619 - ANAPLASTIC THYROID CANCER UNDERGOES GENOMIC AND PHENOTYPIC PLASTICITY IN RESPONSE TO BRAF INHIBITOR TREATMENT Presenter: XIAO ZHAO
	ATA PRIZE LECTURE / GENERAL
	ATA PRIZE LECTURE
13:05 - 13:10	Chair: VICTOR BERNET - UNITED STATES
	Awardees: KRISTIE BOELAERT - UNITED KINGDOM
	Awardees: THOMAS SCANLAN - UNITED STATES
	Awardees: SUSAN MANDEL - UNITED STATES
13:10 - 13:15	ORAL ABSTRACTS / ABSTRACTS
	ORAL SESSION - CLINICAL THYROID CANCER 2
	Chair: ANA LUIZA MAIA - BRAZIL
	Chair: IWAO SUGITANI - JAPAN
13:15 - 13:20	1112621 - A TUMOR-CELL SPECIFIC GENE SIGNATURE DERIVED FROM SINGLE-CELL SEQUENCING IS PROGNOSTIC ACROSS INDEPENDENT COHORTS OF PAPILLARY THYROID CARCINOMA PATIENTS PRESENTER: JENNIFER RUI WANG
	1112553 - GENETIC ANCESTRY OF RET MUTATIONS AT CODON 804 REVEALS A BOTTLENECK EFFECT AMONG BRAZILIANS WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE 2 PRESENTER: VICTOR ALEXANDRE DOS SANTOS VALSECCHI
	1112616 - MOLECULAR PROFILE OF ADVANCED RADIOIODINE-REFRACTORY THYROID CANCER AND RESPONSE TO LENVATINIB TREATMENT PRESENTER: ELISA MINALDI
	1112244 - THE SIGNIFICANCE OF APOPTOSIS DYSREGULATION IN CLINICAL MANAGEMENT OF PAPILLARY THYROID CANCER: IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS PRESENTER: ADAMSKA AGNIESZKA
13:20 - 13:25	
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13:35 - 13:40	
13:40 - 13:45	
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15:30 - 15:45	

15:45 - 16:00	POSTER / GENERAL
	POSTER SESSION/BREAK IN THE EXHIBIT HALL
16:00 - 17:30	SYMPOSIUM / THYROID NODULES
	Alternative approaches to indeterminate nodule management
	Chair: ROSA PAULA MELLO BISCOLLA - BRAZIL
	Chair: KENNICHI KAKUDO - JAPAN
16:00 - 16:25	Active surveillance for indeterminate thyroid nodules
	Speaker: ALVARO SANABRIA - COLOMBIA
16:25 - 16:50	Minimally invasive management of thyroid nodules
	Speaker: GIOVANNI MAURI - ITALY
16:50 - 17:15	Endoscopic surgery
	Speaker: ANTONIO BERTELLI - BRAZIL
17:15 - 17:30	Discussion
Room 2 – Eduardo Gaitán (LATS President 1982–85; Colombia)	
09:45 - 10:45	MEET THE PROFESSOR / REGULATION OF TH M&S
	Transcription and circadian control by thyroid hormone
	Chair: TANIA MARIA RUFFONI ORTIGA - BRAZIL
	Chair: ALEXANDRA DUMITRESCU - UNITED STATES
09:45 - 10:10	Thyroid hormone and genomic regulation in amphibians
	Speaker: LAURENT SACHS - FRANCE
10:10 - 10:35	Thyroid hormone and circadian control
	Speaker: PAULA BARGI SOUZA - BRAZIL
10:35 - 10:45	Discussion
11:15 - 12:00	MEET THE PROFESSOR / THYROID & PREGNANCY
	Hazards of endocrine disruptors in pregnancy
	Chair: ROBIN PEETERS - NETHERLANDS
	Chair: MARIA IZABEL CHIAMOLERA - BRAZIL
	Speaker: LAURA STERIAN WARD - BRAZIL
11:45 - 12:00	Discussion
14:45 - 15:45	ORAL ABSTRACTS / ABSTRACTS
	ORAL SESSION - PEDIATRIC THYROIDOLOGY
	Moderator: FERNANDA VAISMAN - BRAZIL
	Moderator: STEVEN WAGUESPACK - UNITED STATES
14:45 - 15:00	1114004 - TOCILIZUMAB VS METHYLPREDNISOLONE IN MODERATE-SEVERE GRAVES' ORBITOPATHY: RESULTS OF AN ITALIAN MULTICENTER CLINICAL TRIAL PRESENTER: MARIO SALVI
15:00 - 15:15	1112453 - DISEASE PRESENTATION AND DISTINCT GENETIC PROFILES ARE RELATED TO GENDER AND PUBERTY COMPLETION IN PEDIATRIC DIFFERENTIATED THYROID CARCINOMA PRESENTER: Paulo Alonso Garcia Alves
15:15 - 15:30	1112255 - NEWBORNS THYROGLOBULIN IS A MORE SENSITIVE BIOMARKER FOR MONITORING IODINE STATUS THAN NEONATAL TSH PRESENTER: CAMILO FUENTES PEÑA
16:00 to 17:30	SYMPOSIUM / GOITER, IODINE AND OTHER ENVIRONMENTAL FACTORS
	Impact of Radiological and Chemical Exposure on Thyroid Health (78)
	Chair: BYEONG-CHEOL AHN - SOUTH KOREA
	Chair: ROSSELLA ELISEI - ITALY
16:00 to 16:25	Human radiation exposure and thyroid genetic alterations
	Speaker: RAFFAELE CIAMPI - ITALY
16:25 to 16:50	Chemical disruptors and neonatal screening
	Speaker: CAROLINE SERRANO DO NASCIMENTO - SP
16:50 to 17:15	Endocrine Disruptors in Thyroid Disease
	Speaker: AARTI MATHUR - UNITED STATES
17:15 to 17:30	Discussion
Room 3 – Marcos S. Abalovich (LATS President 2011-2013; Argentina)	
09:45 - 11:10	SYMPOSIUM / GOITER, IODINE AND OTHER ENVIRONMENTAL FACTORS
	Iodine, selenium and thyroid diseases
	Chair: LAURA STERIAN WARD - BRAZIL
	Chair: BIRTE NYGAARD - DENMARK
09:45 - 10:10	The structure, function, and mechanism of the Na⁺/I⁻ symporter (NIS)
	Speaker: NANCY CARRASCO - UNITED STATES
10:10 - 10:35	Iodine prophylaxis and its impact on thyroid diseases
	Speaker: PETER KOPP - SWITZERLAND
10:35 - 11:00	Selenium and thyroid function: what is new
	Speaker: SUN WOOK CHO - SOUTH KOREA
11:00 - 11:10	Discussion

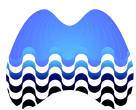
Room 4 – Jorge Maisterrena (LATS President 1986–90; Mexico)	
09:45 - 10:35	MEET THE PROFESSOR / AUTOIMMUNITY
	IgG4 related thyroid disease
	Chair: WON GU KIM - SOUTH KOREA
	Chair: MARIO ROTONDI - ITALY
10:15 - 10:35	Speaker: TAKASHI AKAMIZU - JAPAN
	Discussion
11:15 - 12:00	MEET THE PROFESSOR / GOITER, IODINE AND OTHER ENVIRONMENTAL FACTORS
	Nuclear accidents and thyroid disease
	Chair: MICHAEL TUTTLE - UNITED STATES
11:15 - 11:45	The Effects of Radiation Exposure on the Thyroid Gland in Fukushima, Japan
	Speaker: HIROKI SHIMURA - JAPAN
11:45 - 12:00	Discussion
13:00 - 14:00	SHORT ORAL COMMUNICATIONS / ABSTRACTS
	SHORT ORAL COMMUNICATIONS - Thyroid Cell Biology, Thyroid Hormone Action and Metabolism
	Chair: LAILA Yael BIELSKI - ARGENTINA
	Chair: BALÁZS GEREBEN - HUNGARY
13:00 - 13:05	1112526 - THE NLRP3/TLR2/NFkB PATHWAY IS INVOLVED IN THE OCCURRENCE OF MISCARRIAGE IN AIT PATIENTS
13:05 - 13:10	1112372 - FUNCTIONAL ANALYSIS OF SLC5A5 GENE VARIANTS ASSOCIATED WITH CONGENITAL HYPOTHYROIDISM PRESENTER:GERARDO HERNÁN CARRO
13:10 - 13:15	1112321 - FUNCTIONAL TESTING OF POTENTIAL NOVEL THYROID HORMONE TRANSPORTERS INFORMED BY A LARGE SCALE THYROID FUNCTION GENOME-WIDE ASSOCIATION STUDY MATTHIJS FREUND
13:15 - 13:20	1113717 - GESTATIONAL HYPOTHYROIDISM DAMAGES THE INTESTINAL INTEGRITY IN THE ILEUM OF THE ADULT OFFSPRING MARIA JOSE MENDOZA LEON
13:20 - 13:25	1112598 - TRIIODOTHYRONINE MODULATES DENDRITIC CELL-DERIVED EXTRACELLULAR VESICLES AND THEIR ROLE IN IMMUNE RESPONSE REGULATION MARIANA PIRES CAVALCANTI TEIXEIRA
13:25 - 13:30	1112374 - PATHOGENIC VARIANTS IN CONSERVED RESIDUES OF SLC5A FAMILY MEMBERS REVEALED KEY RESIDUES FOR NIS FUNCTION GERARDO HERNÁN CARRO
13:30 - 13:35	1112276 - NEW INSIGHTS INTO THYROID HORMONE METABOLISM AND AMMONIA DETOXIFICATION IN MASLD USING N-ACETYL CYSTEINE (NAC) AND L-ORNITHINE L-ASPARTATE (LOLA) SIMONE WAJNER
13:35 - 13:40	1112274 - TYPE 3 DEIODINASE IS ACTIVATED IN THE BRAIN OF AN ANIMAL MODEL OF METABOLIC ASSOCIATED STEATOTIC LIVER DISEASE (MASLD). SIMONE WAJNER
13:40 - 13:45	1114179 - Chronic iodine excess induced TSH elevation by inactivating Type 2 deiodinase via ROS/AKT-mTOR-GSK3β/NRF2 signaling pathway XIAOTONG GAO
13:45 - 13:50	1112292 - IFNA TRIGGERS AUTOIMMUNE THYROIDITIS BY RESHAPING THYROGLOBULIN IMMUNOGENIC PEPTIDE REPERTOIRE MIHAELA STEFAN LIFSHITZ
13:50 - 13:55	1112184 - INTEGRATED TRANSCRIPTOMIC AND EPIGENETIC PROFILING OF THYROCYTES IN AUTOIMMUNE THYROIDITIS VIA SINGLE CELL RNA-SEQ, BULK RNA-SEQ AND DNA METHYLATION PROFILING TINGTING LIU
16:00 - 16:50	MEET THE PROFESSOR / REGULATION OF TH M&S
	Current topics in Nonthyroidal Illness Syndrome
	Chair: ANITA BOELEN - NETHERLANDS
16:00 - 16:30	Chair: GABRIELA BRENTA - ARGENTINA
	Understanding the mechanisms behind the disorders
16:30 - 16:50	Speaker: SIMONE WAJNER - BRAZIL
	Discussion
Room 5 – Gustavo Pineda (LATS President 1995–97; Chile)	
09:45 - 10:45	MEET THE PROFESSOR / REGULATION OF TH M&S
	Tissue responses to thyroid hormone
	Chair: LEA MACIEL - BRAZIL
09:45 - 10:10	Chair: ANA MARIA MASINI REPISO - ARGENTINA
	Patients with THRA and THRB receptor defects
10:10 - 10:35	Speaker: CARLA MORAN - IRELAND
	Thyroid hormone and the immune system
10:35 - 10:45	Speaker: MARIA DEL MAR MONTESINOS - ARGENTINA
	Discussion
12:00 to 13:00	ROUND TABLE
	International Round Table - Global challenges in thyroid health
	Chair: LUCA PERSANI - ITALY
	Chair: ANA LUIZA MAIA - BRAZIL
	Panelist: FASANMADE OLUFEMI ADETOLA - NIGERIA
	Panelist: HINDE IRAQI - MOROCCO
	Panelist: FEREIDOUN AZIZI - IRAN
	Panelist: KIRTIDA S. ACHARYA - KENYA
	Panelist: JENNIFER SIPOS - UNITED STATES
	Panelist: ASHOK BHASEEN - CANADA
	Panelist: DONG YEOB SHIN - SOUTH KOREA

13:00 to 14:00	SHORT ORAL COMMUNICATIONS / ABSTRACTS
	SHORT ORAL COMMUNICATIONS - Endocrine Disruptors and Thyroid Dysfunctions (Basic)
	Chair: LISA THOMASZ - ARGENTINA
	Chair: ANTONIO DE LA VIEJA - SPAIN
13:00 - 13:05	1112633 - GESTATIONAL HYPOTHYROIDISM DAMAGES THE INTESTINAL INTEGRITY IN THE ILEUM OF THE ADULT OFFSPRING. Presenter: MARIA JOSE MENDOZA LEON
13:05 - 13:10	1112254 - HISTONE ACETYLTRANSFERASE LOSS-OF-FUNCTION PROMOTES THYROID CANCER PROGRESSION IN VIVO AND SENSITIZES HUMAN THYROID CANCER CELLS TO HIGHLY SPECIFIC PROTEIN DEGRADERS
13:10 - 13:15	1112515 - BISPHENOL A, PERCHLORATE, AND NITRATE MIXTURE DISRUPTS CELL DIFFERENTIATION AND ALTERS EPIGENETIC MECHANISMS AND SIGNALING PATHWAYS IN THYROID CELLS PRESENTER: EVELYN FRANCINY CARDOSO TAVARES
13:15 - 13:20	1112589 - FOXE1 DOMAINS AT THE CROSSROAD BETWEEN EVOLUTION AND THYROID FUNCTIONALITY PRESENTER: ELISA STELLARIA GRASSI
13:20 - 13:25	1112446 - HYPOTHYROIDISM PROMOTES A SARCOPENIA-LIKE PHENOTYPE IN YOUNG BUT NOT IN AGED MICE PRESENTER: THAMIRE SIQUEIRA DE OLIVEIRA
13:25 - 13:30	1112233 - DEVELOPING A TESTING BATTERY FOR DEVELOPMENTAL NEUROTOXICITY MEDIATED VIA DISRUPTED THYROID HORMONE HOMEOSTASIS PRESENTER: NATHALIE DIERICH
13:30 - 13:35	1112514 - MATERNAL EXPOSURE TO TRICLOSAN DURING THE INTRAUTERINE PERIOD DISRUPTS THYROID DEVELOPMENT AND FUNCTION IN THE OFFSPRING ANIMALS PRESENTER: GUILHERME HENRIQUE
13:35 - 13:40	1112511 - POLYCHLORINATED BIPHENYLS DISRUPT GENE EXPRESSION, NIS FUNCTION, AND KEY SIGNALING PATHWAYS IN HUMAN THYROID CELLS PRESENTER: VINICIUS GONÇALVES RODRIGUES
13:40 - 13:45	1112360 - TRANSCRIPTOMIC PROFILING OF THYROID CELLS EXPOSED TO ROUNDUP® ORIGINAL DI REVEALS DOSE-DEPENDENT EFFECTS: IMPLICATIONS FOR SAFETY STANDARDS PRESENTER: IZABELA FERNANDA DAL BO CRUZ
13:45 - 13:50	1113992 - DEHAL1 modulates oxidative stress induced by endogenous and anthropogenic oxidants. PRESENTER: José C. Moreno
13:50 - 13:55	1112208 - THE ROLE OF THYROID HORMONE IN SUSCEPTIBILITY TO TYPE 2 DIABETES IN OFFSPRING: REGULATORY MECHANISMS OF THE PLACENTAL GENOMIC IMPRINT AT THE DLK1-DIO3 LOCUS IN WOMEN WITH HYPOTHYROIDISM. PRESENTER: MARIA BEATRIZ BRAVIN
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	Chair: PETER KOPP - SWITZERLAND
14:45 - 15:00	1112486 - EVALUATING INSULIN'S IMPACT ON THYROID DEVELOPMENT USING HUMAN THYROID ORGANOIDS PRESENTER: SABINE COSTAGLIOLA
15:00 - 15:15	1112269 - INDUCTION OF TYPE 2 AND 3 DEIODINASES IN MUSCLE STEM CELLS OF CRITICALLY ILL PATIENTS: UNVEILING THE IMPLICATIONS FOR HYPERGLYCEMIA AND NON-THYROIDAL ILLNESS SYNDROME PRESENTER: Thalane Carvalho Oliveira
15:15 - 15:30	1112499 - UNREVEALING THE EPIGENETIC MECHANISMS TRIGGERED BY TSH IN THE STIMULATION OF THYROID DIFFERENTIATION MARKERS GENE EXPRESSION PRESENTER: VINICIUS GONÇALVES RODRIGUES
15:30 - 15:45	1113824 - Identification and Characterization of GC-Cells: A Novel Population of Benign Epithelial Cells Involved in Lymph Node Metastasis of Papillary Thyroid Carcinoma PRESENTER: YEFENG CAI
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	Chair: CELIA REGINA NOGUEIRA - BRAZIL
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	Speaker: HELMUT GRASBERGER - UNITED STATES
10:35 - 11:00	Dealing with variants of uncertain significance in the genetic diagnosis of congenital hypothyroidism
	Speaker: JUAN PABLO NICOLA - ARGENTINA
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	Chair: NEMENCIO A NICODEMUS JR - PHILIPPINES
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	Novel Advances in Thyroid Cancer Research
	Chair: CARMELO NUCERA - UNITED STATES
	Chair: CHRIS MCCABE - UNITED KINGDOM

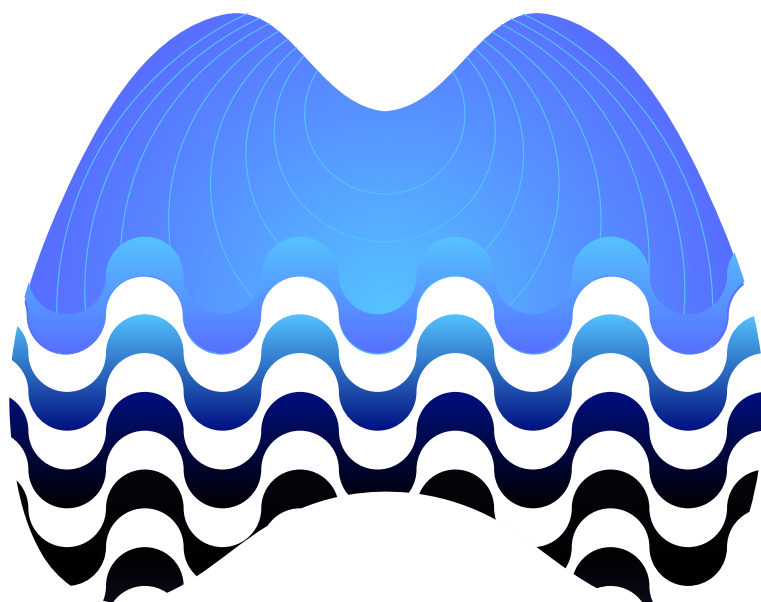
16:00 - 16:25	TERT promoter mutations as a driver of tumor aggression Speaker: NORISATO MITSUTAKE - JAPAN
16:25 - 16:50	Tumor Microenvironment in thyroid cancer differentiation Speaker: LAURA FOZZATTI - ARGENTINA
16:50 - 17:15	The Role of Deiodinases in Thyroid Tumorigenesis Speaker: DOMENICO SALVATORE - ITALY
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	Chair: ANTONIO MATRONE - ITALY
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10:35 - 11:30	Thyroid nodule management in children
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	Chair: ANDRÉ BORSATTO ZANELLA - BRAZIL
	Speaker: ANDREW BAUER - UNITED STATES
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	Chair: NATSUKO WATANABE - JAPAN
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13:10 - 13:15	1112656 - IODINE, HEAVY METALS, AND THYROID FUNCTION IN PREGNANCY: A CROSS-SECTIONAL STUDY IN BOTUCATU, BRAZIL. PRESENTER: ADRIANO FRANCISCO DE MARCHI JUNIOR
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13:20 - 13:25	1112574 - MATERNAL HYPOTHYROXINEMIA IN EARLY PREGNANCY AND OFFSPRING NEURODEVELOPMENT: A PROSPECTIVE INTERVENTION STUDY PRESENTER: YUTONG HAN
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13:30 - 13:35	1112611 - IODINE STATUS QUESTIONNAIRE ASSESSMENT DURING PREGNANCY: A PILOT STUDY. PRESENTER: MARIA IZABEL CHIAMOLERA
13:35 - 13:40	1112323 - TREATMENT PATTERNS AMONG METHIMAZOLE-TREATED PATIENTS WITH GRAVES' DISEASE PRESENTER: LESLEY-ANN MILLER-WILSON
13:40 - 13:45	1112418 - THYROID AUTOIMMUNITY AND PREGNANCY: IMPLICATIONS FOR MATERNAL AND FETAL HEALTH OUTCOMES CAMILA BERGER DE OLIVEIRA CUNHA
13:45 - 13:50	1112587 - CLINICAL IMPLICATIONS FOR OBESITY MANAGEMENT: BARIATRIC SURGERY-INDUCED CHANGES IN TSH AND ITS CORRELATION WITH THE NEW MODEL OF OBESITY CLASSIFICATION PROPOSAL BY SBEM/ABESO, A CROSS SECTIONAL STUDY. PRESENTER: ADRIANO FRANCISCO DE MARCHI JUN
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15:15 - 15:30	1112417 - IMPACT OF ENDOCRINE DISRUPTORS ON THYROID FUNCTION AND REPRODUCTIVE HEALTH: INSIGHTS INTO THE HYPOTHALAMIC-PITUITARY-THYROID AXIS PRESENTER: CAMILA BERGER DE OLIVEIRA CUNHA

15:30 - 15:45	1112313 - MULTIPLE ASSAY INTERFERENCES LEADING TO THE DIAGNOSIS OF LYMPHOPROLIFERATIVE DISORDERS PRESENTER: IRENE CAMPI
16:00 - 17:30	SYMPOSIUM / THYROID DYSFUNCTION
	End-Organ Effects of Hyperthyroidism
	Chair: MARIO VAISMAN - BRAZIL Chair: EIJUN NISHIHARA - JAPAN
16:00 - 16:25	Heart and vascular risk Speaker: JOSE SGARBI - BRAZIL
16:25 - 16:50	Bones and fracture risk Speaker: ROBIN PEETERS - NETHERLANDS
16:50 - 17:15	Mental health and cognition Speaker: ANNE CAPPOLA - UNITED STATES
17:15 - 17:30	Discussion
2025-06-22 (Sunday)	
Room 1 - Geraldo A. Medeiros Neto (LATS President 1974–78; Brazil)	
08:00 - 09:30	EARLY RISER SYMPOSIA / THYROID & PREGNANCY
	Masterclass: Impact of thyroid disease & pregnancy (Reasons not to panic)
	Chair: SPYRIDOULA MARAKA - UNITED STATES Chair: PATRICIA GATBONTON - PHILIPPINES
08:00 - 08:20	Maternal hypothyroxinaemia: treat or observe Speaker: TIM KOREVAAR - NETHERLANDS
08:20 - 08:40	Autoimmunity with assisted reproduction Speaker: KRIS POPPE - BELGIUM
08:40 - 09:00	Uncontrolled Graves' disease Speaker: DANILO VILLAGELIN - BRAZIL
09:00 - 09:20	Treatment of MCT8 Deficiency during Pregnancy Speaker: STEFAN GROENEWEG - NETHERLANDS
09:20 - 09:30	Discussion
09:30 - 10:15	AOTA PRIZE LECTURE
	Chair: WON BAE KIM - SOUTH KOREA Chair: BYEONG-CHEOL AHN - SOUTH KOREA Awardees: WON GU KIM - SOUTH KOREA
	POSTER / Break
10:15 - 10:30	POSTER SESSION/BREAK IN THE EXHIBIT HALL
10:30 - 12:00	SYMPOSIUM / THYROID NODULES
	Indeterminate Nodules: Molecular and Genomic Strategies Across Different Regions
	Chair: JANETE MARIA CERUTTI - BRAZIL Chair: VERONICA ILERA - ARGENTINA
10:30 - 10:50	North America/Canada Speaker: MARKUS ESZLINGER - GERMANY
10:50 - 11:10	Europe Speaker: CARLA COLOMBO - ITALY
11:10 - 11:30	Asia Speaker: KENNICHI KAKUDO - JAPAN
11:30 - 11:50	Latin America Speaker: CAROLINA FERRAZ - BRAZIL
11:50 - 12:00	Discussion
12:00 - 13:00	POSTER / Break POSTER / EXHIBIT HALL BREAK
13:00 - 14:00	DEBATE / THYROID CANCER
	Use of molecular testing for initial treatment decisions in low and intermediate risk thyroid cancers
	Moderator: ANA PAULA SOARES DIAS FERREIRA - PORTUGAL Moderator: MICHAEL MINGZHAO XING - UNITED STATES
13:00 - 13:20	YES Speaker: JANETE MARIA CERUTTI - BRAZIL
13:20 - 13:50	NO Speaker: MATTHEW DAVID RINGEL - UNITED STATES
13:50 - 14:00	Discussion
14:30 - 15:00	CLOSING / EVENT CLOSURE 17th International Thyroid Congress - Concludes

Room 2 – Eduardo Gaitán (LATS President 1982–85; Colombia)	
10:30 - 12:00	DEBATE / AUTOIMMUNITY
	Early definitive treatment of Graves' hyperthyroidism is the gold standard
	Moderator: ALICIA TERESA GAUNA - ARGENTINA Moderator: PRIYA DEDHIA - UNITED STATES
10:30 - 10:50	For the proposal
	Speaker: KRISTIEN BOELAERT - UNITED KINGDOM
10:50 - 11:10	Against the proposal
	Speaker: FEREIDOUN AZIZI - IRAN
11:10 - 12:00	Discussion
12:00 - 13:00	POSTER / Break
	POSTER / EXHIBIT HALL BREAK
13:00 - 13:50	MEET THE PROFESSOR / THYROID DYSFUNCTION
	The Dilemma of Subclinical Hyperthyroidism: Treat or Observe?
	Chair: MARIO VAISMAN - BRAZIL
	Chair: MIN JI JEON - SOUTH KOREA
13:00 - 13:30	Subclinical Hyperthyroidism: Treat or observe?
	Speaker: JENNIFER MAMMEN - UNITED STATES
13:30 - 13:50	Discussion
Room 3 – Marcos S. Abalovich (LATS President 2011-2013; Argentina)	
10:30 - 12:00	SYMPOSIUM / REGULATION OF TH M&S
	Thyroid Hormone and the nervous system
	Chair: NORIYUKI KOIBUCHI - JAPAN
	Chair: THOMAS SCANLAN - UNITED STATES
10:30 - 10:55	Thyroid hormone transport and the CNS
	Speaker: Heike Heuer - GERMANY
10:55 - 11:20	Deiodinases and brain function
	Speaker: ARTURO HERNANDEZ - UNITED STATES
11:20 - 11:45	Thyroid hormone and neuronal differentiation
	Speaker: FREDERIC FLAMANT - FRANCE
11:45 - 12:00	Discussion
12:00 - 13:00	POSTER / Break
	POSTER / EXHIBIT HALL BREAK
13:00 - 13:50	MEET THE PROFESSOR / THYROID DYSFUNCTION
	Thyroid dysfunction with Immune Checkpoint inhibitors
	Chair: DONG YEOB SHIN - SOUTH KOREA
	Thyroid dysfunction with Immune Checkpoint inhibitors
13:00 - 13:30	Speaker: MARIA FABIANA RUSSO PICASSO - ARGENTINA
	Discussion
13:30 - 13:50	Discussion
Room 4 – Jorge Maisterrena (LATS President 1986–90; Mexico)	
13:00 - 14:00	MEET THE PROFESSOR / REGULATION OF TH M&S
	Hypothalamic-pituitary-thyroid axis
	Chair: ARTURO HERNANDEZ - UNITED STATES
	Chair: Heike Heuer - GERMANY
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	Speaker: Antonio C. Bianco - UNITED STATES
13:20 - 13:40	Hypothalamic control of the thyroid axis
	Speaker: CSABA FEKETE - HUNGARY
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	Environmental Factors and Their Impact on Thyroid Autoimmunity
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	Chair: AARTI MATHUR - UNITED STATES
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	Speaker: JEREMYJONES FERNANDEZ ROBLES - PHILIPPINES
10:55 - 11:20	Microbiome in thyroid autoimmunity
	Speaker: CAMILLA VIRILI - ITALY
11:20 - 11:45	Stress and lifestyle in pathogenesis of AITD
	Speaker: LEONIDAS DUNTAS - GREECE
11:45 - 12:00	Discussion



12:00 - 13:00	POSTER / Break
	POSTER / EXHIBIT HALL BREAK
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	Approaches to Managing Toxicity in TKI Treatment
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	Chair: BHAVANA KONDA - UNITED STATES
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	Chair: RAFFAELE CIAMPI - ITALY
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	Speaker: DEBORA DANILOVIC - BRAZIL
10:55 - 11:20	Clinical utility of micro RNA expression
	Speaker: EDNA T. KIMURA - BRAZIL
11:20 - 11:45	Mechanisms of development of drug resistance to targeted therapies
	Speaker: NAIFA LAMKI BUSAIDY - UNITED STATES
11:45 - 12:00	Discussion
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	POSTER / EXHIBIT HALL BREAK
13:00 - 14:30	SYMPOSIUM / THYROID & PREGNANCY
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	Chair: ULLA FELDT-RASMUSSEN - DENMARK
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	Speaker: ALEXANDRA DUMITRESCU - UNITED STATES
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	Speaker: MARIO ROTONDI - ITALY
13:50 - 14:15	TRAb and fetal outcome
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17th

International **Thyroid** Congress

18 – 22 **June 2025**

Rio de Janeiro Brazil

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ENDOCRINE DISRUPTORS AND THYROID FUNCTION

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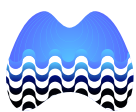
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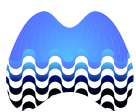
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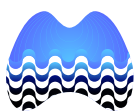
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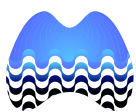
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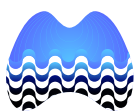
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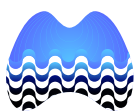
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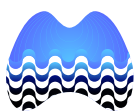
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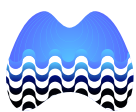
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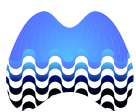
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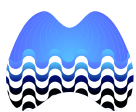
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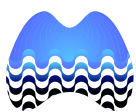
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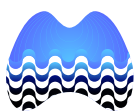
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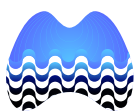
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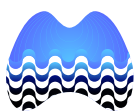
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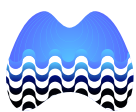
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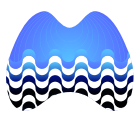
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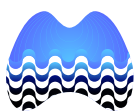
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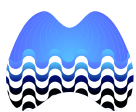
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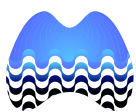
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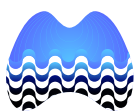
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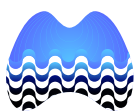
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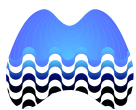
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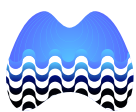
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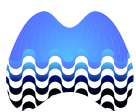
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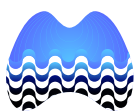
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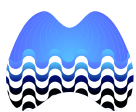
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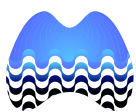
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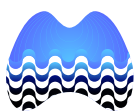
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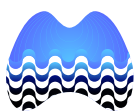
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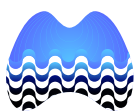
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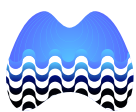
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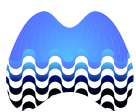
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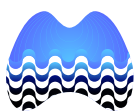
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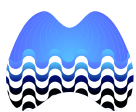
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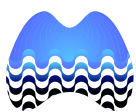
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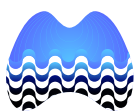
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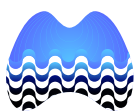
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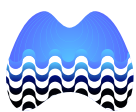
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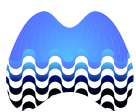
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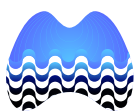
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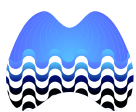
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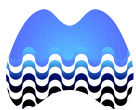
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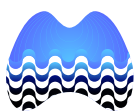
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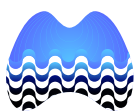
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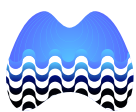
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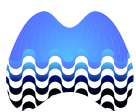
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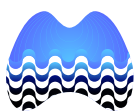
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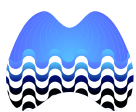
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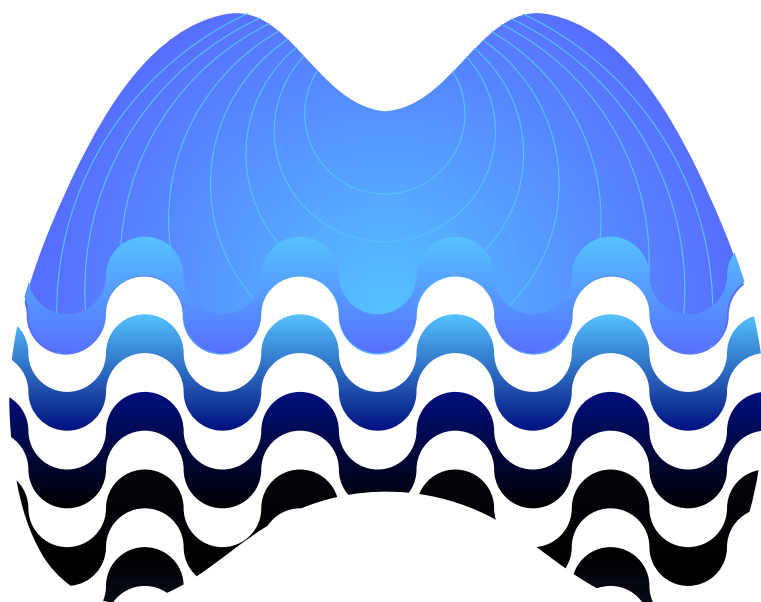
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17th

International **Thyroid** Congress

18 – 22 **June 2025**

Rio de Janeiro Brazil

ORAL PRESENTATION

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112177 - BISPHENOL-A EXPOSURE MAY BE RELATED TO THE GROWING INCIDENCE OF THYROID TUMORS AND THE OCCURRENCE OF MORE AGGRESSIVE CANCER TYPES

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Introduction: Evidence links Bisphenol A (BPA), a widespread synthetic endocrine-disrupting chemical, to an increased risk of cancer. However, little is known about its effects on thyroid cells, particularly on mutated cells. **Methods:** The present study compared the effects of doses lower than the 1.0 µg/mL Specific Migration Limit (SML, maximum permitted amount of a substance in food) on two papillary thyroid carcinoma-derived cell lines (TPC-1 and BCPAP) and one anaplastic thyroid carcinoma cell line (8505C) to a control lineage (Nthy-ori-3-1). **Results:** BPA induced non-monotonic cytotoxic effects at both the membrane (Trypan Blue assay) and metabolism (CCK-8 assay) levels across all thyroid cell lines. Exposure to the SML dose resulted in membrane destruction in 50% of control cells and 48% of 8505-C cells and had an even more pronounced effect on TPC-1 and BCPAP cells, where 75% and 79% of cells, respectively, were affected after 24 h. Moreover, after 48 h of exposure, all the mutant cells displayed a killing rate of approximately 80%. An assay combining double staining with Hoechst 33342 and propidium iodide (Hoechst Double Staining Kit) indicated that the observed effects were partly due to the induction of apoptosis. The anaplastic line exhibited the highest apoptosis rate, with 75% of 8505-C cells undergoing apoptosis at both 24 and 48 hours at 0.8 µg/mL. In contrast, BPA stimulated proliferation of all cells except BCPAP, as demonstrated by the bromodeoxyuridine (BRDU) assay. The SML dose resulted in a 151% increase in the number of 8505-C cells after 48 h. This dose also increased the migration rate of anaplastic cells by 65% at 72 h ($p < 0.0001$). **Conclusion:** Our data demonstrate that BPA exerts important pleiotropic effects on thyroid cells, even at doses considered acceptable. The increasing incidence of thyroid cancer may be related to BPA exposure, which may influence the selection of aggressive cancer types.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112491 - ENDOCRINE DISRUPTORS MIXTURE IMPAIRS THYROID DIFFERENTIATION THROUGH EPIGENETIC MECHANISMS AND DYSREGULATED PKA AND AKT SIGNALING PATHWAYS

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Introduction: Personal care products contain various endocrine disruptors (EDs), including antimicrobials (e.g., triclosan, parabens) and plasticizers (e.g., BPA, phthalates). Our previous studies showed that individual EDs disrupt thyroid function by altering signaling pathways, gene/protein expression and epigenetic mechanisms. However, the combined effects of ED mixtures, more representative of human exposure, have never been studied in thyrocytes. **Objective:** This study aimed to evaluate the molecular mechanisms triggered by an EDs-mixture, commonly found in personal care products in thyrocytes. **Methods:** PCCl3 cells were treated or not with a mixture of: triclosan, methylparaben, BPA, MEHP (10⁻⁷, 10⁻⁹ or 10⁻¹¹M) for 24 h. Gene/protein expression and ROS production were evaluated by qPCR/Western Blotting and flow cytometry. AKT and PKA signaling pathways were assessed through Western Blotting. The participation of these pathways in ED-mixture-induced effects was evaluated using inhibitors of PKA (H89) or PI3K (LY294002). The role of histone post-translational modifications in EDs-induced effects was assessed using inhibitors of histone acetyltransferase (A485) and H3K27 methyltransferase EZH2 (GSK343). **Results:** The EDs-mixture decreased the expression of genes/proteins involved in thyroid hormone synthesis (Slc5a5, Tg, Tpo, Tshr), increased ROS production, and reduced antioxidant enzymes expression (Sod3, Txntr). The treatment upregulated the expression of enzymes involved in transcriptional repression (Kdm5c, Hdac3, Ezh2) and downregulated the expression of enzymes involved in transcriptional activation (Hat1, Kdm6a). Accordingly, increased methylation and reduced acetylation of histones were observed in ED-mixture-treated cells. A485 and GSK343 partially reversed the ED-mixture effects on thyroid differentiation markers. Additionally, the EDs-mixture increased pAKT and decreased pCREB. Notably, H89 and LY294002 reversed the EDs-mixture-induced effects on thyroid gene expression. **Conclusion:** EDs-mixture, commonly found in cosmetics, reduced the expression of thyroid differentiation markers via epigenetic mechanisms associated with transcriptional repression. Additionally, the inhibition of PKA and activation of AKT signaling pathways appear to play an essential role in the EDs-mixture-induced effects.

HYPERTHYROIDISM

1112371 - T3 ANALOGUE TRIIODOTHYROACETIC ACID (TRIAC) TREATMENT AND SURVIVAL IN MCT8 DEFICIENCY: AN INTERNATIONAL REAL-WORLD COHORT STUDY

Floor van der Most¹; Ferdy S. van Geest¹; Stefan Groeneweg¹; Matthijs E. T. Freund¹; Barbara. M. van der Linden¹; Jeremy. A. Labrecque¹; Layal Chaker¹; W. Edward Visser¹

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Introduction: MCT8 deficiency is an X-linked genetic defect in the thyroid hormone monocarboxylate transporter (MCT) 8, characterized by severe neurocognitive disabilities and peripheral thyrotoxicosis. Mortality rates are high with 30% dying during childhood. The T3 analogue triiodothyroacetic acid (Triac) has been proven to safely alleviate peripheral thyrotoxicosis in patients with MCT8 deficiency. **Objective:** As thyrotoxicosis is linked to increased mortality, we investigated whether Triac treatment could improve survival in male patients with MCT8 deficiency. **Methods:** Genetic, biochemical and clinical data were collected from 190 sites in 51 countries through an international consortium on MCT8 deficiency, including Triac Trial, a Triac off-label cohort, and published cases in literature. The impact of mutations on MCT8 transporter function was assessed in transfected cells and classified as mild, moderate or severe loss-of-function (LoF). Baseline characteristics, including age at diagnosis, country of residence, disease features, presence of a feeding tube, and prior treatment targeting thyrotoxicosis were collected. Missing data were imputed with multiple imputation prior to Kaplan-Meier, Log-rank, Accelerated Failure Time and Cox proportional-hazards models carried out to estimate the effect of Triac on survival. Trial emulation through case-matching was performed to minimize confounding and immortal-time bias. **Results:** We screened 540 male patients of whom 265 were selected (141 Triac-treated and 124 untreated). Exclusion was based on (i) being born before the diseases discovery in 2004 (n=182), (ii) limited data (n=62) or (iii) unknown genetic mutation (n=31). Median follow-up after diagnosis was 4.4 years [IQR=2.18.1] and we observed 27 deaths (6 treated vs 21 untreated). Triac-treated patients had a 3-times longer survival time ($\exp(\beta)=3.56$, 95%CI=0.00-2.54, p-value=< 0.05). **Conclusions:** In this international real-world cohort study, we showed that Triac treatment in patients with MCT8 deficiency was associated with a 3-times longer survival time. This corroborates previous findings indicating that Triac sustainably alleviated key features of thyrotoxicosis.

HYPERTHYROIDISM

1112316 - THE FCRN INHIBITOR, BATOCLIMAB, RAPIDLY NORMALIZES THYROID FUNCTION IN GRAVES HYPERTHYROIDISM: A PROOF-OF-CONCEPT STUDY

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Introduction: Thyrotropin receptor autoantibodies (TSH-R-Ab) cause Graves hyperthyroidism (GH) and its extrathyroidal manifestations. Batoclimab, a neonatal fragment crystallizable receptor inhibitor, reduces IgG levels, including TSH-R-Ab. **Objective:** To describe outcomes in batoclimab-treated patients with GH. **Methods:** This phase 2a, proof-of-concept, open-label, single-center study enrolled patients with serologically confirmed GH and elevated TSH-R-Ab. Patients who were hyperthyroid despite ≥ 12 weeks of therapy with moderate-to-high dose anti-thyroid drugs (ATD) received weekly subcutaneous batoclimab 680 mg for 12 weeks, then 340 mg for 12 weeks. **Results:** At the data cutoff, 25 patients completed Week 24 (n=23) or discontinued for non-treatment-related reasons (n=2). Eighty percent (20/25) had pre-existing Graves orbitopathy. Batoclimab was associated with marked reductions in free serum T3 (FT3) and T4 (FT4) by Week 1 (nominal p<0.0001 for both analytes). By Week 2, 15/25 (60%) patients achieved FT3 and FT4 levels $\leq$ upper limit of normal (ULN) without an increase in ATD; this increased to 19/25 (76%) patients at Week 12, including 14/25 (56%) who were off ATD, and to 17/25 (68%) patients at Week 24, including 9/25 (36%) who were off ATD. Median reductions in daily ATD dose were 75% and 100% at Weeks 6 and 12, respectively. Marked reductions from baseline in TSH-R-Ab serum concentration were observed as early as 1 week following initiation of batoclimab (nominal p<0.0001). Mean TSH serum levels improved from baseline (0.008 mIU/L) to Week 24 (0.324 mIU/L). Reductions from baseline in thyroid peroxidase antibody serum levels, thyroid volume, proptosis, lid aperture, and improvements in Thyroid-Related Patient-Reported Outcome-39 assessments (anxiety, daily living) were observed. Adverse events were mild-to-moderate, with no new safety signals. **Conclusions:** Batoclimab rapidly normalized FT3 and FT4, with >50% of patients achieving FT3 and FT4 $\leq$ ULN and discontinuing ATD by Week 12. Strong decreases in TSH-R-Ab levels with amelioration of extrathyroidal signs were noted.

1112518 - THE IMPACT OF TRAB ON GUT MICROBIOTA AND NON-TARGET METABOLITES IN HUMAN AND MURINE MODEL WITH THYROID EYE DISEASE

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Introduction: Thyroid eye disease (TED) is the most common and serious manifestation of GD. **Objective:** This study aims to explore the key differential microbial species and their associated metabolites, investigating their potential mechanisms in the pathophysiology of TED. **Methods:** A prospective study was conducted within a population cohort to explore the changes in gut microbiota and non-target metabolites in patients with TRAB-mediated GD/TED. To further investigate the correlation, as well as the potential underlying mechanisms, murine models of GD/TED were established. The gut microbiota, non-target metabolites, thyroid characteristics, intractable features, peripheral blood immunity, cellular immunity, and intestinal mucosal barrier in the TED mouse model were systematically assessed. These results lay a strong foundation for further investigation into whether these correlations suggest causal relationships. **Results:** In the population study, TED patients exhibited a higher abundance of *Clostridium innocuum* and a lower abundance of *Akkermansia muciniphila* in their gut microbiota compared to the healthy control group. Correlation analysis revealed that *Clostridium innocuum* was positively correlated with oleamide and TRAB, while negatively correlated with inosine. Murine model of GD/TED elevated TRAB and TT4 levels, diffuse thyroid enlargement, and pathological changes. TED murine model exhibited consistent changes in *Clostridium innocuum* and *Akkermansia muciniphila*, which mirrored the alterations observed in human samples and showed significant differences compared to the control group. Furthermore, an imbalance in gut microbiota may disrupt T cell subset equilibrium through metabolite influence, correlating with serum TT4 and TRAB levels, as well as orbital brown adipose tissue content (BAT%). Notably, intestinal mucosal damage, particularly the activation of NLRP3 inflammasomes, plays a crucial role in this process in TED patients. **Conclusions:** These results strongly suggest that the gut microbiota plays a key role in TRAB-induced disease. These findings suggest a potential link between gut microbiota, colonic mucosal barrier dysfunction, and the immune-inflammatory response in TED.

HYPOTHYROIDISM

1112368 - ASSOCIATION BETWEEN SUBCLINICAL HYPOTHYROIDISM AND CHRONIC KIDNEY DISEASE INCIDENCE: INSIGHTS FROM ELSA-BRASIL

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Introduction: Thyroid dysfunction has been associated with declining renal function; however, evidence regarding subclinical thyroid dysfunction remains conflicting, with most data derived from cross-sectional studies. **Objectives:** We aimed to evaluate the association between subclinical hypothyroidism (SCH) and the development of chronic kidney disease (CKD) over an eight-year follow-up in a prospective cohort. **Methods:** Participants without CKD at baseline and with either normal thyroid function or subclinical thyroid dysfunction were included from the ELSA-Brasil. Individuals on medications affecting thyroid function were excluded. CKD was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m² (using the CKD-Epi equation) and/or an albumin-to-creatinine ratio > 30 mg/g. Poisson regression models with robust variance were applied to evaluate associations, calculating incidence rate ratios (IRR) and 95% confidence intervals (CI) in univariate and multivariable analyses adjusting for demographic and CKD-related risk factors. **Results:** A total of 10,177 participants (mean age: 50.91 years) were analyzed, including 9,231 with euthyroidism and 889 with SCH. After eight years, baseline SCH was not significantly associated with a higher incidence of CKD compared to euthyroidism [IRR, 1.18 (0.991.39); p=0.053]. This finding persisted after adjustments for sex, age, and confounders [IRR, 1.17 (0.941.31); p=0.189]. However, in a sex-specific subanalysis, baseline SCH was associated with an increased risk of CKD in women [IRR, 1.31 (1.311.62); p=0.011], even after multivariable adjustments. **Conclusion:** In the general population, SCH was not associated with CKD incidence or deterioration of renal function over eight years. However, a significant association was observed in women, warranting further investigation into sex-specific mechanisms linking thyroid dysfunction and CKD.

1112255 - NEWBORNS THYROGLOBULIN IS A MORE SENSITIVE BIOMARKER FOR MONITORING IODINE STATUS THAN NEONATAL TSH

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Introduction: Thyroglobulin (Tg) is a promising indicator of iodine status in pregnant women and children. **Objective:** This study aimed to evaluate a new method for monitoring iodine status using newborns Tg dried blood spot (DBS). **Methods:** We recruited pregnant women in the third trimester of pregnancy at the Erasme Hospital in Brussels, Belgium. Thyroglobulin concentrations, urine iodine concentrations (UIC), and creatinine concentrations were determined. Cord blood samples were collected to measure cord plasma Tg (Tg-CP), cord Tg in DBS (TgC-DBS), and cord TSH (TSH C-DBS). After delivery, a urine sample from the newborn was collected during the 2nd to 5th day of life, and three additional drops of blood were collected during the routine neonatal screening Tg (TgNS-DBS). **Results:** Median UIC/Cr in pregnant women was 141 (85-210) µg/g, and median UIC/Cr in newborns was 143 (96-210) µg/g (n=382). The median Tg-CP was 31 (21-47) µg/L, median TgC-DBS was 30 (19-46) µg/L (n = 387), median TgNS-DBS was 31.8 (21-50) µg/L (n=355). The difference between the groups was not significant. Neonatal UIC/Cr was significantly and negatively associated with Tg-CP (r=-0.21, p<0.001) and TgC-DBS (r= -0.17, p<0.01) but not with TSH C-DBS (r=0.126, p=0.054). **Conclusion:** Our findings indicate that thyroglobulin concentrations in cord blood correlate significantly and negatively with newborn UIC/Cr but do not correlate with neonatal TSH. These results suggest that newborns Tg is more sensitive than TSH to variations in iodine status.

NONTHYROIDAL ILLNESS SYNDROME (NTIS)

1112269 - INDUCTION OF TYPE 2 AND 3 DEIODINASES IN MUSCLE STEM CELLS OF CRITICALLY ILL PATIENTS: UNVEILING THE IMPLICATIONS FOR HYPERGLYCEMIA AND NON-THYROIDAL ILLNESS SYNDROME

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Introduction: The dysregulation of deiodinases 2 and 3 (D2 and D3) impacts thyroid hormone metabolism in non-thyroidal illness syndrome (NTIS). Alterations in the function of these enzymes in muscle may influence the progression of the syndrome. Moreover, alterations in thyroid hormone metabolism can impact critical patients glycemic control. **Methods:** We collected blood and muscle biopsies from 24 patients admitted to the intensive care unit to investigate these variations. Blood cells were separated, and carbonyl content and GSH levels in muscle were used as redox status indicators. D2 and D3 expression was assessed through in situ hybridization (RNAscope) and real-time PCR. Glucose receptors and transporters were also evaluated. **Results:** Patients were categorized based on T3 levels (< 35 ng/dL, 35-60 ng/dL, and > 60 ng/dL). Carbonyl formation significantly increased in all patients on the first day of ICU admission (P < 0.0001), while GSH levels decreased (P < 0.001). Muscle D2 and D3 expression increased fivefold (P = 0.002). Significant differences in enzyme expression were observed between patients with T3 < 35 ng/dL and 35-60 ng/dL, compared to those with T3 > 60 ng/dL. The presence of D2 and D3 in muscle tissue was confirmed by RNAscope and colocalized with MYOD or PAX7 positive cells. Interestingly, glucose transporter GLUT4 also colocalizes in the muscle stem cells with dio3. **Conclusion:** Critical illness induces D2 and D3 expression in muscle; both enzymes are localized mainly in the stem cells regardless of the underlying condition, contributing to decreased circulating T3 levels, augmented glucose, and worsening sarcopenia.

THYROID AND PEDIATRIC DISEASE

1112453 - DISEASE PRESENTATION AND DISTINCT GENETIC PROFILES ARE RELATED TO GENDER AND PUBERTY COMPLETION IN PEDIATRIC DIFFERENTIATED THYROID CARCINOMA

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Introduction: Pediatric differentiated thyroid carcinoma (DTC) tends to behave more aggressively. The tumor's molecular landscape and the status of puberty completion appear to be associated with clinical presentations and responses to treatment. **Objectives:** This study aimed to evaluate the association between gender and tumor molecular profile with puberty status, disease presentation, and treatment response at the end of follow-up. **Methods:** 97 patients under the age of 19 diagnosed with DTC followed at a reference oncology center were assessed for gender, clinical presentation, puberty completion status, and treatment response at the end of the follow-up. The tumor molecular profile was evaluated using next-generation sequencing (NGS) and associated with the collected data. **Results:** There was a significant difference in the proportion of males and females diagnosed with DTC based on age at diagnosis ($p < 0.001$) and puberty completion ($p < 0.001$). Patients who had completed puberty showed less aggressive disease, evidenced by a lower incidence of distant metastases (36% vs. 10%, $p = 0.003$) and a reduced risk of recurrence ($p = 0.01$). The tumor molecular characteristics were associated with the status of puberty completion and disease aggressiveness. NTRK and AGK::BRAF fusions were more common in patients who had not completed puberty, whereas RET/PTC and BRAF_V600E mutations were more prevalent among those who had completed puberty. At the end of the follow-up, 36% of patients who had not completed puberty and 23% of those who had completed puberty demonstrated incomplete structural responses. **Conclusion:** Distinct molecular genetic profiles were observed based on pubertal status in pediatric DTC patients. This differentiation may explain the variations in clinical presentations and treatment responses. Further studies are needed to understand the mechanisms by which these genetic alterations influence therapy responses and the role of gender in this context.

THYROID AND PREGNANCY

1112344 - ASSOCIATION OF PERCHLORATE, THIOCYANATE, AND NITRATE WITH GESTATIONAL THYROID FUNCTION AND CHILD NEURODEVELOPMENT

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Introduction: Iodine is necessary for the synthesis of thyroid hormones that are essential to normal offspring neurodevelopment. The well-known inhibitors of sodium/iodide symporter (NIS), perchlorate, thiocyanate, and nitrate, can competitively inhibit the thyroidal uptake of iodine. Therefore, exposure to these NIS inhibitors during pregnancy may lower gestational thyroid hormone availability, subsequently affecting child brain development. **Objectives:** To investigate the association of maternal exposure to NIS inhibitors with gestational thyroid function as well as child IQ and brain morphology. **Methods:** We utilized data from Generation R, a population-based prospective birth cohort (Rotterdam, the Netherlands). We included participants with measurements of urinary perchlorate, thiocyanate, and nitrate, including 1,221 pregnant women with data on maternal thyroid function, 1,255 mother-child pairs with data on child IQ acquired at 5 and/or 13 years of age, and 830 mother-child pairs with data on child magnetic resonance imaging (MRI) acquired at 9 and/or 13 years of age. We studied the association of NIS inhibitors with maternal thyroid function, child IQ, and child brain MRI using multivariable linear regression models and weighted quantile sum regression. **Results:** Exposure to perchlorate was not associated with maternal thyroid function tests. Higher exposure to thiocyanate was associated with higher thyroid stimulating hormone (TSH) concentrations (beta: 0.03, 95% CI: 0.01, 0.06) and lower free thyroxine (FT4) concentrations (beta: -0.16, 95% CI: -0.31, -0.003). Higher exposure to nitrate was associated with higher TSH concentrations (beta: 0.04, 95% CI: 0.002, 0.08). We identified that the mixture of perchlorate, thiocyanate, and nitrate was negatively associated with FT4 concentrations (beta: -0.26, 95% CI: -0.46, -0.07). Maternal exposure to perchlorate, thiocyanate, or nitrate was not associated with child IQ or brain morphology. **Conclusion:** Higher maternal exposure to NIS inhibitors may interfere with the thyroid system during pregnancy. No association of NIS inhibitors with child neurodevelopment was observed.

THYROID AND PREGNANCY

1112606 - CHARACTERIZATION AND IMPACT OF THE GESTATIONAL HYPOTHYROXINEMIC ENVIRONMENT ON MACROPHAGE POLARIZATION AND FUNCTION

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Introduction: Maternal hypothyroxinemia is characterized by a hormone tetraiodothyronine (T4) deficiency with normal levels of triiodothyronine (T3) and thyroid-stimulating hormone (TSH). More recent evidence indicates that affects the immune system function of the fetus and offspring. **Objective:** This study identified changes in protein expression in serum from pregnant women with hypothyroxinemia compared to sera from euthyroid pregnant women during the first trimester of pregnancy. Furthermore, we evaluated the effect of sera on the macrophages polarization and function, one of the main cells located at the maternal-fetal interface. **Methods:** Serum samples were obtained from pregnant women over 18 years of age during the first trimester of pregnancy (Scientific and Ethical Committee of the Health Service, Resolution 17-12-88). Serum proteins were depleted, prepared, and analyzed using mass spectrometry. Moreover, THP-1 cells were differentiated into macrophages to evaluate the impact of sera from hypothyroxinemic pregnant women on macrophage polarization by qPCR and FACS, and the reactive oxygen species (ROS) production by FACS, with respect to sera from euthyroid pregnant women. **Results:** 230 proteins were identified by mass spectroscopy, but only 64 proteins were significantly expressed in serum samples from hypothyroxinemic pregnant women, compared to sera from euthyroid pregnant women. Of the latter, 38 and 26 proteins were overexpressed or underexpressed, respectively, in hypothyroxinemic sera compared to euthyroid sera. Moreover, macrophages treated with hypothyroxinemic sera were polarized towards an M1 phenotype and generated more ROS, compared to macrophages treated with euthyroid sera. **Conclusions:** Sera from hypothyroxinemic pregnant women present differential protein expression with respect to euthyroid sera. Macrophages treated with hypothyroxinemic sera polarize to a pro-inflammatory phenotype and produce more ROS, causing a sustained inflammatory state that could be involved in the negative impact that gestational hypothyroxinemia has on the fetus and the offspring development.

THYROID AND PREGNANCY

1112577 - TOTAL TRIIODOTHYRONINE AND TOTAL THYROXINE LEVELS ARE POSITIVELY ASSOCIATED WITH PREGNANCY LOSS OF CHROMOSOME NORMAL (EUPLOID) FETUSES

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Introduction: Approximately 55% of pregnancy losses are due to lethal chromosome abnormalities (aneuploid losses), whereas fetuses with a normal number of chromosomes (euploid) are potentially viable. Pregnancy loss of a euploid fetus could be due to maternal comorbidity. **Objectives:** We aimed to investigate if thyroid function and autoimmunity were associated with fetal chromosome status in pregnancy loss. **Methods:** Prospective cohort study of women experiencing pregnancy loss at three Danish hospitals (2020-2024). Blood collected at the time of pregnancy loss was analyzed for thyroid stimulating hormones (TSH), free and total thyroxine (FT4, TT4), total triiodothyronine (TT3), human chorionic gonadotropin (hCG), thyroid peroxidase and thyroglobulin antibodies (TPOAb, TgAb). Antibody positivity: > 60 kIU/L. Fetal chromosome status was determined by cell-free fetal DNA or fetal tissue sequencing to detect aneuploidy. Logistic regression covariates: age, body mass index, gestational week, and thyroid medication use. **Results:** Among 2,018 pregnancy losses, 1,031 (51%) were euploid. The risk of euploid pregnancy loss was not associated with TSH (adjusted odds ratio (aOR) 0.9, 95% confidence interval (CI) 0.8; 1.1), FT4 (aOR 1.0, 95%CI 1.0; 1.0), TPOAb positivity (aOR 0.99, 95%CI 0.68; 1.43), nor TgAb positivity (aOR 0.96, 95%CI 0.66; 1.41). However, TT3 (aOR 2.0, 95%CI 1.5; 2.6) and TT4 (aOR 1.09, 95%CI 1.05; 1.13) were positively associated with increased euploidy risk, and this persisted after adjusting for TSH, TPOAb, TgAb, and hCG (TT3 aOR 2.7, 95%CI 1.44; 5.33; TT4 aOR 1.16, 95%CI 1.06; 1.27). The proportion of euploid pregnancy losses were higher in women with TT3 > 2.6 nmol/L (laboratory cut-off) vs TT3 ≤ 2.6 nmol/L (n=61/85, 71.8% vs. n=470/1,521 48.6%, p=5.4x10⁻⁵) and TT4 > 140 nmol/L (laboratory cut-off) vs ≤ 140 nmol/L (n=248/425 58.4% vs. n=552/1,180 46.8%, p=5.5x10⁻⁵). **Conclusion:** Higher maternal TT3 and TT4 levels are associated with euploid pregnancy loss. We hypothesize that gestational thyrotoxicosis is a lethal risk factor to potentially viable fetuses. Future studies should explore causality.

THYROID AND REPRODUCTION

1112417 - IMPACT OF ENDOCRINE DISRUPTORS ON THYROID FUNCTION AND REPRODUCTIVE HEALTH: INSIGHTS INTO THE HYPOTHALAMIC-PITUITARY-THYROID AXIS

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Introduction: Endocrine disruptors (EDs) are environmental chemicals that interfere with hormonal systems, particularly the hypothalamic-pituitary-thyroid (HPT) axis. Alterations in this axis can lead to thyroid dysfunction, contributing to infertility, pregnancy complications, and impaired fetal development. This study investigates the relationship between chronic ED exposure, thyroid dysfunction, and reproductive health outcomes. **Objective:** To evaluate the impact of EDs on thyroid function and their association with reproductive and gestational outcomes in chronically exposed women. **Methods:** This prospective study involved 200 women aged 1840 years living in regions of high ED exposure. **Biological Sampling:** EDs (bisphenol A, phthalates, and pesticides) were quantified via mass spectrometry in blood and urine samples. Thyroid hormones (TSH, free T3, free T4) and autoantibodies (anti-TPO, anti-TG) were measured using immunoassays. **Reproductive Assessment:** Ovarian reserve was assessed through ultrasonography and anti-Müllerian hormone (AMH) levels. Reproductive histories and pregnancy outcomes (e.g., preeclampsia, miscarriage) were recorded. **Statistical Analysis:** Correlations between ED exposure, thyroid dysfunction, and reproductive outcomes were analyzed using Pearson's correlation and logistic regression. **Results:** Elevated ED levels were found in 65% of participants, exceeding WHO safety thresholds. Organophosphate exposure was significantly associated with increased TSH levels (mean: 4.8 mIU/L, $p < 0.01$). Subclinical hypothyroidism was identified in 38%, with anti-TPO positivity in 22%. Thyroid dysfunction correlated with a 2.5-fold increase in unexplained infertility ($p < 0.05$) and 41% of pregnancies showed adverse outcomes. **Conclusion:** Preliminary findings suggest increased neurodevelopmental delays in children born to exposed mothers.

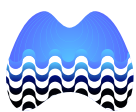
THYROID AUTOIMMUNITY

1112232 - DIFFERENT INHIBITING MECHANISMS OF AN ANTI-IGF-1R SMALL MOLECULE VERSUS AN ANTI-IGF-1R MONOCLONAL ANTIBODY

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Introduction: The insulin-like growth factor 1 receptor (IGF-1R) and the thyrotropin receptor (TSH-R), co-expressed on orbital fibroblasts, mediate thyroid eye disease (TED) pathophysiology. **Objectives:** This in-vitro study compared the inhibitory actions on cell proliferation and apoptosis induction of an anti-IGF-1R small molecule (Linsitinib) that targets the intracellular domain with those of an anti-IGF-1R monoclonal antibody (Teprotumumab), which binds to the extracellular subunit. **Methods:** The IGF-1R-expressing cell line NCI-H295R (ATCC, USA) and a TSH-R overexpressing CHO cell line (QuidelOrtho, USA) were incubated with five increasing concentrations of Linsitinib (Sling Therapeutics, USA), or Teprotumumab (BioVision, USA). Cell proliferation was microscopically and functionally (tetrazolium absorbance, GloMax, USA) tested; while apoptosis was evaluated by the caspase-3/7 activity. **Results:** Linsitinib strongly inhibited the proliferation of both cell lines at concentrations of 15,806.25 ng/mL (IGF-1R cells -63%, $P=0.0029$, TSH-R cells -63%, $P=0.0026$), 31,612.5 ng/mL (IGF-1R cells -71%, TSH-R cells -67%, $P < 0.0001$), and at 63,225 ng/mL (IGF-1R cells -72%, TSH-R cells -79%, $P < 0.0001$). Linsitinib exclusively induced apoptosis in both cell lines, confirmed morphologically and with increased caspase-3/7 activity at concentrations of 15,806.25 ng/mL (+3.5-fold in IGF-1R and TSH-R cells, $P=0.0029$), 31,612.5 ng/mL (+6.0-fold in IGF-1R and +5.3-fold in TSH-R cells, $P < 0.0001$) and 63,225 ng/mL (+6.3-fold in IGF-1R and +5.5-fold in TSH-R cells, $P < 0.0001$). On Linsitinib, cell proliferation negatively correlated with apoptosis in both IGF-1R ($r = -0.9429$, $P=0.0167$) and TSH-R cell lines ($r = -1.00$, $P=0.0028$). Compared to Teprotumumab, Linsitinib inhibited markedly more the proliferation of IGF-1R cells at all concentrations ($P=0.0002$). Teprotumumab showed no significant inhibition, with proliferation ranging from -12 to +11% relative to control in IGF-1R cells and -12 to +23% in TSH-R cells. **Conclusions:** Linsitinib by targeting the intracellular ATP-binding site inhibits the IGF-1R markedly more than Teprotumumab by targeting the extracellular cysteine-rich domain. Linsitinib is a promising therapeutical option for TED.



1113894 - EFFICACY AND SAFETY OF VELIGROTUG (VRDN-001), A FULL ANTAGONIST HUMANIZED MONOCLONAL ANTIBODY TO IGF-1 RECEPTOR, IN CHRONIC THYROID EYE DISEASE (TED): THRIVE-2 PHASE 3 RESULTS AT 15 WEEKS

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Introduction: Significant unmet needs remain for chronic TED. Veligrotug is being assessed in two ongoing phase 3 RCTs, THRIVE (active TED) and THRIVE-2 (chronic TED). **Objectives:** Here we present efficacy and safety data of veligrotug vs placebo at 15 weeks from THRIVE-2 (NCT06021054). **Methods:** Adults with moderate-to-severe chronic TED (onset >15 months, proptosis ≥ 3 mm, and any clinical activity score [CAS] ≥ 3) were randomized to 5 IV infusions Q3W of either 10 mg/kg veligrotug or placebo. Efficacy outcomes and treatment-emergent adverse events (AEs) were assessed through 15 weeks (primary timepoint). **Results:** 188 patients received veligrotug (n=125) or placebo (n=63). Baseline values for veligrotug vs placebo were balanced, including diplopia in 52% vs 59% and CAS ≥ 3 in 57% vs 52%. At 15 weeks, veligrotug vs placebo proptosis responder rate (PRR; ≥ 2 -mm reduction vs baseline by Hertel exophthalmometry) was 56% vs 8% ($p < 0.0001$), with a mean reduction of 2.34 mm vs 0.46 mm ($p < 0.0001$). In patients reporting diplopia on the Gorman subjective diplopia scale at baseline, improvement was reported in 56% vs 25% ($p = 0.0006$) and complete resolution in 32% vs 14% ($p = 0.0152$). Exploratory analyses were nominally significant for treatment effect as early as 3 weeks in overall population and for achievement of CAS 0/1 at 15 weeks in patients with CAS ≥ 3 at baseline (54% vs 24%; $p = 0.0060$). Most AEs were mild; most common was muscle spasms (36% vs 6%). Hearing impairment AEs occurred in 13% vs 3% and serious AEs in 2% vs 3% (1 treatment-related/group). **Conclusion:** THRIVE-2, assessing 5 IV infusions of veligrotug vs placebo, is the first RCT of IGF-1R inhibition in chronic TED to show statistically significant improvement not only in proptosis but also in diplopia, with a generally well-tolerated safety profile. Follow-up through 52 weeks is ongoing.

THYROID AUTOIMMUNITY

1112483 - IMPACT OF MICROBIOTA-NLRP3 INFLAMMASOME INTERACTIONS ON PROGRESSION OF AUTOIMMUNE THYROIDITIS

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Introduction: Emerging evidence highlights the gut microbiotas role in autoimmune thyroiditis (AIT) pathogenesis via the microbiota-gut-thyroid axis. It is noteworthy that the NLRP3 inflammasome may be at the crossroads of the thyroid-gut-microbiota axis. **Objectives:** The aim of our study is to investigate the role of crosstalk between NLRP3 and the gut microbiota in the development of AIT. **Methods:** We establish a spontaneously developed thyroiditis mouse model using NOD.H-2h4 mice as well as NLRP3 knockout mouse (KO) models. We use 16SrRNA sequence and fecal microbiota transplantation (FMT) in antibiotic-treated mice to investigate the role of microbiota in the pathogenesis of AIT. We detect short-chain fatty acid in the intestine by GC-MS. HE staining of the thyroid gland and serum TgAb concentrations were used to prove the AIT model. **Results:** The composition of the gut microbiota was significantly different between NLRP3 KO mice and wild-type (WT) NOD.H-2h4 mice, suggesting that NLRP3 deficiency counteracts AIT-induced dysbiosis. The relative abundance of *Lactobacillus reuteri* is significantly increased in NLRP3 KO mice compared with WT mice, which may be responsible for the pathogenesis of AIT. The concentration of butyric acid is significantly decreased in AIT group than that in control and NLRP3 KO groups. With a strengthened gut barrier and decreased inflammation, NLRP3 KO mice showed lower TgAb and less lymphocyte infiltration in thyroid. Here we found that AIT could be alleviated by *Lactobacillus reuteri* supplementation or by transferring from NLRP3 KO donor mice to WT recipient mice via FMT. Moreover, we found *Lactobacillus reuteri* supplementation and transfer from NLRP3 KO mice via FMT could protect against Treg/Th17 imbalance in AIT pathogenesis. **Conclusion:** Our results identified the bidirectional modulation between the gut microbiota and NLRP3 in the progression of AIT.

THYROID AUTOIMMUNITY

1112615 - MECHANISMS IN THYROID EYE DISEASE (TED) – TSH RECEPTOR ANTIBODIES ENHANCE THE EXPRESSION OF BOTH TSH RECEPTORS AND IGF-1 RECEPTORS IN FIBROBLASTS

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Introduction: It has long been known that TSH signaling is enhanced by IGF-1 in fibroblasts which is now thought to help explain the role of stimulating TSH receptor (TSHR) antibodies acting as TSH agonists in TED. **Methods:** We have developed a new approach to assessing TSHR expression using a monoclonal antibody to the TSHR hinge region (MC-1) which is not affected by the binding of TSH or TSHR antibodies. Molecular Dynamic simulations showed clear access to the TSH and antibody binding sites in the leucine rich repeat region of the TSHR ectodomain in the presence of MC-1 binding thus giving us a way for the first time to measure TSHR expression in the presence of ligand binding. **Results:** Using this approach with 3T3-L1 fibroblasts we found that TSH ligand induced a dose dependent increase in binding at the TSHR with a 3-fold increase at 100uU/mL TSH as measured by flow cytometry. Furthermore, parallel assessments of IGF-1 receptor (IGF-1R) expression also showed a dose dependent 2-fold increase. Similar studies with a monoclonal human stimulating antibody (M22) demonstrated a 3-fold increase in TSHR expression and up to 4-fold increases in IGF-1R with peak expression at 48 hours. These data could not be explained by cell proliferation or transcriptional changes as measured by digital PCR. However, further analysis of additional Molecular Dynamic simulations indicated that upon TSH binding there were a number of changes to the entire TSHR structure including the linker region and increased curvature of transmembrane helix 3 and altered angles between helices 7 and 8. **Conclusion:** These data provide further evidence for the role of TSH receptor antibodies in TED by their action on both the TSHR and the IGF-1R in fibroblasts where they induce structural changes which most likely result in greater access to the receptor binding sites.

THYROID AUTOIMMUNITY

1114004 - TOCILIZUMAB VS METHYLPREDNISOLONE IN MODERATE-SEVERE GRAVES' ORBITOPATHY: RESULTS OF AN ITALIAN MULTICENTER CLINICAL TRIAL

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Introduction: In this trial (NCT04876534) we compared the efficacy of Tocilizumab (TCZ) to methylprednisolone (MP). **Objective:** Improvement of Graves' Orbitopathy (GO) (CAS - 3 points, primary endpoint), proptosis (>2 mm), quality of life, diplopia and safety. **Methods:** 56 patients with active GO (<9 months) were randomized to receive TCZ (n. 28) or MP (n.28). TCZ was administered IV in 4 monthly doses (8 mg/Kg), while MP in 12 weekly doses (500 mg for 6 weeks, then 250 mg). **Results:** Mean age, sex distribution and thyroid treatment were not different in the 2 groups. Mean baseline CAS was 4.4 (±1.3) and 4.4 (±0.8), and proptosis in the study eye (more severe) was 25.2 and 25.5 mm, for patients randomized to TCZ and MP, respectively. In the intention to treat analysis population, CAS decreased in 75% and 79% of patients at 12 and 24 weeks, respectively, with TCZ treatment compared to 36% and 29% with MP (P<0.003). At 36 and 48 weeks, 75% and 86% of patients after TCZ, respectively, remained inactive (P<0.003). Proptosis decreased ≥2 mm in 61% of patients after TCZ, compared to 29% after MP at 24 weeks (P<0.02). At 36 and 48 weeks proptosis responders were 57% and 61% after TCZ and 18% and 25% after MP, respectively (P<0.01). No SAE were reported, MP was discontinued in 2 patients due to allergic reaction. Quality of life (GO-QoL), improved after TCZ compared to MP (P<0.01) for both appearance and visual function. Diplopia improved in 56 and 57% of patients at 12 and 24 weeks, respectively, after TCZ and in 9 and 24% after MP (P<0.0005 and P<0.02, respectively). **Conclusion:** TCZ is more effective than MP in inactivating GO, but also improving proptosis (>60%), diplopia (>55%) and patients' QoL, at 48 months follow-up. Support by funds of Roche Italia to Fondazione IRCCS Cà Granda, Milan, Italy.

1112357 - TRAB DYNAMICS AND SURGICAL OUTCOMES IN GRAVES' ORBITOPATHY: A RETROSPECTIVE ANALYSIS

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Introduction: Thyroid-stimulating hormone receptor antibodies (TRAb) are central to the pathogenesis and clinical presentation of Graves orbitopathy (GO). Orbital surgery is typically reserved for inactive or low-TRAb states, except vision-threatening cases. However, our experience includes surgery in active GO with elevated TRAb when immunosuppressive therapies failed to achieve disease inactivity. **Objective:** This study aims to evaluate the TRAb dynamic and relationship with outcomes in GO surgery. **Methods:** A retrospective analysis was conducted on 32 patients undergoing orbital surgery from 2015 to 2022 at our institution. Indications included vision risk (n=6), resistance to corticosteroids (n=7), functional/aesthetic concerns (n=17), and ocular globe subluxation (n=1). Pre- and post-surgery TRAb levels (612 months) were assessed using RIA, EQLIA, and Q assays, with results expressed as multiples of the upper reference limit. Outcomes were analyzed based on median TRAb changes and CAS (clinical activity score). **Results:** Preoperative TRAb levels were positive in 88% of cases (active GO: 100%; inactive GO: 80%, p=NS). TRAb medians decreased postoperatively by 34%62%, irrespective of baseline CAS. TRAb reduction was greater in inactive GO (p=0.049). Notably, 72% of patients exhibited TRAb declines or seronegativity post-surgery, with no recorded TRAb increases. Surgery was successful in 72 % of active and 94.4 % of inactive OG (p:NS) and independent of baseline TRAb. All patients achieving TRAb seronegativity reported satisfactory surgical outcomes. **Conclusion:** Orbital surgery yielded favorable outcomes in both active and inactive GO, independent of baseline TRAb levels. Over 70% of patients experienced TRAb reductions or seronegativity, potentially reflecting decreased antigen or antibody production from tissue removal. These findings challenge the paradigm of high TRAb as a contraindication for surgery, warranting reconsideration of TRAbs role in surgical decision-making for GO.

THYROID CANCER BASIC

1112461 - ANAPLASTIC THYROID CANCER CELL-SECRETED TGFβ1 UPREGULATES THE EXPRESSION OF THE IMMUNE CHECKPOINT TIM3 IN HUMAN MONOCYTES

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Introduction: Anaplastic thyroid cancer (ATC) is the most aggressive thyroid cancer (TC) with poor prognosis and limited treatment options, highlighting the urgent need to identify novel molecular targets. Macrophages (Mo) are a major component of TC infiltrating cells, and their presence is associated with a poor prognosis. We recently identified the upregulation of the immune checkpoint TIM3 on M2-like Mo in vitro and of ATC xenografts in vivo. In addition, TGFβ1 promoted Mo polarization towards an M2-like phenotype. **Objective:** To investigate the role and clinical significance of TGFβ1 on TIM3 upregulation in Mo of TC. **Methods:** THP-1 cells (human monocytes) were treated with conditioned media from ATC 8505C cells (8505C- CM), recombinant TGFβ1 protein and/or the TGFβ receptor inhibitor (SB-431542). Peripheral blood mononuclear cells (PBMCs) were isolated from PTC patients (n=21) and healthy donors. TIM3 expression in tumors was analyzed using RT-qPCR and/or immunofluorescence (IF) in FFPE biopsies from TC patients. **Results:** TIM3 mRNA expression in THP-1 cells was promoted by treatment of 8505C-CM and TGFβ1, and the effect of 8505C-CM was inhibited by SB-431542. No significant difference in TIM3 expression was observed in PBMCs from PTC patients. Tumor-infiltrating Mo were detected in both PTC and ATC. Notably, TIM3 expression on Mo was observed in ATC. These findings are consistent with scRNA-seq data (database GSE193581) revealing a significant increase in CD68+CD163+ myeloid cells in both ATC and PTC. Additionally, while no significant difference was found, we observed an increased median number of CD68+CD163+TIM3+ myeloid cells in ATC than in normal thyroids. In line, ATC cells exhibited higher TGFβ1 expression, which had a tendency to positively correlate with TIM3 expression. **Conclusions:** Our results revealed an association between TIM3 and tumor-infiltrating Mo in a TGFβ1-rich microenvironment in ATC. Collectively, our findings identify novel therapeutic targets for the treatment of advanced TC.

1113896 - CELL INTRINSIC IFN-I SIGNATURE CORRELATES WITH DEDIFFERENTIATION OF THYROID CANCER AND DETERMINES ITS IMMUNOLOGICAL FATE

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Introduction: Anaplastic thyroid cancer (ATC) is an undifferentiated malignancy that can originate either de novo or through dedifferentiation of a previously more differentiated thyroid tumor such as papillary thyroid cancer (PTC). Mechanisms of dedifferentiation and how this affects anti-tumoral immune response remain poorly understood. **Objective:** This study aims to elucidate the role of the intrinsic Type I Interferon (IFN-I) signature in thyroid cancer dedifferentiation and its influence on tumor immunology, as well as to explore potential therapeutic strategies to restore anti-tumoral immunity. **Methods:** By isolating thyroid cells at sequential time points from an in situ mouse model harboring a thyrocyte-specific anaplastic lymphoma kinase mutation (AlkF1174L) and a TP53 knockout (Trp53^{-/-}), we found that the development of ATC occurred in a two-step process. In the first step, mutated cancer cells exhibit a low Type I Interferon (IFN-I) signature and maintain a cell-intrinsic PTC-like phenotype (IFN-I_{lo}). In a second step mutated cancer acquires a high IFN-I signature transitioning to an ATC-like phenotype (IFN-I_{hi}). **Results:** Immunologically, IFN-I_{lo} PTC-like cancer cells showed limited expression of PD-L1 and initiated an effective anti-tumor T cell response leading to rapid T cell dependent tumor control in an established subcutaneous mouse model. In contrast, IFN-I_{hi} ATC-like cancer cells upregulated PD-L1 expression, resulting in limited anti-tumoral immunity and accelerated tumor growth. Treatment of IFN-I_{hi} ATC-like cancers with an anti-PDL1 antibody or the Janus kinase (JAK) inhibitor Ruxolitinib revived the anti-tumoral immune response and reduced tumor progression. In conclusion, these findings suggest that an increase of the intrinsic IFN-I signature is a critical step in thyroid cancer dedifferentiation and immunological escape. **Conclusion:** Our findings identify the intrinsic IFN-I signature as a potential critical driver of thyroid cancer dedifferentiation and immune escape, offering new therapeutic targets to restore immune surveillance in aggressive thyroid cancers.

THYROID CANCER BASIC

1112267 - CHARACTERIZATION OF PATIENT DERIVED XENOGRAPTS (PDX) MOUSE MODELS AND THEIR RESPECTIVE CELL LINES FROM ANAPLASTIC THYROID CANCER (ATC)

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Introduction: Anaplastic thyroid cancer is an ultra-rare, most lethal, resistant and aggressive endocrine cancer. Due to the rarity of ATC and limitations of specimen availability and size, researchers are directing towards patient derived xenograft models. **Objectives:** The main objective was to Generate and characterise PDX mouse models and their derived cell lines from our ATC patients to confirm their ability to recapitulate disease heterogeneity. **Methods:** Fresh tumor biopsies were collected from patients enrolled in MATCH-R clinical trial (NCT02517892) or STING study (NCT04932525). Seven PDX models were established in NOD/SCID Gamma mice, five cell lines were derived from them. We analyzed the tissue architecture, IHC characterization and immune myeloid infiltrate of the PDX models. Whole exome sequencing and transcriptome analysis were done on each group "patient, PDX model, cell line" to examine their genomic/transcriptomic correlation. Cell lines were characterized in terms of morphology, proliferation, metabolic activity, drug sensitivity, MAPK/PI3K signaling pathways (2D) and Tumoroid formation (3D). **Results:** Our models of diverse mutational backgrounds (BRAFV600E, BRAFT/AKT, BRAF-AFAP1L2 fusion, NF1 and RET-NCOA4 fusion) recapitulated human tumor architecture, differentiation marker expressions and mouse myeloid infiltration mimicking macrophage infiltration in patients. Preliminary analysis of NGS showed high correlation/clustering between each PDX model and their corresponding patient. PDX cell lines show diverse morphologies (4 epidermoid & 1 fusiform) that resemble the cell morphologies of patients. These cell lines share similar proliferation and metabolic activation profiles but show different activation levels of MAPK and PI3K signaling. BRAF mutant cell lines show different sensitivity to clinically used drugs (ex. dabrafenib/trametinib) compared to others. We successfully set up Tumoroid formation of these cell lines and their characterization is ongoing. **Conclusion:** Our characterized models are promising tools that will permit significant advances in preclinical research for anaplastic thyroid cancer.

THYROID CANCER BASIC

1112581 - UNRAVELING THYROID CANCER ORIGINS: A CUTTING-EDGE HUMAN THYROID ORGANOID MODEL

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Introduction: Thyroid carcinomas, primarily those arising from follicular cells, represent the most prevalent endocrine malignancies, with Papillary Thyroid Carcinoma (PTC) constituting 85% of cases and the aggressive Anaplastic Thyroid Cancer (ATC) accounting for approximately 2%. A pivotal factor in the development of these cancers is the BRAFV600E mutation, present in 7080% of PTCs and 3050% of ATCs. Despite advancements in our understanding of advanced cancer biology, the initial triggers of thyroid carcinogenesis remain poorly understood. **Objective:** To bridge this knowledge gap, our research team has pioneered the creation of mature and functional human thyroid organoids derived from human embryonic stem cells. **Methods:** Utilizing these organoids, we have established a groundbreaking model to explore the early stages of tumorigenesis. By employing low-efficiency electroporation alongside an integrative PiggyBac vector system, we successfully introduced the BRAFV600E mutation into fully differentiated thyroid follicular cells. This innovative methodology replicates the early onset of PTC, wherein a limited number of cells begin to express the oncogenic mutation. **Results:** Our findings indicate that the expression of BRAFV600E initiates profound cellular de-differentiation, morphological changes, and altered migratory behaviors, shining a light on the dynamic interactions between normal thyrocytes and emerging cancerous cells. This model not only accurately reflects the initial phases of thyroid carcinogenesis but also underscores the critical role of BRAFV600E in undermining thyroid cell identity and functionality. **Conclusion:** By providing a robust experimental platform to dissect the molecular and cellular mechanisms driving the transformation of thyroid follicular cells, this system paves the way for the identification of early key drivers of thyroid cancer. It holds significant potential for unveiling critical pathways and innovative strategies to intervene prior to the progression of the disease.

THYROID CANCER CLINICAL

1112369 - CLINICAL AND PATHOLOGICAL CHARACTERISTICS OF DIFFERENTIATED THYROID CANCER ACCORDING TO DISTANT METASTASIS STATUS

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Introduction: Differentiated thyroid carcinomas (DTC) often have an indolent course. However, the diagnosis of distant metastases represents a critical turning point in a patients trajectory and is the most frequent cause of death related to thyroid cancer. **Objective:** This study aimed to compare the clinical and tumor characteristics of patients with and without distant metastasis from DTC. **Methods:** This study involved a cohort review of DTC patients aged ≥ 18 years at the time of diagnosis from two referral centers in southern Brazil. **Results:** Out of the 1,872 patients with DTC, 1,808 were included in this study. Among them, 154 (8%) patients had distant metastases. Compared to patients without distant metastases, those with distant metastases were more likely to be male (30.5% vs. 17.3%, $p < 0.01$), older at diagnosis (55.9 ± 15 years vs. 46.9 ± 13 years, $p < 0.01$), and present with a larger initial tumor ($4.0 [2.56.0]$ cm vs. $2.0 [1.03.0]$ cm, $p < 0.01$). Although the most prevalent histological type in our cohort was papillary thyroid cancer, patients with distant metastases had a higher prevalence of follicular cancer (25.3% vs. 6.6%, $p < 0.01$), oncocytic carcinoma (14.3% vs. 3.2%, $p < 0.01$), and poorly differentiated thyroid cancer (3.2% vs. 0%, $p < 0.01$). The most common site of metastasis was the lung (53.9%), followed by the bone (9.1%). Furthermore, 46 patients (29.9%) had both lung and bone metastases, whereas 11 patients (7.1%) presented with metastases at other sites associated with lung and/or bone metastases. **Conclusion:** Patients with distant metastases were more often male, older, and had larger tumors with aggressive histological subtypes (follicular, oncocytic, and poorly differentiated thyroid carcinomas). The lungs are the most common metastatic sites, frequently with bone involvement. Early detection and aggressive management may improve the care of high-risk DTC patients.

THYROID CANCER CLINICAL

1112616 - MOLECULAR PROFILE OF ADVANCED RADIOIODINE-REFRACTORY THYROID CANCER AND RESPONSE TO LENVATINIB TREATMENT

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Introduction: Tumor genetics can influence response to multikinase inhibitors in radioiodine-refractory thyroid cancer (RAIR-TC). **Objective:** We evaluated the association between molecular signature of RAIR-TC and response to lenvatinib. **Methods:** We evaluated 49 RAIR-TC patients (25 PTC, 14 FTC, 5 PDTC, 5 Oncocytic-TC) treated with first-line lenvatinib. We performed an NGS on primary/metastatic tumor tissue. Response to lenvatinib was assessed using RECIST. **Results:** TERT (57.1%), BRAF (38.7%), RAS (22.4%), TP53 (6.1%) were the most frequent mutations. Drivers co-occurred with TERT or TP53 in 44.9%. No driver mutations were found in 34.6%. Seven cases lacked driver mutations (only TERT in 6 and TP53 in 1). In 10/49 (20.4%), no mutations were found. Cases with ≥ 1 mutation had longer PFS than non-mutated [HR 0.34(0.16-0.75); $p=0.004$]. Group 1 (single driver mutation) showed longer PFS than Group 3 (no driver mutations) [HR 3.095(1.06-8.99); $p=0.04$] but no difference with Group 2 (driver + TERT or TP53) ($p=0.13$). Group 1 showed longer OS than Group 2 [HR 3.552 (1.17-10.79); $p=0.026$] and 3 [HR 3.516 (1.10-11.2); $p=0.034$]. In multivariate analysis, the absence of driver mutations and the coexistence of TERT/TP53 with a driver mutation were associated with worse OS, regardless of histotype. **Conclusions:** The RAIR-TC molecular profile is heterogeneous, with TERT being the most frequent mutation. Cases negative for any mutation and cases presenting both a driver and TERT mutation had poor prognosis and response to lenvatinib, while patients with a single driver mutation showed a better response to the drug.

THYROID CANCER CLINICAL

1112243 - REAL WORLD RESULTS OF IMMUNE CHECKPOINT BLOCKERS IN ANAPLASTIC THYROID CARCINOMA PATIENTS: INSIGHT FROM THE COMEDIMS COMPASSIONATE PROGRAM AT GUSTAVE ROUSSY

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1 - Gustave Roussy

Introduction: Anaplastic thyroid carcinoma (ATC) is an ultrarare undifferentiated cancer with a poor prognosis (median overall survival (OS) of 6-12 months). Immune checkpoint blockers (ICB) targeting PD-1/PD-L1 provide prolonged survival in a subset of patients. However, these drugs are off-label for ATC. *Comité du Médicament et des Dispositifs Médicaux* (COMEDIMS) has granted a compassionate access to ICB for Gustave Roussy ATC patients. **Methods:** Monocentric retrospective study of ATC patients diagnosed and treated at Gustave Roussy between December 2018 and January 2024. The main objective is to evaluate the results of compassionate immunotherapy in terms of OS. Baseline clinical, molecular, pathological and immunological characteristics as well as therapies were collected. **Results:** Fifty-two ATC patients were included: 50% female, median age 70 years, 78% ECOG PS 0-1, 15 stage IVB (29%) and 37 stage IVC at diagnosis (71%). The histology was pure, mixed and transformed ATC in 55, 31 and 14% of the cases and 83% had a PDL1 expression. The main drivers were RAS (29%), BRAF (29%) and NF1 (14%). Overall, patients received best supportive care (9.6%), chemoradiation (58%), dabrafenib + trametinib (29%) and ICB ($n=25$, 48%) including durvalumab ($n=5$), nivolumab ($n=15$) and pembrolizumab ($n=5$). ICB were administered at disease progression ($n=20$), at first-line ($n=2$) and as maintenance ($n=3$). ICB-treated patients had a lower neutrophil-to-lymphocyte ratio (median 3.73 vs 5.90, $p=0.048$), a more frequent expression of PD-L1 (96% vs 68%), a higher 18-months OS rate (44% vs 19%, $p=0.047$) and similar BRAF mutation frequency (32 vs 27%). Median OS in the whole cohort ($n=52$) was 10.3 months (95%CI 8.11) and 20.1 months (95%CI 10.5 NA) in patients who received ICB ($n=25$). **Conclusion:** ICB may provide clinical benefit in a compassionate access program for ATC patients. Further trials and approvals are required for these patients with dismal prognosis.

THYROID CANCER CLINICAL

1112237 - REAL-WORLD EXPERIENCE WITH LENVATINIB PLUS PEMBROLIZUMAB IN METASTATIC BRAF WILD-TYPE ANAPLASTIC THYROID CARCINOMA (BRAFWT-ATC)

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Introduction: BRAFWT-ATC has a poor prognosis due to limited effective therapies. The phase II ATLEP trial showed promising results with lenvatinib plus pembrolizumab (L/P). **Objective:** We aimed to confirm the real-world efficacy of L/P in BRAFWT-ATC. **Methods:** Retrospective study of patients with BRAFWT-ATC treated with first-line L/P between 11/2016-7/2024 off trial. Primary endpoints were overall response rate (ORR), progression-free survival (PFS) and overall survival (OS). **Results:** 36 patients were eligible for inclusion. Median age was 64 years (range, 41-84), all patients had distant metastases and 46% had suspicion of locoregional invasion including in the trachea, esophagus and/or jugular vein. Most common driver mutations were in RAS (39%) and NF1 (19%); 61% had co-occurring TP53 mutations, 50% TERT promoter mutations. In evaluated specimens: PD-L1 was > 1 in 96%, median TMB 2 mut/Mb (range, 0-16), and MSI-H in 7%. Previous therapies: surgery (69%), definitive radiation (33%), palliative radiation (28%) and therapeutic-dose cytotoxic chemotherapy (9%). Median initial dose of lenvatinib was 16 mg (range, 10-24 mg). Pembrolizumab dosing was 200 mg Q3 weeks in 64%, 400 mg Q6 weeks in remaining. Median time between lenvatinib and pembrolizumab initiation was 0.5 days (range, -105-61). With a median follow-up of 39 months (95%CI, 3.09-74.90), median OS was 8 months (95%CI, 5.24-10.77). In 29/36 patients evaluable for response, ORR was 45% and median PFS 7 months (95%CI, 4.82-9.18). Median duration of response was 16 months (95%CI, 3.22-28.78). Best overall response was confirmed CR in 3 (10%), confirmed PR in 9 (31%), unconfirmed PR in 1 (3%), SD in 10 (35%) and PD in 6 (21%). Safety profile was similar to previous studies. Five patients stopped pembrolizumab due to immune-related toxicity including pneumonitis (n=2) and colitis (n=3). Two patients discontinued lenvatinib due to esophageal and tracheal fistula formation. **Conclusion:** Our real-world experience of L/P in BRAFWT-ATC is comparable to the ATLEP trial, confirming safety and efficacy of this combination. A prospective clinical trial in the US is ongoing (NCT#04171622).

THYROID CANCER CLINICAL

1112402 - REDIFFERENTIATION OF REFRACTORY THYROID CANCER OF FOLLICULAR ORIGIN: NATIONAL FRENCH REAL LIFE EXPERIENCE

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Introduction: Targeted treatment to redifferentiate refractory differentiated thyroid cancers have shown promising results in the French phase 2 study MERAIODE. **Objective:** This study reports outcomes of the real-world application of the redifferentiation strategy. **Methods:** A multicenter, national, retrospective French study collected all cases not included in the MERAIODE trial and treated with targeted therapy followed by radioiodine treatment between 2018 and 2024. Patients continuing targeted treatment after radioiodine were excluded. **Results:** Seventy-four patients were recruited (median age at diagnosis 58.5 yo, 90% PTC, 7% PDTC, 3% FTC). Molecular drivers included BRAF mutations (N=67; 61 BRAFV600E), HRAS (N=3) and NRAS (N=4). Common metastatic sites were: lung (89%), neck lymph nodes (69%), mediastinum (35%) and bone (16%) with a median size of the largest lesion being 17,5 mm. Disease progression prior to redifferentiation occurred within 12 months for 33 patients (44.5%), in ≥12 months for 39 (53%) and unknown in 2. Dabrafenib and trametinib were prescribed in 73 cases and trametinib in one (48 weeks), followed by 150 mCi radioiodine after rhTSH. Two courses of redifferentiation treatment were performed in 11 patients and 3 courses in 3. Uptake was restored in 65 (88%) patients (in all lesions in 33, 51%). Among these patients 20 (31%) had partial response and 33 (51%) stable disease, while 10 (15%) had disease progression (unknown in 2). Median progression free survival (PFS) was longer in patients with restored uptake in all lesions (26 months) compared to those with uptake only in some lesions (15 months) and no uptake (8 months) (P=0.04). PFS improved compared to that observed before redifferentiation in 17 with restored uptake. Gender, age, histology, metastasis size, molecular driver were not predictive of redifferentiation efficacy. **Conclusion:** Redifferentiation can provide partial response and prolonged PFS when uptake is restored, predictive factors remain to be identified.

THYROID CANCER CLINICAL

1112439 - SURGERY FOR THYROID CANCER WITH OR WITHOUT AUTOFLUORESCENCE TO PREVENT HYPOPARATHYROIDISM - A RANDOMIZED, CONTROLLED TRIAL

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Introduction: Hypoparathyroidism (HypoPT) is the main chronic complication after thyroid cancer surgery, particularly in patients undergoing total thyroidectomy (TT) or completion hemithyroidectomy (cHT). While surgeon expertise is key to reducing risk, HypoPT remains significant, especially in advanced cases requiring central neck dissection. Near-infrared autofluorescence (NIRAF) imaging systems have been introduced as intraoperative tools to improve parathyroid gland (PG) identification, potentially reducing HypoPT risk. **Objective:** This study evaluates whether NIRAF-assisted surgery reduces HypoPT risk following TT or cHT for thyroid cancer. **Methods:** This randomized controlled trial (RCT) included thyroid cancer patients randomized 1:1 to surgery with or without a NIRAF camera system (EleVision IR, Medtronic). Three high-volume thyroid/parathyroid surgeons conducted all surgeries. The primary outcome was immediate post-operative HypoPT requiring active vitamin D treatment, defined by postoperative $\text{Ca}^{2+} < 1.00 \text{ mmol/L}$ or $\text{Ca}^{2+} \leq 1.18 \text{ mmol/L}$ with $\text{PTH} \leq 1.2 \text{ pmol/L}$. Secondary outcomes included permanent HypoPT (6 and 12 months), intraoperative PTH reduction, hospitalization length, and disease-free survival. The study aims to enroll 110 patients over two years (ClinicalTrials.gov Identifier: NCT06222606). **Results:** By 11 months, 65 patients were enrolled. Primary endpoint data were available for 57 patients (28 NIRAF, 29 control). Ten patients (17%) developed HypoPT: 7/28 (25%) in the NIRAF group vs. 3/29 (10%) in controls (risk ratio 2.4, 95% CI: 0.78.4, $p=0.15$). Intraoperative PTH reduction and hospitalization length were similar between groups. **Conclusion:** Preliminary findings suggest NIRAF does not reduce HypoPT risk in high-volume settings. Low enrollment and potential confounder imbalance limit conclusions. Final results are expected by June 2025.

THYROID CANCER CLINICAL

1112557 - THE ROLE OF ADJUVANT VOLUMETRIC MODULATED ARC RADIOTHERAPY (VMAT) IN THE TREATMENT OF LOCALLY ADVANCED DIFFERENTIATED THYROID CANCER: A SINGLE INSTITUTION EXPERIENCE

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Introduction: The use of adjuvant external beam radiotherapy (EBRT) in the management of locally advanced differentiated thyroid cancer (DTC) is debated. **Objective:** This study aims to evaluate the efficacy of EBRT with volumetric modulated arc radiotherapy (VMAT) in improving locoregional relapse-free survival after surgery and radioiodine therapy (RAI). Secondary objective was to assess the tolerability of the adjuvant treatment. **Methods:** This monocentric, retrospective study included patients with locally advanced DTC, positive resection margins (R1) or lymph node metastases with extra-nodal extension who had undergone total thyroidectomy followed by RAI. Patients identified, although homogenous in terms of risk factors, followed two distinct therapeutic strategies: those who received only RAI after surgery and those who, after RAI, underwent adjuvant EBRT. Outcomes between the two groups were compared. **Results:** 25 patients were included in the study, 10 who received EBRT and 15 who did not. None of the patients in the EBRT group experienced locoregional recurrence, compared to 60% in the non-EBRT group. Comparison of the survival curves showed a statistically significant difference between the groups ($p=0.043$). Additionally, no severe (grade 3 or higher) treatment-related adverse effects were reported in the EBRT group, indicating good tolerability. Distant Disease-Free Survival (DDFS) was similar between the two groups, suggesting that the addition of EBRT did not impact the control of distant disease. **Conclusions:** Adjuvant EBRT using VMAT improves locoregional control in patients with locally advanced DTC without adding significant toxicity. These findings support the integration of EBRT into treatment protocols for selected high-risk patients to minimize the risk of locoregional relapse, thereby potentially reducing the need for repeated surgeries and improving overall patient outcomes. Further studies are needed to confirm these results and to evaluate the long-term impact of EBRT on survival and quality of life.

THYROID CANCER CLINICAL

1112244 - THE SIGNIFICANCE OF APOPTOSIS DYSREGULATION IN CLINICAL MANAGEMENT OF PAPILLARY THYROID CANCER: IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS

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Introduction: Dysregulations in apoptosis in papillary thyroid cancer (PTC) may significantly impact treatment outcomes. Basic research indicates disturbances in apoptosis activation pathways in PTC, underscoring the importance of identifying novel therapeutic targets. **Objective:** This study aimed to evaluate apoptotic dysregulations in PTC patients to support the development of personalized treatment strategies based on apoptosis profiling. **Methods:** The study included 137 women: 108 diagnosed with PTC (28 with angioinvasion and 80 without) and 29 healthy controls. Serum concentrations of FAS ligand (FASL), Bcl-2-associated x protein (BAX), p53-upregulated modulator of apoptosis (PUMA), apoptosis-inducing factor (AIF), and TP53-induced glycolysis and apoptosis regulator (TIGAR) were measured using ELISA. Platelet count (PLT), fasting glucose, and bone parameters via dual-energy X-ray absorptiometry (DXA) were also analyzed. **Results:** PTC patients exhibited elevated PUMA levels (angioinvasive PTC: $p=0.0007$; non-angioinvasive PTC: $p=0.04$) and increased BAX concentrations in non-angioinvasive PTC compared to controls ($p=0.04$). Notably, insufficient activation of BAX by PUMA was observed in angioinvasive PTC. Strong correlations were found between BAX and FASL (angioinvasive PTC: $r=0.63$; non-angioinvasive PTC: $r=0.76$), AIF and FASL (angioinvasive PTC: $r=0.76$; non-angioinvasive PTC: $r=0.79$), BAX and AIF (angioinvasive PTC: $r=0.82$; non-angioinvasive PTC: $r=0.86$) ($p < 0.0001$ for all) and TIGAR and PLT (angioinvasive PTC $r=0.63$; $p < 0.0001$; non-angioinvasive PTC: $r=0.27$; $p=0.01$). AIF correlated with bone mineral content ($r=0.5$; $p=0.008$) and fasting glucose ($r=-0.5$; $p=0.006$) in angioinvasive PTC. **Conclusion:** These findings highlight significant dysregulations in apoptosis-related pathways in PTC. Elevated PUMA and BAX levels and AIFs dual systemic role suggest its involvement in tumor invasiveness, skeletal health, and metabolism. Apoptosis profiling may guide the identification of therapeutic targets and the development of personalized treatment strategies for PTC.

THYROID CELL BIOLOGY

1112486 - EVALUATING INSULIN'S IMPACT ON THYROID DEVELOPMENT USING HUMAN THYROID ORGANIDS

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Introduction: The Insulin/IGF signaling pathway is a critical regulator of various physiological processes, including mammalian growth, metabolism, and reproduction. Both the IGF1 receptor (IGF1R) and the insulin receptor (INSR) are vital for thyroid function, influencing gene expression, proliferation and survival of epithelial cells. Notably, the conditional knockout of both IGF1R and INSR in the thyroid during development results in smaller neonatal thyroid glands and impaired folliculogenesis. Despite substantial evidence highlighting the essential role of Insulin/IGF1 pathways in the thyroid proper formation and function, the specific cellular and molecular mechanisms involved during different developmental stages remain largely unexplored. **Methods:** In this study, we utilized human embryonic stem cell-derived thyroid organoids treated with insulin (INS) to evaluate its effects on thyroid development. **Results:** Transcriptomic analyses revealed sustained high expression levels of INSR throughout thyroid organoids development. By using single-cell RNA (scRNA) and ATAC (scATAC) sequencing, we found that at an early stage of thyroid organogenesis in vitro, INS significantly enhances the differentiation of thyroid progenitors (NKX2.1, PAX8, FOXE1, HHEX+) into more mature cells (TG, TSHR+) compared to control conditions (-INS). Furthermore, INS-treated organoids exhibited a higher proportion of proliferating thyroid cells (TOP2A, MKI67+). Differential expression analyses indicated that INS leads to an upregulation of glycolysis-associated genes, particularly marked by increased levels of GLUT1 (SLC2A1) and HK2. Additionally, transcription factor and motif enrichment analyses suggested that at progenitor stage, TEAD4 plays a differential role in cell state maintenance in the absence of INS, whereas transcription factors related to the AP-1 family are linked to a more differentiated thyrocyte status in the presence of INS. **Conclusion:** These findings suggest that insulin signaling plays a pivotal role during the early stages of human thyroid development in vitro, facilitating the differentiation of thyroid progenitors into TG/TSHR+ thyrocytes through mechanisms involving glucose metabolism and chromatin remodeling.

1112250 - PATIENT-DERIVED HIPSC MODEL OF HUMAN BRAIN REVEAL MOLECULAR MECHANISMS OF CLINICAL CONSEQUENCES OF CEREBRAL SBP2 DEFICIENCY

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Introduction: Selenocysteine insertion sequence-binding protein 2 (SBP2) plays a key role in the synthesis of selenoproteins. Selenoproteins are essential for antioxidant defense, thyroid hormone metabolism, and cellular homeostasis. SBP2 deficiency presents variable features including abnormal thyroid hormone metabolism, growth delay and aortopathy. Clinical features and molecular mechanisms underlying the consequences of SBP2 deficiency for the human brain are unknown. **Objective:** To investigate the clinical features and molecular mechanisms of SBP2 deficiency for the human brain. **Methods:** Two adult patients with SBP2 deficiency underwent clinical and neurological examinations and repeated brain MRI-scans. Cells from patients and unaffected family members were reprogrammed to human induced pluripotent stem cells (hiPSCs). Patient and control hiPSCs were differentiated into neural progenitor cells (NPCs) and NGN2-neurons, co-cultured with wild-type astrocytes to model the human brain. Immunohistochemistry, gene expression, deiodinase assays and multielectrode arrays for neuronal functionality were employed to study structural and functional differences between patient and control lines. **Results:** Both patients had compound heterozygous SBP2 mutations and exhibited a range of features compatible with SBP2 deficiency. In addition, both had neurodevelopmental delay and, clinical and imaging features of neurodegeneration. Patient-derived NPCs showed absent DIO3 activity with a concomitant increased response to T3 in the T3-responsive gene KLF9. Patient-derived NPCs exhibited decreased GPX4 levels accompanied by ~50% reduction in their proliferation rate in the presence of iron and oxidative stress. Patient-derived neurons required antioxidants for survival but exhibited significantly reduced electrophysiological activity despite the antioxidant support. In contrast, control neurons showed time-dependent increase in their mean firing rate and number of spikes. **Conclusions:** We describe neurodevelopmental and neurodegenerative abnormalities as new features in SBP2 deficiency. Our patient-derived hiPSCs modelling SBP2 deficiency in brain suggest abnormal thyroid hormone signaling possibly underlying abnormal neurodevelopment as well as ferroptosis-mediated neurodegeneration, which could be alleviated by antioxidant therapy.

THYROID CELL BIOLOGY

1112290 - PD-L1 ACTIVATES INTRINSIC CELLULAR FUNCTIONS IN THYROID CELLS: IMPLICATIONS FOR IMMUNE CHECKPOINT INHIBITOR INDUCED THYROIDITIS

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Introduction: Immune related adverse events (irAE), affect 55% of patients receiving immune checkpoint inhibitors (ICI). Thyroid dysfunctions are the most common irAEs and they are predominantly associated with anti-PD-L1/PD-1 therapies. The ICI-induced thyroiditis mechanisms are unknown. **Objective:** To test the hypothesis that blockade of thyrocyte PD-L1 causes thyrocyte stress and apoptosis by dysregulating intrinsic thyrocyte functions. **Methods:** We generated two human thyroid cell lines: one over-expressing PD-L1 (PD-L1-H) and another with downregulated PD-L1 expression (PD-L1-L). To examine PD-L1 role in thyrocyte responses to cytokines we exposed PD-L1-H and PD-L1-L cells to IFN γ and assessed apoptosis, ER-, mitochondrial-stress and autophagy using western blot, flow cytometry and immunofluorescence assays. To identify cell-intrinsic pathways controlled by PD-L1 we performed proximity labeling via BioID-mass spectrometry (MS). We created a mouse model of anti-PD-L1(α PD-L1)-induced thyroiditis and evaluated pathways dysregulated by PD-L1 blockade in thyroid. **Results:** IFN γ treatment triggered significant apoptosis in PD-L1-L compared with PD-L1-H and control (CTR) cells. IFN γ induced increased levels of ER-stress markers (e.g., BiP) and impaired mitochondrial function in PD-L1-L compared with PD-L1-H and CTR cells. Autophagy assessment by measuring LC3-II flux revealed blunted autophagic response to IFN γ in PD-L1-L cells. IFN γ -induced ER- and mitochondrial-stress was reversed by autophagic activator rapamycin, suggesting that defective autophagy due to PD-L1 suppression was causal to IFN γ -induced cellular-stress. BioID-MS and pathway analyses identified ERK and AKT as critical mediators of defective autophagy in PD-L1-L cells. In vivo, treatment of NOD.H-2h4 mice with α PD-L1 triggered thyroiditis evidenced by increased fT4, T-cell activation and thyroid lymphocytic infiltration. Autophagic flux was decreased in thyroids of α PD-L1-treated mice and RNA-seq revealed upregulation of immune and phagosome pathways. **Conclusion:** Thyroidal PD-L1 has immune-independent functions promoting cell-intrinsic survival signals. PD-L1 suppression dysregulates autophagy sensitizing thyrocytes to IFN-induced stress. Restoring PD-L1 intracellular functions may protect the thyroid from ICI-induced thyroid destruction.

1112499 - UNREVEALING THE EPIGENETIC MECHANISMS TRIGGERED BY TSH IN THE STIMULATION OF THYROID DIFFERENTIATION MARKERS GENE EXPRESSION

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Introduction: It is well known that thyroid-stimulating hormone (TSH) is the main regulator of thyroid function, promoting the upregulation of proteins/enzymes that participate in thyroid hormone production. However, the epigenetic mechanisms underlying TSH-induced stimulation of thyroid gene expression have yet to be elucidated. **Objective:** This study aimed to investigate the epigenetic mechanisms triggered by TSH exposure involved in regulating the expression of thyroid differentiation markers. **Methods:** PCCl3 cells were maintained in starved condition (0.2% FBS, without TSH and insulin) for 4 days. Thereafter, the cells were treated or not with TSH (1 mU/mL) for 24 h. Gene and protein expression were evaluated by RT-qPCR and Western Blotting, respectively. Moreover, the involvement of epigenetic alterations in TSH-induced effects was assessed by using inhibitors of DNA methylation (azacitidine), histone methylation (GSK343), and histone acetylation (A485). **Results:** As expected, starved cells exposed to TSH presented a significant increase in the gene/protein expression of thyroid differentiation markers, NIS, TPO, TG, and TSHR. TSH also increased histone acetylation and H3K4me3 content, markers of transcriptional activity, correlating with reduced expression of Hdac3 and Kdm5c. Additionally, TSH-treated cells exhibited decreased expression of DNMT1, DNMT3, and reduced H3K27me3 content, a classical marker of transcriptional repression. These results were consistent with reduced mRNA expression of Dnmt1, Dnmt3a, Dnmt3b, and Ezh2 in TSH-treated cells. The HDAC inhibitor A485 blocked the TSH-induced stimulation of thyroid differentiation markers. Treatment with GSK343 concomitantly with TSH impaired the stimulation of NIS and TSHR. Finally, azacitidine treatment abrogated the TSH-induced stimulation of TSHR expression only. **Conclusion:** This study highlights the role of epigenetic mechanisms in regulating thyroid differentiation markers, providing crucial insights into thyrocyte physiology. Finally, these findings could also be useful for developing new treatment strategies for thyroid cancer, which frequently involves reduced expression of thyroid differentiation markers.

THYROID GENETICS

1112621 - A TUMOR-CELL SPECIFIC GENE SIGNATURE DERIVED FROM SINGLE-CELL SEQUENCING IS PROGNOSTIC ACROSS INDEPENDENT COHORTS OF PAPILLARY THYROID CARCINOMA PATIENTS

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Introduction: Gene expression alterations may provide prognostic information in papillary thyroid carcinoma (PTC). However, bulk RNAseq data contain mixed signals from tumor and non-tumor cells. Using single cell/nucleus RNAseq data from 37 thyroid cancers and 9 adjacent normal thyroids, we derived a PTC tumor cell specific gene signature [Prognostic RNA Expression Cell-specific Integrated Signature – PRECISE]. **Objective:** To assess the prognostic significance of a multigene signature [PRECISE] in two independent cohorts of PTC patients with long durations of follow-up (MDACC and VUMC cohorts). **Methods:** PTC tumor samples were submitted to bulk RNAseq. PRECISE scores were calculated using a single sample rank-based method. Primary outcome was progression-free survival (PFS). Disease-specific survival (DSS) was a secondary outcome. Predictive models incorporating PRECISE-PTC score were developed in the MDACC cohort and validated in the VUMC cohort. Associations between PRECISE-PTC and survival outcomes were evaluated using multivariable cox regression. **Results:** In the MDACC cohort (N=111, median follow-up 14.2 years), PRECISE scores [median -2.1; IQR -2.9-1.7] were significantly associated with PFS [HR=2.5; P< 0.001] in a univariable model. The association remained significant after adjusting for stage, age, and TERT status [aHR=2.14; P=0.002]. In the VUMC cohort [N=63, median follow-up 5.2 years], PRECISE scores [median -3.1; IQR -3.7-2.3] were also significantly associated with PFS in univariable and multivariable models [HR=2.5; P< 0.001 and aHR=3.52; P< 0.001]. In both cohorts, predictive models incorporating the multigene PRECISE score were superior to models incorporating age, stage and TERT only (C-index 0.81 vs. 0.91 with PRECISE). PRECISE scores were also associated with DSS in both cohorts [MDACC HR=3.4; P<0.001 and VUMC HR=2.7; P=0.002]. **Conclusion:** Our novel tumor-specific gene signature demonstrates potential utility as a prognostic biomarker for detecting recurrent/progressive disease and PTC-related death, providing additional information beyond currently used clinicopathologic information, such as age, TNM, and TERT promotor mutation status.

1112222 - AN UNBIASED, AI-DRIVEN, QUANTITATIVE SURVEY OF HISTOLOGY IN HUMAN ASYMPTOMATIC THYROID GLANDS REVEALS THE EXTENT OF NATURAL MORPHOLOGICAL VARIATION AND HISTOLOGICAL QTLs

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Introduction: Rationale: While healthy tissue states are traditionally defined by population norms, understanding the range of morphological variations in asymptomatic individuals remains crucial. **Objective:** This study presents for the first time an unbiased quantitative survey of histological variations in human thyroid tissue from individuals without diagnosed thyroid disease. It rests on artificial intelligence (AI) to analyze morphological variation, and its association with transcriptome and genome variations. **Methods:** We developed an automated pipeline to analyze gigapixel whole slide images from the GTEx database, processing approximately 7 million 110x110 microns tiles from 893 thyroid slides. The AI-driven approach, operating without human supervision, successfully classified and quantified various tissue morphologies including epithelium, fibrosis, and immune foci. **Results:** Our methodology revealed distinct morphological clusters corresponding to major thyroid tissue features, enabling spatial mapping of these structures across tissue samples. Notably, we identified significant correlations between morphological features and clinical annotations, such as the association between immune cluster presence and incidental post-mortem thyroiditis diagnosis. Gene set enrichment analysis demonstrated strong concordance between morphological clusters and their corresponding gene expression profiles. Furthermore, we conducted the first histological quantitative trait loci (hQTL) analysis, identifying 120 SNPs associated with morphological variations. The most significant loci overlapped with FOXE1, a key thyroid transcription factor, and PTCSC2, a lincRNA previously linked to papillary thyroid cancer risk. **Conclusion:** This study establishes a novel framework for unsupervised quantitative histological analysis and reveals the extent of morphological variation in asymptomatic thyroids, while identifying genetic variants associated with tissue architecture. These findings provide insights into the spectrum of “normal” tissue states and suggest potential mechanisms linking genetic variation to cancer susceptibility through altered tissue architecture.

THYROID GENETICS

1112553 - GENETIC ANCESTRY OF RET MUTATIONS AT CODON 804 REVEALS A BOTTLENECK EFFECT AMONG BRAZILIANS WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE 2

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Introduction: Pathogenic variants in codon 804 of the RET gene, associated with multiple endocrine neoplasia type 2A (MEN2A), hold significant clinical and genetic relevance. Understanding the genetic structure and evolutionary dynamics of these pathogenic variants can provide valuable insights into their role in MEN2A and inform targeted genetic counseling and management strategies. **Objective:** This study aimed to investigate the genetic structure of populations carrying the p.Val804Met (c.2410G> A), p.Val804Leu (c.2410G> C), and p.Val804Leu (c.2410G> T) variants by evaluating signals of genetic bottlenecks, linkage disequilibrium, and phylogenetic relationships among subpopulations. **Methods:** A total of 146 individuals were analyzed, divided into three subpopulations (A c.2410G> A: n=97, C c.2410G> C: n=42, T c.2410G> T: n=7). Genotyping included microsatellite loci within the RET gene. Bottleneck effects were assessed using the Infinite Allele Model (IAM) and Stepwise Mutation Model (SMM) with Bottleneck software. Linkage disequilibrium was analyzed using GENEPOP, and genetic distances based on FST values were calculated in PopTree2 for phylogenetic tree construction. **Results:** Bottleneck tests revealed significant effects in population A under IAM (T2=2.107; p=0.017) and in population C under SMM (T2=-2.823; p=0.002). In both cases, Wilcoxon tests indicated heterozygote excess or deficiency (p<0.05). For linkage disequilibrium analysis, population A showed highly significant associations between loci (p<0.000001), while population C exhibited heterogeneous patterns. Phylogenetic trees indicated genetic proximity among families within each subpopulation, suggesting a recent common ancestor. **Conclusion:** The findings suggest that historical events, such as genetic bottlenecks, contributed to the structuring of the studied populations. Significant linkage associations and phylogenetic distances support the hypothesis of shared ancestry and restricted gene flow. These insights enhance the understanding of population dynamics in rare hereditary conditions.

THYROID HORMONE ACTION

1112666 - REGULATION OF ADULT NEUROGLIOGENESIS BY DIO2 IN MOUSE BRAIN: A TALE OF TWO WAVES

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Introduction: Thyroid hormones (THs) are essential for neurodevelopment and adult brain function regulation. In rodents, we previously demonstrated a key role of THs in the neuron/glia determination of neural stem cell (NSC) located in the subventricular zone (SVZ), the brain's largest NSC niche. Among the key TH-availability regulators expressed in the murine SVZ, the role of type two deiodinase (DIO2), the main enzyme responsible for locally activating T4, remains underexplored. **Objective:** Our study aims to investigate DIO2's role in the adult SVZ, particularly in NSC activation, proliferation, and neuroglial cell fate determination. **Methods:** Unexpectedly, using single-cell RNA sequencing, we found a strong link between Dio2 expression and NSC quiescence, further clarified by RNAscope, which revealed that NSC Dio2 expression was almost exclusive to quiescent NSCs. To better unravel the function of DIO2, we exposed proliferating neurospheres to DIO2 inhibitors, revealing increased SVZ-derived progenitor proliferation. Then, we analyzed the adult SVZ of DIO2-lacking mice (Dio2 KO), showing an enhanced number of cycling cells without an increase in cell division, suggesting hindrances in progenitor cell cycle progression. Furthermore, we explored the functional impact of DIO2 absence by analyzing consequences on endogenous regeneration of SVZ cell types after exposure to an antimetabolic drug. Preliminary data highlighted a key role of Dio2 in SVZ maintenance and regeneration. Finally, we examined Dio2 KO mice for alterations in progenitor fate determination, migration, and integration into target tissues. **Results:** Showed premature oligodendroglial maturation in white matter and disrupted neuroblast integration into the olfactory bulb, correlating with functional impairments in odor memory. **Conclusion:** Our findings underline two waves of DIO2's influence in the adult SVZ: NSC quiescence and activation, and committed progenitor differentiation and maturation, providing a dynamic basis for further exploration of DIO2's implications in brain function, and more generally in the function and disease of TH target tissues.

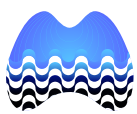
THYROID HORMONE ACTION

1112197 - RHGH PARTIALLY IMPROVES CORTICAL AND HIPPOCAMPAL DEVELOPMENTAL IMPAIRMENTS IN TRA1 MUTANT MICE BY RESTORING THE GH/IGF-1 AXIS

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Introduction: The ThraE403X mutant mice exhibit reduced GH synthesis and significant developmental impairments in the cerebral cortex and hippocampus. **Objective:** This study aims to explore the potential value of restoring the GH/IGF1 axis in treating neurological abnormalities caused by resistance to thyroid hormone alpha (RTH α). **Methods:** From postnatal day 3 to day 21, ThraE403X mutant mice received subcutaneous injections of human recombinant growth hormone (rhGH) at a dose of 8 μ g/g/day. The therapeutic effects were assessed by evaluating morphological changes in the cerebral cortex and hippocampus, cortical proteomics, hippocampal long-term potentiation (LTP) electrophysiology, conditioned fear tests, and molecular changes before and after rhGH supplementation in P21 ThraE403X mice. **Results:** After rhGH treatment, the height and weight of ThraE403X mice recovered. GH and IGF-1 levels in the peripheral blood, hippocampus, and cortex of ThraE403X mutant mice returned to those of wild-type mice. Key protein levels in the MAPK, PI3K/AKT/mTOR, and STAT5 pathways increased. The number of pyramidal cells in the CA1 region of the hippocampus significantly increased. Hippocampal LTP experiments indicated that the learning and memory abilities of 3-week-old ThraE403X/+ mutant mice improved. Conditioned fear tests suggested improved learning and memory abilities in 10-week-old ThraE403X/+ mutant mice. Western blot analysis confirmed that abnormalities in neurofilament proteins and long-term potentiation-related proteins ARC and p-CREB improved, but abnormalities in myelin-related proteins MOG and MBP did not improve. **Conclusions:** Supplementing rhGH can restore the GH/IGF1 axis and partially improve the neurodevelopmental impairments caused by the ThraE403X mutation in mice. This suggests that rhGH has potential therapeutic value for RTH α , although further basic and clinical research is needed to confirm this.



1112488 - ROLE OF T3 IN DENDRITIC CELL ACTIVATION: INSIGHTS INTO THE METABOLIC REPROGRAMMING AND ITS FUNCTIONAL IMPACT

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Introduction: Dendritic cells (DCs) integrate environmental signals to orchestrate the adaptive immune responses. We demonstrated that T3 activates DCs, favouring pro-inflammatory and cytotoxic T cells profiles, and enhancing anti-tumor responses in T3-treated DC vaccination protocols against melanoma and colon carcinoma in mice. However, how T3 impacts DC functionality remain incompletely understood. **Objective:** Given recent advances highlighting cellular metabolism as a key regulator of immune cell function, we aimed to evaluate T3 effects on DC metabolism and its functional implications. **Methods:** Bone marrow-derived DCs from C57BL/6 mice were treated with T3 (10 nM, 18 h) ± L-NAME (5 mM, 18 h). Glucose, lactate and nitrite (nitric oxide NO production) levels were measured in supernatants. Mitochondrial respiration parameters were assessed via high-resolution respirometry (Oroboros) using mitochondrial inhibitors. Protein expression of Ser2448p-mTOR, mTOR, HIF1α and inducible NO synthase (iNOS) was determined by WB. DC activation and maturation markers (CD86, MHC-II, IL-12p40p70) were analysed by flow-cytometry. T cell activation (CD25 expression) was assessed after 3-day co-culture of pre-treated DCs with allogenic splenocytes (BALB/c mice) by flow-cytometry. **Results:** Statistical analysis: T-test, two-way ANOVA with Tukeys post hoc test ($p < 0.05$). T3 increased glucose consumption and lactate production ($p < 0.01$) but suppressed mitochondrial respiration, reducing basal ($p < 0.01$), ATP-linked ($p < 0.001$), maximal ($p < 0.01$), and spare respiratory capacity ($p < 0.01$). T3 also induced iNOS expression and NO production ($p < 0.0001$). Inhibition of iNOS with L-NAME restored mitochondrial respiration parameters ($p < 0.05$) while preserving enhanced glycolysis ($p < 0.01$). Mechanistically, although p-mTOR/mTOR expression remained unchanged following T3 treatment, T3 induced HIF1α expression ($p < 0.001$) in an iNOS-dependent manner, evidenced by the absence of HIF1α in L-NAME-treated T3-DCs. Notably, iNOS inhibition did not affect T3-DC activation and maturation markers but significantly decreased their capacity to activate CD4⁺ T cells. **Conclusion:** In conclusion, T3 reprograms DC metabolism, promoting glycolysis and suppressing mitochondrial bioenergetics, likely through a HIF1α/iNOS-dependent mechanism. These findings may unveil new strategies to potentially modulate DC immunogenicity.

THYROID HORMONE ACTION

1112314 - THE RELEVANCE OF CO-REPRESSOR BINDING FOR THE RESISTANCE TO THYROID HORMONE ALPHA PHENOTYPE AS REVEALED BY A FAMILY CARRYING AN H175R VARIANT IN THE THYROID HORMONE RECEPTOR ALPHA

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Introduction: Resistance to thyroid hormone (TH) alpha (RTH α), caused by mutations in the T3-receptor (TR) TR α 1, is characterized by discordant thyroid function tests and clinical features due to tissue-specific resistance to TH, including neurocognitive impairments, disproportionate short stature and bradycardia. Mutations in TR α 1 reduce T3-binding affinity resulting in impaired transcriptional activity. Dominant negative inhibition resulting from a failure of mutant receptors to release corepressors is a key pathophysiological feature in RTH. **Objective:** To describe a novel H175R-TR α 1 mutation that disrupts corepressor binding in absence of T3. **Methods:** Receptor function and association with corepressors NCoR1 and SMRT γ were measured in Jeg-3 cells using luciferase-based reporter assays, and corepressor binding confirmed by co-immunoprecipitation. TR α 1H175R/+ mice were analyzed for heart rate, skeletal growth and gene expression. WT-TR α 1 or H175R-TR α 1 RNA was injected in zebrafish embryos; morphology, skeletal development and thyroid function in larvae were assessed at dpf 2 and 5. **Results:** H175R-TR α 1 patients have short stature, but lack other classical features. H175R-TR α 1 showed impaired T3-dependent transcriptional activity (EC50 ~19-fold higher than WT, $p < 0.001$), but no dominant negativity over WT-TR α 1. No binding of H175R-TR α 1 to NCoR1 or SMRT γ was observed, either unliganded or at any concentration of T3. Preliminary data from TR α 1H175R/+ mice showed no cardiac abnormalities. Compared to WT-TR α 1 injected zebrafish, H175R-TR α 1 RNA injected embryos showed morphological and skeletal abnormalities at any dose of RNA, and discordant thyroid function only at the highest dose. **Conclusion:** Replacing His175 with Arg in TR α 1 disrupts corepressor binding, compatible with previous in vitro studies using artificial receptor mutants. Our data may explain the limited phenotype in this family, providing the first human evidence for the concept that impaired, T3-dependent dissociation of corepressors from TR α 1 is a key determinant of the typical RTH α phenotype. Further analysis of H175R-TR α 1 animal models should confirm this hypothesis.

THYROID HORMONE METABOLISM

1112513 - PHENYLBUTYRATE INCREASES THYROXINE UPTAKE IN PRIMARY ASTROCYTES FROM MICE CARRYING A MCT8 MISSENSE MUTATION

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Introduction: Monocarboxylate transporter 8 (MCT8, SLC16A2) contributes to the transport of thyroid hormones (TH) across plasma membranes. Mutations in the X-chromosomal MCT8 lead to a rare genetic disorder resulting in severe intellectual and motor disability. **Objective:** We wanted to investigate whether the chemical chaperone sodium phenylbutyrate (NaPB) can rescue TH transport in a mouse model expressing MCT8-P253L. **Methods:** We studied Mct8-P253L/y mice by quantifying MCT8 expression in kidney and brain, measured deiodinase type 2 (DIO2) activity in brain, and characterized TH import into primary astrocytes. We tested whether NaPB can enhance protein expression and TH transport activity in astrocytes. **Results:** Expression of mutant MCT8-P253L depended on cell type with reduced expression in kidney and primary astrocytes and unaffected expression in whole brain, while Slc16a2 mRNA levels remained unchanged. DIO2 activity in brain was induced in Mct8-P253L/y mice, while mRNA levels remained normal. In primary astrocytes, we demonstrated that not only MCT8 but also OATP1C1 is involved in the uptake of T4. NaPB treatment of primary astrocytes from Mct8-P253L/y mice enhanced T4 uptake, which was silychristin-dependent. T3 uptake as well as MCT8-P253L expression remained unaffected by NaPB in primary astrocytes. **Conclusion:** Differential expression of mutant MCT8-P253L is cell type-dependent and posttranscriptionally regulated. The positive effect of NaPB on T4 uptake in primary mutant astrocytes supports the idea of repurposing NaPB for treatment of patients with MCT8-deficiency. The lack of effect of NaPB on T3 uptake suggests the expression of an unknown silychristin-sensitive T4 transporter.

THYROID HORMONE METABOLISM

1112247 - THE ROLE OF TYPE 3 DEIODINASE IN A HUMAN MODEL FOR EARLY BRAIN DEVELOPMENT

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Introduction: THs are critical signaling molecules in neurodevelopment, acting on differentiation of neural cells and synaptogenesis, with deiodinases governing intracellular TH concentrations in a spatiotemporal manner. It is remarkable that fetal neural cells, while being key target cells of TH, exhibit strong activity of the TH inactivating enzyme DIO3. Currently, the molecular mechanisms underlying TH action in brain are mainly derived from animal models. **Objective:** To investigate the role of DIO3 in a human model for early brain development utilizing human induced pluripotent stem cells (hiPSCs). **Methods:** We generated a complete DIO3 knock-out (KO) using the CRISPR/Cas9 technology in hiPSCs. hiPSC were differentiated to neurons by NGN2 overexpression as a model for fetal human neurons. In parallel, we inactivated DIO3 in neural cells using iopanoic acid (IOP). Cells were cultured with different T3 concentrations (0-3-10 nM). We used immunocytochemistry, qPCR and RNAseq, DIO3 and metabolism assays and multi-electrode assays as readouts. **Results:** CRISPR/Cas9-generated DIO3 KO neurons presented a complete absence of DIO3 activity. Upon T3 addition, there was an enhanced response in gene expression of T3-dependent genes such as KLF9 in DIO3 KO vs wild-type NGN2 neurons. Reduced DIO3 activity accompanied by an enhanced KLF9 induction were validated in IOP-treated neurons. We also examined the differentiation potential of neural progenitor cells to neural networks in absence of DIO3 by IOP treatment. Our preliminary immunocytochemistry data showed an increase in cells containing neuronal nuclear protein (NeuN), a biomarker for neurons, when the activity of DIO3 is diminished. Preliminary data suggests altered electrophysiology in DIO3 KO neurons. **Conclusion:** Our results suggest that impaired DIO3 activity may lead to excessive TH action in neural cells and, thereby, compromising normal brain development. We hypothesize that a high DIO3 activity is required in early brain development to maintain stemness and prevent premature neural differentiation.

1112207 - CORE-NEEDLE BIOPSY IS A SAFE AND VALUABLE OPTION. FIRST 532 PROCEDURES IN ROMANIA

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Introduction: There are two types of thyroid nodule biopsy: fine-needle aspiration (FNAB) and core-needle (CNB). Multiple studies mainly from Eastern Asia demonstrate safety and efficacy of CNB, however it is rarely used in Europe and America. **Methods:** Retrospective analysis of the first 532 thyroid nodule CNBs performed in Romania. All CNBs were performed using 18G semi-automatic biopsy instruments. We used the Korean Thyroid Association reporting system (KTA-CNB) for histology reports. **Results:** Of 532 CNBs, there were only 5 non-diagnostic results, category I, (0.9%), 30 category III results (5.6%) and 56 category IV results (10.5%). Among nodules which previously underwent FNAB, CNB offered a conclusive result (either benign or malignant, KTA II, V and VI categories) in 80% of Bethesda 1, 75% of Bethesda 3, 62.5% of Bethesda 4 nodules. There were no non-diagnostic results in these nodules. We performed on average 2.3 passes per lesion. There were no major complications (none of complications required hospitalisation), some minor adverse events were limited to bruising, perithyroidal hematoma and pain during or after procedure. Four patients had intrathyroidal hematoma, three patients developed transitory hoarseness which resolved spontaneously in 20-90 minutes. **Conclusion:** The CNB is a safe and reliable diagnostic procedure for thyroid nodules. It offers very low chance of non-diagnostic results, lower chance of inconclusive results with a better stratification of risk between different subcategories (III a-d, IV a-c). CNB is a procedure which improves patient experience by reducing the number of procedures needed to make a clinical decision. It is a useful and cost-efficient tool, especially in the absence of molecular testing. CNB offers additional advantage of immunohistochemistry in cases suspected for medullary thyroid cancer, lymphoma or metastatic lesions.

THYROID NODULE

1114232 - PROSPECTIVE RESULTS FOR ACTIVE SURVEILLANCE OF RAS-POSITIVE INDETERMINATE THYROID NODULES WITH BETHESDA III AND IV CYTOLOGIES

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Introduction: Resection of all RAS-positive nodules is a low-yield strategy resulting in overtreatment for up to 50% of patients. Our approach incorporates clinical findings, standardized cytology and ultrasound results into shared decision-making with patients. **Objective:** We report the prospective four-year outcomes of our diagnostic strategy. **Methods:** Routine reflex ThyroSPEC molecular testing (MT) for Bethesda III and IV indeterminate thyroid nodules (ITNs) was implemented in July 2020. The study included 233 consecutive RAS-positive patients diagnosed through September 2024, with 200 Bethesda III and 33 Bethesda IV nodules. Of these, 162 (70%) underwent surgery while 71 (30%) underwent surveillance (median follow-up: 27 month, IQR 19-38). Nodule stability was evaluated in 47 surveillance patients with at least one post-MT ultrasound and one-year follow-up. **Results:** Median maximum nodule size was larger in the surgery group (2.9 cm, IQR 1.9-4.0) than the surveillance group (2.4 cm, IQR 1.7-3.0; $p = 0.003$). Bethesda III nodules were more common in the surveillance patients (94%, $n=67$) than the surgery patients (82%, $n=133$; $p=0.023$). Nuclear atypia was reported in 52% ($n = 85$) of surgery patients and 38% ($n=27$) of surveillance patients ($p=0.059$). Seven patients crossed over to surgery due to patient preference, nodule growth, or symptoms; 4 patients had malignant histology comprising of ATA low-risk cancers. Using a 72% volume increase threshold, 2/47 (4%) nodules exhibited growth, and 29/47 (62%) were stable or decreased. Using a 50% volume increase threshold, 5/47 (11%) exhibited growth, with a cumulative incidence of growth of 2% at 1 year, 2% at 2 years, and 24% at 4 years. **Conclusion:** RAS mutation should not be used the sole determinant for surgery. Clinical factors such as Bethesda category and cytologic atypia should also guide management decisions. Observation of RAS-positive patients is a viable option, though further long-term data are needed.

1112465 - RESULTS OF A SERIES OF 167 CASES OF MICROWAVE ABLATION FOR BENIGN THYROID NODULES

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Objective: Evaluate the efficacy and safety of ultrasound-guided microwave ablation of benign thyroid nodules. **Methods:** Patients 160 patients (167 nodules) treated with ultrasound-guided microwave ablation between April 2022 and May 2023. The treatment was performed with the microwave surgical ablation system ECO200G using antennas with diameters of 17G and 16G. The technique used was moving shot under local anesthesia with 1.0% lidocaine and light intravenous sedation when necessary. All cases were discharged from the hospital on the same day and returned for ultrasound control of the volumetric reduction of the nodules at one, three, six and twelve months. Thyroid function tests were performed in the second month after procedure. **Results:** 167 nodules were treated. The mean volume of the nodules was 22.5 mL (0.60 107.00 mL). Nodules were predominantly solid (83.5%). The average ablation time was 11.14 minutes and the average power was 33.2 Watts. There were eleven cases of immediate complications, three of which were considered major and eight considered minor. The mean volumetric reduction of the treated nodules was 63.3% in the 1st month, 77.1% in the 3rd month, 82.5% in the 6th month, and 87.2% in the 12th month. When subdivided by volume (less than 10 mL, between 10 and 20 mL, between 20 and 30 mL and greater than 30 mL) there was a difference only in the group with more than 30 mL, which presented a smaller reduction in volume when compared to the others (75%). Three cases showed increased TSH levels requiring thyroxine replacement. **Conclusion:** ablation of benign thyroid nodules is a safe procedure with high resolution rates and few complications. Nodules larger than 30 mL should be carefully followed and more likely to require a new ablative procedure.

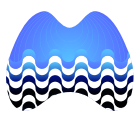
THYROID PHYSIOLOGY

1112313 - MULTIPLE ASSAY INTERFERENCES LEADING TO THE DIAGNOSIS OF LYMPHOPROLIFERATIVE DISORDERS

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Introduction: Paraproteins of clonal origin can cause spurious results in hormonal immunoassays, resulting in diagnostic pitfalls and inappropriate treatments due to false-positive or false-negative results. **Objective:** in this study, we sought to describe four cases, in whom the identification of analytical interferences led to the discovery of previously undiagnosed lymphoproliferative disorders. **Methods:** We studied 133 cases referred to our center for discrepant hormonal results compatible with central hyperthyroidism from 2017 to 2024. The diagnosis of analytical artifact was made by 1. Reassessment of discrepant results in the thyroid, adrenal, gonadal and somatotrophic function by different analytical platforms with different architecture or by liquid chromatography-tandem mass spectrometry; 2. Serial dilution of patients serum; 3. PEG precipitation. Rheumatoid factor, serum electrophoresis and cryoglobulins were measured for differential diagnosis. **Results:** In our monocentric cohort of patients referred for central hyperthyroidism, the overall prevalence of assay interference was 56% (74/133) with one, four, thirty-one and six patients diagnosed with biotin interference (0.75%), macro-TSH (3.0%), familial dysalbuminemic hyperthyroxinemia (23.3%) and clonal paraproteins (4.5%), respectively. In 32 cases (24%) the spurious results were not confirmed at reassessment. The remaining patients had genuine results due to RTHβ (N=46; 34.6%), TSH-secreting adenomas (N=8; 6.0%), amiodarone treatment (N=1; 0.75%), resistance to TSH or congenital hypothyroidism (N=4; 3.0%). In 4/6 patients with clonal paraproteins the interferences uncovered the previously unknown diagnosis of lymphoproliferative disorders. Three patients with spurious hyperthyroxinemia and falsely positive TSHR antibodies (TRAb) were diagnosed with monoclonal gammaglobulinemia of uncertain significance (MGUS; n=2) or type 1 cryoglobulinemia due to indolent non-Hodgkin lymphoma (n=1). A fourth patient with spurious hypothyroxinemia and hyperandrogenemia and unilateral adrenal hyperplasia was subsequently diagnosed with MGUS. In all cases the clonal paraprotein was an IgM light chain. **Conclusion:** In the workout of patients with multiple assay interferences serum electrophoresis and hematological investigations are highly recommended.



1114060 - PREDICTING REOPERATION OUTCOMES IN PAPILLARY THYROID CARCINOMA USING INTERPRETABLE MACHINE LEARNING

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Introduction: Reoperation for papillary thyroid carcinoma (PTC) is technically challenging and associated with a high risk of complications. Early identification of patients likely to respond to reoperation is essential for optimizing clinical decision-making and improving outcomes. **Objective:** To develop and validate interpretable machine learning (ML) models for early prediction of reoperation response in patients with PTC. **Methods:** This retrospective study included 670 patients with PTC who underwent reoperation at Wuhan Union Hospital between January 2012 and December 2023. Multiple ML algorithms, including random forest (RF), were used to construct predictive models. Model performance was assessed by the area under the receiver operating characteristic curve (AUC), and the SHapley Additive exPlanations (SHAP) method was used to evaluate feature contributions. **Results:** Among the 12 ML models tested, the RF model demonstrated the highest predictive accuracy. In internal validation, the RF model achieved an AUC of 0.904 (95% CI, 0.881-0.927); in the test set, the AUC was 0.876 (95% CI, 0.842-0.910). Calibration analysis showed strong agreement between predicted and actual outcomes. Eleven variables were retained in the final model, including age, body mass index, total tumor size, primary positive lymph node, gross extrathyroidal extension, reoperation interval, reoperative lymph node ratio, neutrophil to lymphocyte count ratio, the systemic immune-inflammation index, and levels of thyroglobulin and thyroglobulin antibody. **Conclusion:** This study developed and validated an interpretable ML model capable of accurately predicting reoperation outcomes in patients with PTC. The model may aid clinicians in identifying high-risk individuals and tailoring personalized treatment strategies.

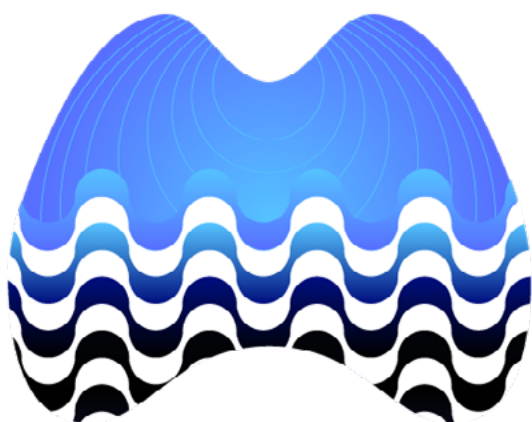
THYROID SURGERY

1114099 - TREATMENT OF CHRONIC HYPOPARATHYROIDISM POST THYROID CANCER SURGERY THROUGH INTER VIVO PARATHYROID TRANSPLANTATION

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Introduction: Hypoparathyroidism after total thyroidectomy is a possible and feared complication. Associated with cramps, tingling, a feeling of imminent death, often mistakenly received in emergency rooms as panic syndrome and wrongly treated with anxiolytics. **Objectives:** Report of a case of chronic hypoparathyroidism post total thyroidectomy that did not respond to clinical treatment and was finally treated with inter vivo parathyroid transplant, with the mother being the donor. **Methods:** 43-year-old female patient, undergoing total thyroidectomy in 2022 for papillary thyroid carcinoma developing hypoparathyroidism 4 months after surgery, being treated initially with calcitriol (up to 2.25 mcg/day) and calcium carbonate (3 g/day), later associated with renal tubulopathy. She continued to maintain symptoms and needed frequent admissions to emergency rooms to replace venous calcium and finally, she started to use analog PTH, therapeutic without complete response to symptoms. It was decided to attempt a living parathyroid transplant, a genetic and immunological study was carried out on possible donors in the family, with the patient's mother being selected as the donor, being defined by the donation of two parathyroid glands from the mother and fragmentation of 30 units for implantation under the fascia in the recipient's left forearm. **Results:** Haploidentity 50% HLA similarity. Negative cross match. Surgery without complications, both in the donor recovery and in the recipient's graft. Donor discharged in 24 hours and recipient in 4 days. Starts weaning off calcium and calcitriol, using only 1 g of calcium and without sismatriol after three weeks and with PTH of 46 pg/mL on day 30 post transplant. **Conclusion:** Chronic hypoparathyroidism is a complication of total thyroidectomy that is difficult to manage and has a great impact on the quality of life of patients. Inter vivo parathyroid transplantation requires specific criteria and can be a treatment tool for patients who do not respond to clinical treatment.



17°
International
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**SHORT ORAL
COMMUNICATION**

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112515 - BISPHENOL A, PERCHLORATE, AND NITRATE MIXTURE DISRUPTS CELL DIFFERENTIATION AND ALTERS EPIGENETIC MECHANISMS AND SIGNALING PATHWAYS IN THYROCYTES

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Introduction: Bisphenol A (BPA), nitrate, and perchlorate are endocrine disruptors (EDs) commonly found in drinking water. Our previous data indicated that these disruptors can individually affect gene expression and function in thyroid cells. However, the molecular effects triggered by the combined exposure to these compounds have not been evaluated. **Objective:** This study aimed to assess the impact of a mixture of BPA, perchlorate, and nitrate on gene and protein expression, as well as signaling pathways in thyrocytes. **Methods:** PCCl3 cells were treated for 48 hours with a mixture of BPA, nitrate, and perchlorate at concentrations of 10^{-7} , 10^{-9} , and 10^{-11} M. Gene and protein expressions were evaluated using qPCR and Western blotting, respectively. NIS activity was assessed through a non-radioactive iodine uptake assay. Signaling pathways, including MAPK, PI3K/AKT, and PKA, were analyzed via Western blotting. **Results:** EDs mixture exposure decreased the expression of genes involved in thyroid hormone synthesis, such as NIS, TG, TPO, and TSHR. Consistently, treated cells exhibited reduced NIS expression and diminished iodide uptake. Interestingly, the treatment increased the expression of epigenetic enzymes involved in transcriptional repression mechanisms (Dnmt1, Dnmt3a, Ezh2) and decreased the expression of enzymes related to the activation of transcription (Hat1, Kdm6a). Additionally, the EDs mixture activated MAPK and PI3K/AKT signaling pathways, which are associated with thyroid cell dedifferentiation. The treatment also reduced the phosphorylation of CREB, a transcription factor that stimulates the expression of thyroid differentiation genes. Notably, some of the most significant effects were observed at the lowest treatment dose. **Conclusion:** Exposure to a mixture of BPA, perchlorate, and nitrate, commonly found in drinking water, disrupts signaling pathways in thyroid cells, potentially leading to decreased expression of thyroid differentiation markers. These findings underscore the importance of evaluating the combined effects of environmental contaminants on thyroid function.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112233 - DEVELOPING A TESTING BATTERY FOR DEVELOPMENTAL NEUROTOXICITY MEDIATED VIA DISRUPTED THYROID HORMONE HOMEOSTASIS

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Introduction: Maternal thyroid hormone (TH) dysfunction is associated with lower IQ and decreased motor function in children. Endocrine disrupting chemicals (EDCs) are associated with disruption of maternal thyroid function and neurodevelopmental effects during pregnancy. Animal data has limited relevance for toxicity prediction in humans. **Objective:** Our aim is to develop a human-based testing battery to assess the safety of chemicals for developmental neurotoxicity mediated by disrupted TH signaling. **Methods:** Testing battery tier 1 consists of human cell lines representing neurons (SK-N-AS), oligodendrocytes (MO3.13) and astrocytes (H4) exposed to 12 different chemicals. TH transport and deiodinase-mediated metabolism were tested using 1 nM radiolabeled TH. T3-receptor activation was measured using qPCR of the T3-responsive gene KLF9. Tier 2 entails differentiation of human stem cells into neuron-astrocyte co-cultures. Effect of chemicals on T3-receptor response and neuronal differentiation was measured using qPCR. **Results:** Silychristin inhibited TH uptake up to 50% in all cell models. Whole-cell metabolism showed inhibition of deiodinase type 3 by iopanoic acid in MO3.13 and SK-N-AS cells. T3-induced KLF9 expression decreased 38% by TRα1 antagonist NH-3, and TBBPA exposure resulted in a fold change increase of ~8. Inhibition of T3-transport by 10 μM silychristin reduced KLF9 expression by 39%. Preliminary data on neuronal differentiation show that TBBPA exposure increases KLF9 expression after differentiation. **Conclusion:** The selected cell lines are suitable models to test the effect of EDCs on transport, metabolism and receptor activation. The human stem cells are a promising model to study the effect of EDCs on neuronal differentiation. Together, these models can form a two-tier testing battery to assess whether EDCs can disrupt the TH balance in the developing brain. The VHP4Safety project (NWA 1292.19.272) is part of the NWA research program Research along Routes by Consortia (ORC) and is funded by the Netherlands Organization for Scientific Research (NWO).

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112514 - MATERNAL EXPOSURE TO TRICLOSAN DURING THE INTRAUTERINE PERIOD DISRUPTS THYROID DEVELOPMENT AND FUNCTION IN THE OFFSPRING ANIMALS

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Introduction: Triclosan (TCS) is widely used in personal care products and food packaging. Our previous results indicated that intrauterine TCS exposure dysregulates the hypothalamus-pituitary thyroid axis of the offspring animals during adulthood. Nevertheless, the consequences of TCS exposure in the programming of thyroid development have not been studied. **Objective:** To investigate the impact of maternal exposure to TCS on the intrauterine development of the thyroid gland in the offspring rats. **Methods:** Pregnant Wistar rats were orally treated with corn oil (control) or corn oil supplemented with TCS (10 or 30 mg/kg/day) throughout the gestation. Female and male offspring rats were weighted and euthanized at gestational day 20 (GD20). Gene/protein expression was evaluated by RT-qPCR and Western Blotting. Thyroid T4/T3 levels and iodine content were measured through chemiluminescence immunoassay and a modified Sandell-Kolthoff colorimetric assay, respectively. **Results:** In the female offspring rats, the intrauterine exposure to TCS increased the mRNA expression of Tpo, Tshr, and Pax8 exclusively in the lowest treatment dose. In the male rats, TCS exposure stimulated the expression of Tg, Tpo, Tshr, Foxe1, Pax8, and Nkx2.1, especially in the highest dose. Interestingly, TCS-exposed male and female rats presented reduced gene/protein expression of NIS, and decreased content of T4, T3 and iodine in the thyroid in comparison to the control group. DNA methyltransferase expression was decreased in TCS-exposed animals. Additionally, Hat1 expression was increased both in male and female rats. Finally, TCS-treated animals presented a higher content of acetylated histones H3 and H4 than the control animals. These epigenetic changes are commonly involved in increased transcriptional activity. **Conclusion:** TCS exposure during a critical development period disrupted thyroid gland development and function. Specific epigenetic alterations seem to be involved in the activation of thyroid gene expression in TCS-exposed animals.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112511 - POLYCHLORINATED BIPHENYLS DISRUPT GENE EXPRESSION, NIS FUNCTION, AND KEY SIGNALING PATHWAYS IN HUMAN THYROID CELLS

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Introduction: Polychlorinated Biphenyls (PCBs) are persistent environmental contaminants known to disrupt thyroid function by altering serum levels of thyroid hormones and TSH in both humans and rodents. Previous studies of our group demonstrated that PCBs disrupt thyroid gene expression in rat cell lines through epigenetic mechanisms and dysregulation of PKA and MAPK signaling pathways at nanomolar doses. **Objectives:** To evaluate the molecular mechanisms triggered by PCB exposure in human thyrocytes. **Methods:** Nthy-ori 3-1 cell line (normal human thyrocytes) was treated or not (control), for 24h, with different doses (10⁻⁷, 10⁻⁹, 10⁻¹¹ M) of Aroclor 1254, a mixture of PCBs. Gene expression of epithelial-mesenchymal transition (EMT) markers and NIS were evaluated through RT-qPCR. Additionally, NIS function was assessed using a non-radioactive iodine uptake assay. PI3K/AKT, MAPK, and PKA signaling pathways were evaluated by Western Blotting. Cell viability was assessed by MTT assay. **Results:** PCB exposure increased the gene expression of E-cadherin, an epithelial marker, and reduced the expression of Vimentin, a mesenchymal marker. No significant alterations were observed in other evaluated EMT markers. Interestingly, PCB increased the phosphorylation of AKT, but did not significantly alter other signaling pathways studied. Moreover, PCBs exposure reduced the thyrocytes viability at different doses. Finally, PCBs significantly increased NIS gene expression and iodide uptake at the nanomolar dose. **Conclusions:** PCBs mixture modulates thyroid cell physiology by enhancing NIS gene expression and activity while inducing changes in EMT marker expression. The increased phosphorylation of AKT suggests that the PI3K/AKT pathway may play a role in mediating these effects. However, the observed reduction in thyrocyte viability underscores the cytotoxic potential of PCBs, even at low doses. These findings provide new insights into the molecular mechanisms underlying PCB-induced thyroid disruption and highlight the dual impact of these contaminants on thyroid cell function and survival.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112360 - TRANSCRIPTOMIC PROFILING OF THYROID CELLS EXPOSED TO ROUNDUP® ORIGINAL DI REVEALS DOSE-DEPENDENT EFFECTS: IMPLICATIONS FOR SAFETY STANDARDS

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Thyroid nodules are a major global health concern because of their high prevalence, and the incidence of malignant nodules is increasing. Endocrine disruptors are considered risk factors for thyroid cancer and include glyphosate, which has been classified as probably carcinogenic to humans and is the active ingredient of the most widely used herbicide worldwide. However, it remains unclear how different doses of glyphosate-based herbicides influence molecular pathways in normal thyroid cells and those already harboring mutations. We performed RNA-seq analyses on Nthy-ori 3-1 human cell line and papillary-derived thyroid cell (TPC-1) lines exposed to 65, 160, and 830 µg/L of Roundup® for 24h, in triplicate. Differentially expressed genes (DEGs) were identified with $p < 0.05$ and fold-regulation > 2 or < -2 . In Nthy-ori, we identified 116, 126, and 146 DEGs in the cells exposed to 65, 160, and 830 µg/L, respectively. Most genes were down-regulated (64%, 63% and 75%, respectively). ENSG00000289226, annotated as a long non-coding RNA (lncRNA) in Ensembl, was the only upregulated at all concentrations. lncRNAs are known to play critical roles in gene regulation and cellular responses to chemical stressors. Dysregulation of ENSG00000289226 may reflect alterations in regulatory pathways sensitive to glyphosate, such as epigenetic processes or oxidative stress responses. In TPC-1 cells, the groups treated with 65, 160, and 830 µg/L contained 152, 192, and 178 DEGs, respectively. However, unlike Nthy-ori 3-1, most genes were up-regulated (60%, 79% and 61%, respectively). Of the 11 common DEGs across concentrations, eight were upregulated, suggesting that Roundup® differentially affects the transcriptomes of control and mutant thyroid cells at different doses. Notably, a dose of 160 µg/L, corresponding to the acceptable daily intake established by regulatory agencies, resulted in the highest number of upregulated genes in both the control and papillary cell-derived cell lines, highlighting the potential molecular impacts associated with levels considered safe.

HYPERTHYROIDISM

1112436 - INFILTRATED MACROPHAGES CONTRIBUTE TO CARDIAC HYPERTROPHY ASSOCIATED WITH HYPERTHYROIDISM

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Introduction: Recent research has revealed the essential roles of leukocytes in cardiac homeostasis and stress-induced responses. Thus, new therapeutic approaches for treating cardiac disease that target the strength of immune response have shown promise. **Objective:** Considering that the heart is one of the main targets of thyroid hormone (TH) and that patients with hyperthyroidism present increased episodes of arrhythmia, cardiac hypertrophy, and cardiovascular dysfunction, we aimed to verify the role of immune cells in TH-induced cardiac alterations. **Methods:** Hyperthyroidism was mimicked in mice by daily injections (i.p.) of triiodothyronine (14 µg/100 g BW) for 7 or 14 days. **Results:** Here we observed that elevated heart mass and heart rate in hyperthyroidism were accompanied by an increase in the cardiac neutrophils, dendritic cells, monocytes, and macrophages when assessed by flow cytometry. No changes in leukocytes were detected in the blood of hyperthyroid mice. In vitro studies revealed a shift towards pro-inflammatory polarization in bone marrow-derived macrophages upon stimulation with TH. Macrophage depletion inhibited cardiac hypertrophy, tachycardia, and the elevated expression of the pro-inflammatory cytokine interleukin-(IL)-6 in mice induced to hyperthyroidism. In conclusion, these new findings highlight the involvement of macrophage in cardiac changes associated to hyperthyroidism. **Conclusion:** Considering that sustained cardiac growth and tachycardia can potentially progress to heart failure, our findings may provide new insights for future therapeutic studies in hyperthyroidism.

1112664 - MOLECULAR AND CLINICAL UPDATE IN THYROTOXIC PERIODIC PARALYSIS: A COMPREHENSIVE 30-YEAR STUDY OF A LARGE BRAZILIAN COHORT

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Introduction: Thyrotoxic periodic paralysis (TPP) is a well-documented complication of hyperthyroidism, predominantly affecting Asian males but increasingly recognized in Western populations. This condition is characterized by hypokalemia and episodic muscle paralysis due to a sudden intracellular shift of potassium. Timely potassium supplementation is critical to prevent severe cardiopulmonary complications and can expedite recovery, with definitive control of hyperthyroidism leading to symptom resolution. Genetic factors, particularly mutations in the KCNJ18 gene (Kir2.6 channel), have been implicated, with our research revealing this mutation in a subset of patients. **Objectives:** This study aimed to assess the presence of Kir pathogenic variants in a cohort of Brazilian patients diagnosed with TPP, dating back to our first case in 1994 at the University Hospital. **Methods:** We evaluated patients with TPP at our institution and those referred for genetic testing. Clinical data were collected, and genetic testing for germline variants in Kir2.6 was conducted using Sanger sequencing. **Results:** A total of 73 patients were included, with 97.2% being male. Ethnic backgrounds consisted of 7 Asians, 22 Caucasians, 5 Black, 28 admixture Black and White, and 1 Indigenous, with 4 cases lacking ethnicity data. Graves's disease was the leading etiology of thyrotoxicosis (66/69 cases, 95.6%). However, 49/66 (74.2%) patients were first diagnosed with paralysis and were unaware of their thyroid condition. Importantly, no patient presented new TPP crises after thyrotoxicosis treatment. Kir2.6 variants were identified in 8 out of 67 patients (11.9%), including Gln407Stp, Thr354Met, Arg399Stp, Arg386Cys, Asn252Asp and Phe263Leu. **Conclusion:** TPP remains an underdiagnosed endocrine emergency. With increasing recognition of TPP in Western countries, early diagnosis and treatment are vital in preventing life-threatening complications associated with hypokalemia. Assessing thyroid function in patients with hypokalemic paralysis is essential for distinguishing TPP from other hypokalemic periodic paralysis forms.

HYPERTHYROIDISM

1112560 - NEUTROPENIA IN CHILDREN WITH GRAVES' DISEASE TREATED WITH METHIMAZOLE: A CHINESE CHILDREN COHORT (3C) STUDY

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Introduction: Hyperthyroidism caused by Graves disease (GD) is a rare disease in children. Methimazole (MMI) was recommended as the first-line therapy for children with GD. However, few studies have focused on MMI-associated neutropenia. We conducted a large-sample, long-term and closely monitored cohort study, aiming to investigate the clinical characteristics and risk factors of MMI-associated neutropenia. **Methods:** A cohort study was carried out to analyze the longitudinal clinical and biochemical data of 382 pediatric patients with GD who received MMI treatment. All patients were followed up at 0.5, 1, 2, 3, 4, 5, 6, 9 and 12 months after treatment. Data were collected both retrospectively and prospectively. Neutropenias were categorized as mild (absolute neutrophil count [ANC] $1.0-1.5 \times 10^9/L$), moderate (ANC $0.5-1.0 \times 10^9/L$), and severe (ANC $< 0.5 \times 10^9/L$, agranulocytosis). Multivariate logistic regression analysis was used to determine the risk factors for MMI-associated neutropenia. The study was registered in the Clinical Trial Registry (NCT06570967). **Results:** Among the 382 patients with GD, 94 patients (24.6%) developed neutropenia. Specifically, 56.3% and 69.1% of them occurred within the first 2 weeks and 1 month following the treatment, respectively. Among the 94 patients, 76 (80.9%) had mild neutropenia, 16 (17.0%) moderate neutropenia, and 2 (2.1%) severe neutropenia (agranulocytosis). Subsequent to the reduction of MMI dosage and the administration of granulopoietic agents, the ANC levels in the patients with agranulocytosis normalized. Small thyroid size (OR=1.525, 95%CI: 1.140-1.783) was a risk factor for MMI-associated neutropenia, whereas, age (OR=0.909, 95%CI: 0.836-0.987), and baseline levels of ANC (OR=0.792, 95%CI: 0.674-0.932) exhibited a negative association with neutropenia. **Conclusions:** Neutropenia is prevalent in GD children treated by MMI, which often occurs within the first month following the treatment, particularly within the first 2 weeks of treatment. ANC levels should be closely monitored in GD children who are younger or whose baseline ANC levels are less than $3 \times 10^9/L$.

1112530 - RESTING CARDIAC SYMPTOMS CAN PERSIST IN PATIENTS WITH GRAVES' DISEASE TREATED TO STABLE EUTHYROIDISM

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Introduction: Patients with Graves disease often experience cardiac symptoms which improve when hyperthyroidism is adequately treated with antithyroid drugs. A subgroup of patients has persisting symptoms despite achieved euthyroidism. **Objective:** The study aimed to describe the subgroups cardiac symptoms and investigate their origin with a thorough cardiac work up. **Methods:** 75 patients (median age 42 years, interquartile range (IQR): 35-49 years; 89.3% female) with Graves disease and cardiac symptoms were included. All had achieved euthyroidism at least 3 months prior (median 31 months, IQR: 13-50 months). The patients underwent resting 12-lead electrocardiogram, 24-hour ambulatory electrocardiogram monitoring, transthoracic echocardiography, and an exercise stress test. **Results:** The cardiac symptoms were palpitations (98.7%), chest discomfort (50.7%), dyspnoea (42.7%) and near syncope (16.0%). Symptoms primarily occurred during rest. 24-hour ambulatory electrocardiogram monitoring showed normal sinus rhythm. 33.3% of the patients registered symptoms during the 24 hours with a few of the symptoms being associated with supraventricular ectopic beats (8.0%), ventricular ectopic beats (9.0%), or sinus tachycardia (8.0%). No cardiac symptoms were reported during the exercise stress test and no pathological electrocardiographic changes were observed. A significant echocardiographic finding was left atrial enlargement (13.3%). **Conclusion:** Cardiac symptoms persisted in some patients with Graves disease despite achievement of euthyroidism. The symptoms were not caused by structural or functional changes of the heart nor by cardiac arrhythmias other than ectopic beats.

HYPERTHYROIDISM

1112364 - TIME-DEPENDENT CHANGES OF THE RISK OF ATRIAL FIBRILLATION IN PATIENTS WITH HYPERTHYROIDISM RECEIVING RADIOACTIVE IODINE TREATMENT COMPARING TO ANTI-THYROID DRUG: A NATIONWIDE COHORT STUDY

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Introduction: Graves disease (GD) has been known for the increased risk of atrial fibrillation (AF) compared to the general population. However, whether treatment modalities, especially for radioactive iodine (RAI) therapy for GD are associated with the risk of AF remains controversial with discordant results. **Methods:** Using the Korean National Health Insurance Service-National Health Information Database (NHIS-NHID, 2002-2020), we investigated time-dependent hazard ratios (HRs) of overall cardiovascular disease (CVD) and AF in patients with GD receiving RAI therapy compared to the age-, sex-, and health check-up data matched patients with GD receiving only anti-thyroid drugs (ATD) in a 1:5 ratio. **Results:** Of 54,012 patients with GD (36,258 women and 18,754 men; mean age [SD], 42 ± 12 years), 9,002 received RAI therapy and 45,010 received only ATD therapy. During 2004-2020, the overall CVD incidence rates were 3.36 and 3.52 per 1,000 person-years in the RAI and ATD groups, respectively, with an unadjusted HR of 0.96 (95% CI, 0.841-0.9); this remained at 0.93 (95% CI, 0.781-1.1) after adjustment for multiple clinical confounding factors. For AF, incidence rates were 2.44 and 2.83 per 1,000 person-years in the RAI and ATD groups, respectively, with an adjusted HR of 0.86 (95% CI, 0.701-0.6); however, the risk of new-onset AF peaked at 1 year since RAI therapy (HR 1.75, 95% CI, 1.232-5.0) and gradually declined thereafter, with an HR of 0.61 (95% CI 0.450-0.84) observed after 3 years. **Conclusion:** This study identified that the overall CVD and AF risks in GD patients with RAI therapy compared to those with ATD only were not significant. However, the risk of a new onset AF increased until 1 year and then decreased significantly. Further long-term studies are needed in terms of CVD risks and the advantages of RAI in patients with GD.

1114179 - CHRONIC IODINE EXCESS INDUCED TSH ELEVATION BY INACTIVATING TYPE 2 DEIODINASE VIA ROS/AKT-MTOR-GSK3B/NRF2 SIGNALING PATHWAY

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Introduction: Prolonged high iodine intake can increase the prevalence of non-autoimmune subclinical hypothyroidism, associated with accelerated degradation of pituitary type 2 deiodinase (D2) ubiquitination. D2 is a selenoprotein, activating by selenocysteine (Sec) activation centre. **Objective:** We aim to explore D2 biosynthesis variations in the pathogenesis. **Methods:** Male Wistar rats were administered with normal iodine (NI group) and 50-fold high iodine (HI group), respectively. When serum TSH elevation was detected in the HI group, single-cell sequencing (scRNAseq) were performed on the rat pituitary. Protein detection were validated in vivo and vitro GH4C1 experiments. **Results:** Separately 14044 and 6121 pituitary cells were subjected to scRNAseq in the HI and NI groups. In the HI group, the proportion of cells with TSH synthetic ability was raised, and the differentiation and transdifferentiation from stem cells, multi-hormone cells and other endocrine-hormone cells to TSH cells was also increased. Comparing with the NI group, subgroup analysis and pseudotime analysis revealed that TSH α and TSH β were continuous high expression in the HI group. Differential expression analysis found that D2 and a series of Sec synthetic genes SBP2, Sars2, Pstk, Sephs2, Sepsecs, and Ecfsec were low expressed. Pathway enrichment analysis showed high accumulation of oxygen reactive species (ROS), while the antioxidant pathway AKT-mTOR-GSK3 β /NRF2 was significantly downregulated ($P < 0.05$). The above results were validated in vivo and vitro experiments. In vitro experiment, blocking ROS, or activating NRF2 could obviously improve the D2 suppression induced by high iodine. Blocking NRF2 could remarkably inhibit the D2 high-expression in normal iodine ($P < 0.05$). **Conclusion:** In the pituitary gland, the proliferation of TSH cells was increased, and more cells were differentiate and transdifferentiate into TSH cells. In the pituitary cell, excess iodine-induced oxidative stress and the inhibition of AKT-mTOR-GSK3 β /NRF2 antioxidant pathway, leading to D2 inactivation and a weaken of the negative feedback of TSH synthesis.

HYPOTHYROIDISM

1112446 - HYPOTHYROIDISM PROMOTES A SARCOPENIA-LIKE PHENOTYPE IN YOUNG BUT NOT IN AGED MICE

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Introduction: Hypothyroid patients commonly present skeletal muscle dysfunction. Interestingly, hypothyroidism prevalence and age-related myopathies increase with age. However, little is known about the relationship between hypothyroidism and skeletal muscle aging. **Objective:** Investigate whether hypothyroidism contributes to sarcopenia development. **Methods:** Hypothyroidism was induced by a standard diet supplemented with 0.15% propylthiouracil in young (2 months) and aged (18 months) C57BL/6 male mice for four months. Following euthanasia, the tibialis anterior (TA) muscle was dissected for gene expression analysis using qPCR. Data were expressed as mean $\pm$ standard deviation and analyzed by Two-way ANOVA. **Results:** At months 2 and 3, hypothyroidism reduced the forelimb grip strength in young mice, and decreased the locomotion in both ages. The Thra1 mRNA levels increased, while Hr mRNA levels reduced in HYPO groups of both ages. Only young mice showed increased Myh7 (MyHC I) mRNA levels in the HYPO group, but Myh2 (MyHC IIa) mRNA levels increased in HYPO groups of both ages. No changes in mRNA levels were observed in Myh4 (MyHC IIb) and Myh1 (MyHC IIx). The TA predominant fibers are the glycolytic type IIx/b. Thus, an increase in oxidative fibers (MyHC I and IIa) suggests a shift in the glycolytic-to-oxidative fiber profile in both young and aged mice. Hypothyroidism reduces muscle mass in young and increases the atrophic myokine myostatin mRNA (Mstn) levels in both ages. Although Foxo3 mRNA levels doubled in the HYPO-young group, no changes were observed in Foxo3-induced genes: Fbox32 (Murf-1), Trim63 (Atrogin), and Map1lc3b (LC3B). **Conclusion:** Our results show that hypothyroidism reduces muscle strength and mass in young mice, and decreases locomotion activity in both ages. Furthermore, hypothyroidism induces atrophic myokine Mstn and fast-to-slow fiber type shift in the TA muscle. Our data suggest that hypothyroidism promotes a phenotype sarcopenia-like, especially in young mice.

1114292 - SUBCLINICAL HYPOTHYROIDISM AS A RISK FOR CORONARY ARTERY BYPASS GRAFTING

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Introduction: The relationship between hypothyroidism and cardiovascular disease is well established. However, data on subclinical hypothyroidism (SH) and its impact on major adverse cardiovascular events (MACE) and postoperative complications following coronary artery bypass grafting (CABG) remain limited. **Objective:** This study aimed to evaluate whether SH is associated with an increased risk of these outcomes. **Methods:** From 2010 to 2019, 863 patients who underwent CABG for cardiovascular diseases at a reference center were recruited. The primary outcomes included MACE (composite and individual events: all-cause death, cardiovascular death, stroke, acute myocardial infarction [AMI], and new revascularization) and postoperative complications, including atrial fibrillation (AF), pleural effusion (PLE), pericardial effusion (PCE), infections at any site (IAS), and mediastinitis. **Results:** SH patients had higher rates of MACE (20.3% vs. 8.2%, $p=0.001$), MACE 4p (22.0% vs. 12.9%, $p=0.002$), and stroke (10.2% vs. 3.0%, $p=0.013$) than those of euthyroid patients. No significant differences were observed in all-cause death, cardiovascular death, AMI, or new revascularization. Postoperative complications were also more frequent in the SH group: AF (18.6% vs. 9.7%, $p=0.043$), PLE (52.6% vs. 19.2%, $p<0.0001$), PCE (20.3% vs. 7.8%, $p=0.03$), and IAS (28.8% vs. 16.9%, $p=0.032$). However, no significant difference was noted in the incidence of mediastinitis. **Conclusion:** Subclinical Hypothyroidism patients who underwent CABG had a higher frequency of MACE and postoperative complications than those of euthyroid patients.

HYPOTHYROIDISM

1112223 - THE IMPACT OF HEALTH LITERACY ON HYPOTHYROIDISM MANAGEMENT IN PATIENTS UNDERGOING LEVOTHYROXINE THERAPY

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Introduction: Hypothyroidism, a prevalent endocrine disorder, affects quality of life and requires effective management through levothyroxine (L-T4) therapy. Despite its effectiveness, challenges in treatment adherence and disease control persist, often linked to patients' health literacy levels. **Objective:** This study aimed to evaluate the relationship between health literacy and thyroid-stimulating hormone (TSH) levels in patients undergoing L-T4 treatment, exploring its potential influence on disease management. **Methods:** A cross-sectional study was conducted with 355 adult patients diagnosed with primary hypothyroidism at a specialized clinic in São Paulo, Brazil. Health literacy was assessed using the Newest Vital Sign (NVS) scale, and TSH levels were obtained from medical records. Regression analyses examined the association between health literacy and TSH, adjusting for age, sex, education level, and treatment duration. Additional chi-square tests explored categorical variables. **Results:** Health literacy was significantly associated with lower TSH levels (coefficient = -0.20, $p < 0.001$), suggesting a 20% reduction in TSH for each additional point on the NVS scale. Age, sex, and treatment duration were not statistically significant predictors. The model explained 19% of TSH variation ($R^2 = 0.19$). Interactions between health literacy and age or sex did not improve the model. Exploratory analyses revealed that non-linear models, such as a quadratic regression, slightly enhanced explanatory power ($R^2 = 0.285$), while additional variables like comorbidities (hypertension, diabetes, dyslipidemia) were not significant contributors. **Conclusion:** Health literacy emerges as a key factor in hypothyroidism management, directly influencing TSH control. These findings underscore the importance of tailored educational interventions to enhance health literacy, particularly in vulnerable populations, to optimize treatment adherence and clinical outcomes. Future strategies should integrate personalized education to bridge gaps in disease understanding and promote effective self-management.

1112656 - IODINE, HEAVY METALS, AND THYROID FUNCTION IN PREGNANCY: A CROSS-SECTIONAL STUDY IN BOTUCATU, BRAZIL

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Introduction: Iodine is essential for the synthesis of thyroid hormones, which play a crucial role in fetal development during pregnancy. Maternal iodine deficiency during gestation has been linked to adverse outcomes such as preterm birth, low birth weight, and increased risk of maternal and fetal thyroid dysfunction. Similarly, exposure to endocrine-disrupting chemicals (EDCs) like lead and arsenic has been associated with comparable adverse obstetric outcomes. **Objective:** To assess the median urinary iodine concentration (UIC), urinary lead and arsenic levels, and their association with thyroid-stimulating hormone (TSH) levels in pregnant women. **Methods:** A cross-sectional study was conducted involving 53 pregnant women using the public health system in the municipality of Botucatu, Brazil, from 2021 to 2024. Eligible participants were pregnant aged ≥ 18 years, while those with reported thyroid disorders were excluded. UIC, lead, arsenic, and TSH levels were stratified into tertiles for analysis. Statistical methods included Pearson's correlation coefficient and agreement analysis between tertiles, with a 95% confidence interval. **Results:** Among the 46 participants eligible for iodine analysis, the median UIC was 227.6 $\mu\text{g/L}$, indicating adequate iodine nutrition. However, 48% of the women exceeded the recommended intake, while 26% had levels below the recommendations. No statistically significant association was observed between urinary iodine tertiles and TSH levels ($p > 0.05$). Urinary lead levels were elevated in 66% of participants, while 7.55% had arsenic levels above safety thresholds. No association was found between the levels of these heavy metals and TSH. **Conclusion:** While most participants exhibited adequate iodine nutrition, nearly one-quarter had insufficient intake. Despite this, no significant alterations in thyroid function were observed. Elevated lead levels were prevalent, yet no significant correlation with TSH levels was observed. Even so, exposure to these substances can cause postnatal changes, which would require some future recommendations in local health policies.

IODINE DEFICIENCY

1112508 - MILD IODINE DEFICIENCY DURING THE INTRAUTERINE PERIOD DISRUPTS THE PITUITARY-THYROID AXIS OF THE OFFSPRING DURING ADULT LIFE

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Introduction: Iodine is crucial for thyroid hormone biosynthesis and development. While the consequences of severe iodine deficiency are well-documented, the impact of mild iodine deficiency (MID) during pregnancy remains unclear. Additionally, although previous studies showed adverse effects of MID on offsprings neurological development, data on thyroid function is still lacking. **Objective:** This study aimed to investigate the consequences of MID during pregnancy on the programming of pituitary-thyroid axis dysfunction in offspring animals during adulthood. **Methods:** Female CD1 mice were subjected to iodine-deficient animal chow and iodine-supplemented water, either at normal (NI; 0.2 mg NaI/L) or MID (0.08 mg NaI/L) levels during the intrauterine period. Pituitary and thyroid gene/protein expression of adult (PND90) male and female offspring were assessed using qPCR and Western blotting. The study also explored the role of epigenetic mechanisms in MID-induced programming of offspring thyroid gene expression. **Results:** Maternal MID exposure increased the gene/protein expression of the beta subunit of TSH (TSHB) in the pituitary of MID-exposed animals. The offspring from MID-exposed dams presented increased thyroid gene/protein expression of NIS, TSHR, TPO, MCT8, and TG. Interestingly, a decrease in T4 serum levels was observed in female animals, whereas no significant changes were detected in males. Thyroid expression of epigenetic enzymes involved in transcriptional repression (Dnmt1, Hdac3, Kdm5c) was reduced in MID-exposed animals. Conversely, the expression of enzymes involved in transcriptional activation (Kdm6a, Hat1) was increased exclusively in the thyroid of MID-exposed male animals. Additionally, MID-exposed offspring exhibited an increased content of H3K4me3, a marker of transcriptional activation, and a decreased content of H3K27me3, a marker of transcriptional repression. **Conclusion:** MID exposure during pregnancy disrupted the pituitary-thyroid axis function of the offspring animals during adulthood. These findings reinforce the importance of monitoring iodine intake throughout pregnancy to prevent thyroid disorders in offspring during adulthood.

THYROID AND PEDIATRIC DISEASE

1112574 - MATERNAL HYPOTHYROXINEMIA IN EARLY PREGNANCY AND OFFSPRING NEURODEVELOPMENT: A PROSPECTIVE INTERVENTION STUDY

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Introduction: Maternal hypothyroxinemia is associated with adverse neurodevelopmental outcomes in offspring, but the evidence is inconclusive. **Objective:** This study aims to investigate the relationship between hypothyroxinemia and child neurodevelopment and to explore the impact of levothyroxine treatment. **Methods:** This is a prospective cohort study that recruited women in the first 8 weeks of pregnancy for thyroid function screening. Maternal hypothyroxinemia in pregnancy is defined as normal TSH levels with low FT4 (<10th). Severe hypothyroxinemia is defined as FT4 below the 5th percentile. The LT4 treatment group received adjusted dosages of LT4 to maintain euthyroid status. Their offspring was assessed using the CBCL2-3 scale at 2-3 years of age and the SRS and ABC scales at 5-6 years of age. **Results:** A total of 147 mother-child pairs were included in this study, with 51 pairs in the hypothyroxinemia group, of which 38 were severe; 42 pairs in the LT4 treatment group, and 54 in the normal control group. The results from the CBCL scale indicated that offspring with hypothyroxinemia had significantly higher scores in withdrawal, depression, and aggression, as well as significantly higher total T-scores, with no significant differences between the treatment and control groups. The SRS showed that offspring with hypothyroxinemia had significantly higher scores in social perception, social cognition, social communication, social motivation, and total scores. The ABC indicated that the language ability, self-care ability, and total scores of the offspring in hypothyroxinemia group were significantly higher. Early pregnancy hypothyroxinemia (OR=4.81) and severe hypothyroxinemia (OR=6.37) were significantly associated with an increased risk of behavioral problems in offspring. There was no significant correlation between the LT4 treatment group and offspring behavioral problems. **Conclusion:** Offspring of mothers with hypothyroxinemia exhibit more cognitive and behavioral problems, which are more pronounced in male offspring. LT4 treatment in early pregnancy can improve behavioral problems.

THYROID AND PEDIATRIC DISEASE

1112225 - NEWBORN SCREENING FOR CONGENITAL HYPOTHYROIDISM: WORLDWIDE COVERAGE 50 YEARS AFTER ITS START

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Introduction: Congenital hypothyroidism (CH) is a preventable cause of neurodevelopmental delay in children, detectable by newborn screening programs (NBS) for CH. Since NBS for CH was started in Canada in 1974, numerous countries have successfully implemented this public health strategy. However, in 2014, only 29.3% of newborns worldwide were screened by NBS for CH. **Objective:** This study aimed to assess the implementation of new NBS for CH programs over the past decade, and screening methods and coverage rates of current programs. Additionally, it sought to update the worldwide iodine status. **Methods:** We reviewed literature data on NBS programs for CH and their coverage rates for each country, using PubMed, Embase and Google searches. **Results:** Currently, 29.6% of children worldwide are screened for CH. Europe, North America, Oceania, China, Japan and Israel have efficient programs with optimal coverage. Recently, some countries of Central and Western Asia implemented NBS for CH programs, and coverage has increased in several Asian countries. South America has also seen substantial improvements in coverage. In contrast, almost none of the African countries has widespread screening programs, but some attempts with pilot studies and local initiatives have been witnessed. Global iodine sufficiency has improved, with 149 of 193 countries achieving adequate iodine levels by 2023. **Conclusions:** Over the past decades several countries have launched NBS programs for CH or conducted pilot studies, and the coverage of most existing NBS programs increased. Nevertheless, approximately 70% of newborns worldwide still lack access to NBS for CH, predominantly in African and Asian countries, accounting for a significant part of annual births.

THYROID AND PREGNANCY

1113717 - GESTATIONAL HYPOTHYROXINEMIA DAMAGES THE INTESTINAL INTEGRITY IN THE ILEUM OF THE ADULT OFFSPRING

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Introduction: Gestational hypothyroxinemia (HTX) is a frequent thyroid condition that occurs earlier in pregnancy, characterized by low levels of L-3,5,3',5'-tetraiodothyronine (T4) with normal levels of L-3,5,3'-triiodothyronine (T3) and thyroid-stimulating hormone (TSH). It has been reported in humans and in animal models that the offspring gestated in HTX has a low intelligence quotient (IQ) and increases the probability of developing autistic spectrum disorder (ASD). **Objective:** Given that it has been reported that ASD patients have altered intestinal permeability, we aim to evaluate the intestinal integrity and permeability in offspring gestated under HTX. **Methods:** Gestational HTX was induced in C57BL/6 pregnant mice during E10th-14th with 0.025% methimazole in the tap-drinking water. The control pregnant mice received only tap-drinking water. Levels of tT4, tT3, and TSH were analyzed at E14th in pregnant dams. The intestinal permeability was analyzed in vivo and ex vivo at P55. The cellular structure and the content of vesicles and granules from Goblet and Paneth cells were analyzed by transmission electron microscopy. The expression of transcripts that codify for Muc2 and antimicrobial peptides like Cryptidin-1, Cryptidin-4, and lysozyme were analyzed by RT-qPCR. The content of lysozyme was analyzed using western blot and immunofluorescence. The levels of secretory IgA (sIgA) were measured by ELISA. **Results:** Our results show increased paracellular permeability in the ileum of the HTX offspring, less expression of Muc2 and increased Cryptidin-1, Cryptidin-4, and lysozyme mRNA transcripts, and altered Paneth cell granules ultrastructure. The HTX-offspring also showed low levels of sIgA. **Conclusion:** This work shows for the first time that gestational HTX damages the integrity of the intestinal mucosa of offspring. These findings could be responsible, at least in part for the development of inflammatory responses that are associated with ASD

THYROID AND PREGNANCY

1112633 - GESTATIONAL HYPOTHYROXINEMIA DAMAGES THE INTESTINAL INTEGRITY IN THE ILEUM OF THE ADULT OFFSPRING

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Introduction: Gestational hypothyroxinemia (HTX) is a frequent thyroid condition that occurs earlier in pregnancy, characterized by low levels of L-3,5,3,5-tetraiodothyronine (T4) with normal levels of L-3,5,3-triiodothyronine (T3) and thyroid-stimulating hormone (TSH). It has been reported in humans and in animal models that the offspring gestated in HTX has a low intelligence quotient (IQ) and increases the probability of developing autistic spectrum disorder (ASD). **Objective:** Given that it has been reported that ASD patients have altered intestinal permeability, we aim to evaluate the intestinal integrity and permeability in offspring gestated under HTX. **Methods:** Gestational HTX was induced in C57BL/6 pregnant mice during E10th-14th with 0.025% methimazole in the tap-drinking water. The control pregnant mice received only tap-drinking water. Levels of tT4, tT3, and TSH were analyzed at E14th in pregnant dams. The intestinal permeability was analyzed in vivo and ex vivo at P55. The cellular structure and the content of vesicles and granules from Goblet and Paneth cells were analyzed by transmission electron microscopy. The expression of transcripts that codify for Muc2 and antimicrobial peptides like Cryptidin-1, Cryptidin-4, and lysozyme was analyzed by RT-qPCR. The content of lysozyme was analyzed using western blot and immunofluorescence. The levels of secretory IgA (sIgA) were measured by ELISA. **Results and Conclusion:** Our results show increased paracellular permeability in the ileum of the HTX offspring, less expression of Muc2, and increased Cryptidin-1, Cryptidin-4, and lysozyme mRNA transcripts, and altered Paneth cell granules ultrastructure. The HTX offspring also showed low levels of sIgA. This work shows for the first time that gestational HTX damages the integrity of the intestinal mucosa of offspring. These findings could be responsible, at least in part, for the development of inflammatory responses that are associated with ASD. Acknowledgements: ANID 21211419. IMII-ICN2021_045, Advanced Microscopy Facility UMA UC, ECOS230036. FONDECYT #1191300, 1231905.

THYROID AND PREGNANCY

1112611 - IODINE STATUS QUESTIONNAIRE ASSESSMENT DURING PREGNANCY: A PILOT STUDY.

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Introduction: Iodine is essential for thyroid function, particularly during pregnancy when it impacts both maternal and fetal health. **Objective:** This study aimed to assess iodine status among pregnant women in São Paulo, Brazil, by measuring urinary iodine concentration (UIC) and examining its association with nutritional and lifestyle factors. **Methods:** The study included 38 pregnant women. Urinary iodine concentration was determined using a single sample and a colorimetric assay, a standard method for assessing iodine status. Additionally, participants completed a detailed questionnaire addressing dietary habits, iodine supplementation, and lifestyle factors. Data analysis focused on identifying potential associations between iodine levels and socioeconomic and nutritional variables. **Results:** The iodine status of the participants showed significant variability: Deficiency: UIC ≤ 149 $\mu\text{g/L}$ - 35.8% of the participants, Adequacy: UIC 150-299 $\mu\text{g/L}$ - 28.2%, and Excess: UIC ≥ 300 $\mu\text{g/L}$ - 36.0%. Statistical analysis revealed a significant association between iodine status and family income ($p < 0.05$). No other factors, including dietary intake or supplementation, showed significant correlations with UIC levels. **Conclusion:** The findings indicate that iodine deficiency, sufficiency, and excess coexist among pregnant women in São Paulo, reflecting potential imbalances in iodine intake. While the positive association with family income suggests socioeconomic disparities in access to iodine-rich foods or supplements, other factors assessed in the questionnaire did not show significant relationships. These results underscore the need for tailored public health interventions to ensure adequate iodine intake during pregnancy. Further research with larger sample sizes and more comprehensive dietary assessments is recommended to better understand the determinants of iodine status and guide effective nutritional policies.

THYROID AND PREGNANCY

1112526 - THE NLRP3/TLR2/NFkB PATHWAY IS INVOLVED IN THE OCCURRENCE OF MISCARRIAGE IN AIT PATIENTS

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Introduction: Autoimmune thyroiditis (AIT) is a common disease of the endocrine system. Accumulating evidence suggests that NOD-like receptor protein 3 (NLRP3) inflammasomes are involved in the pathogenesis of AIT. At the same time, many studies have shown that NLRP3 is associated with spontaneous abortion (SA). **Objective:** The objectives of this study were to investigate the expression of NLRP3 in patients with AIT and SA, and to further explore the mechanism of NLRP3-mediated AIT-related miscarriage. **Methods:** According to thyroid function, the patients were divided into SA group, AIT combined with SA group, and control group. Proteomics techniques were used to look for differential proteins associated with AIT amiscarriage in decidua tissues. The expression of NLRP3 in decidua tissue, peripheral whole blood and serum was further studied in the AIT combined with SA group. Peripheral blood mononuclear cells (PBMCs) in the AIT combined with SA group and PBMCs in the control group were co-cultured with human peripheral blood mononuclear cell line (THP-1) to explore the mechanism of NLRP3-mediated AIT-related abortion. **Results:** In the proteome, it was found that the proteins related to HMGB and NOD-like receptor signaling pathways in the decidua tissue of patients with AIT and SA were significantly increased. Analysis of decidua tissue, peripheral whole blood and serum showed that NLRP3 inflammasome and its activated inflammatory cytokines IL-18 and IL-1 β were involved in the occurrence of AIT-related miscarriage. In cell experiments, it was found that AIT can directly transcribe and regulate M1 macrophages through NLRP3/TLR2/NFkB or regulate the glycolytic pathway to increase M1 macrophages, resulting in miscarriage. Specific blockade of NLRP3 can change the direction of macrophage polarization, which may reduce the occurrence of AIT-related miscarriage. **Conclusion:** AIT can directly transcribe M1 macrophages through NLRP3/TLR2/NFkB or regulate the glycolytic pathway to increase M1 macrophages, resulting in miscarriage.

1112418 - THYROID AUTOIMMUNITY AND PREGNANCY: IMPLICATIONS FOR MATERNAL AND FETAL HEALTH OUTCOMES

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Introduction: Thyroid autoimmunity is a common condition among women of reproductive age, marked by the presence of thyroid antibodies, such as anti-thyroperoxidase (anti-TPO) and anti-thyroglobulin (anti-TG). During pregnancy, thyroid autoimmunity can lead to complications like miscarriage, preeclampsia, preterm delivery, and developmental issues in the child. This study explores how thyroid autoimmunity affects pregnancy outcomes and the health of the baby. **Objective:** To assess the impact of thyroid autoimmunity on pregnancy complications and the early neurodevelopment of children. **Methods:** We conducted a cohort study with 250 pregnant women, all recruited during their first trimester. Thyroid Function: Blood tests measured TSH, free T4, anti-TPO, and anti-TG levels. Participants were classified as having subclinical hypothyroidism, overt hypothyroidism, or euthyroid autoimmunity. Pregnancy Outcomes: Data was collected on miscarriage, preeclampsia, preterm birth, and birth weight. Child Development: Babies were assessed at 12 months using standardized developmental tests. Analysis: Statistical models were used to understand the link between thyroid autoimmunity and the outcomes observed. **Results:** Anti-TPO antibodies were found in 27% of the women, and 11% developed thyroid dysfunction during pregnancy. Women with thyroid autoimmunity had a higher risk of miscarriage (2.3 times more likely) and preeclampsia (1.9 times more likely) compared to those without antibodies. Preterm births were also more common (15% vs. 8%), and babies born to mothers with thyroid autoimmunity scored lower on language and motor development tests. **Conclusion:** Thyroid autoimmunity increases the risk of complications during pregnancy and impacts the early development of children. These findings highlight the importance of thyroid screening and careful monitoring during pregnancy to improve outcomes for both mother and baby.

THYROID AUTOIMMUNITY

1112239 - COMPARATIVE ANALYSIS OF ORBITAL TISSUE MICROENVIRONMENTS IN ACTIVE VERSUS INACTIVE THYROID EYE DISEASE: A SINGLE-CELL TRANSCRIPTOMICS APPROACH

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Introduction: Thyroid eye disease (TED) is a complex autoimmune disease. **Objective:** Single-cell RNA sequencing (scRNA-seq) can comprehensively map the cellular and molecular landscapes of TED during active and inactive phases. **Methods:** scRNA-seq was performed on retro-orbital tissues from patients (n=6) with active, inactive TED, and healthy controls. Cell clustering and Milo algorithm were employed to identify cell subsets and differential abundance. Gene set scoring, pathway enrichment and pseudotime trajectory analysis were utilized to investigate dynamic cellular changes. Multicolour immunofluorescence validated the identified cell subtypes and their roles across different stages of TED, while cellular experiments confirmed the functions of these molecules. **Results:** Seven major cell types were identified in 57,850 cells, including fibroblasts, T cells, endothelial cells, and macrophages. Retro-orbital fibroblasts (OFs) exhibited significant heterogeneity, with a CD34⁺THY1⁺BGN⁺ fibroblast subset prominently enriched in active TED. These cells exhibited high expression of fibrosis-associated genes (e.g., COL1A1, FN1), and Gene set scoring revealed that these fibroblasts were highly active in inflammatory and fibrotic pathways. CD4⁺ and CD8⁺ memory T cells were significantly enriched in active TED, showing enhanced cytokine secretion and T cell receptor signaling activity. Inflammatory endothelial cells (ACKR1⁺, SELP⁺) were enriched in active TED, demonstrating strong pro-inflammatory and immune-regulatory characteristics. Macrophages in active TED upregulated immune activation-related genes (e.g., IFI44L, ISG15), while those in the inactive phase exhibited anti-inflammatory and tissue repair features (e.g., FOS, CD163). Additionally, Multicolor immunofluorescence validated that CD34⁺THY1⁺BGN⁺ fibroblasts, IL-32⁺CD8⁺Tm and ACKR1⁺SELP⁺ endothelial cells subsets were increased in active TED orbital tissues, and cellular experiments demonstrated that BGN and IL-32 promote fibrosis and inflammation progression. **Conclusion:** This study constructed a comprehensive single-cell atlas of retro-orbital tissues across different stages of TED, revealing the dynamic cellular and molecular features of the disease. These findings provide a foundation for understanding TED pathogenesis and identifying novel therapeutic targets.

1112238 - HIGH-THROUGHPUT PROTEOMICS COMBINED WITH IMMUNOHISTOCHEMISTRY OF ORBITAL CONNECTIVE TISSUE IN THYROID EYE DISEASE

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Introduction: High-throughput proteomics (HPT) helps identify characteristic signaling networks specific to certain diseases. Immunohistochemistry can uncover local orbital immunity and correlate microscopic changes with macroscopic clinical features in TED. **Objective:** Identifying biomarkers of disease progression and offering a range of potential applications in basic research and precision medicine. **Methods:** Thirty-one orbital connective tissue samples from patients with thyroid eye disease (TED, 11 with clinically severe and 12 with mild TED) and from eight control subjects were examined using HPT. We focused on the intersection of differentially expressed proteins (DEPs) that differ between severe TED and both mild TED and control. Gene ontology and the Kyoto Encyclopedia of Genes and Genomes were used to analyze DEPs. Up-regulated DEPs were subsequently verified using immunohistochemistry in another 20 orbital connective tissue samples, including 13 severe TED and 7 mild TED. **Results:** A total of 4,579 proteins were identified: 208, 790, and 847 DEPs were noted when comparing severe versus mild TED, severe TED vs control, and mild TED vs. control, respectively (all $p < 0.05$). Using a cut-off threshold of fold change ≥ 2.0 during screening, five significantly up-regulated DEPs (Latent-transforming growth factor β -binding protein 2, Lysyl oxidase homolog, Ras-interacting protein 1, Integrin beta 3, Coagulation factor XII) overlapped between severe TED and both mild TED and control. Within the TED tissue, 163 up-regulated DEPs were involved in various biological processes. Subsequent immunohistochemical validation revealed that the above five up-regulated DEPs were overexpressed in severe TED compared to mild TED, which was consistent with the HPT results and further confirmed that these five proteins were highly expressed in severe TED. **Conclusion:** For the first time, our proteomics combined with immunohistochemistry study revealed in orbital tissue of TED patients five proteins potentially implicated in disease progression, inflammation, angiogenesis, tissue remodeling and fibrosis.

THYROID AUTOIMMUNITY

1112292 - IFN α TRIGGERS AUTOIMMUNE THYROIDITIS BY RESHAPING THYROGLOBULIN IMMUNOGENIC PEPTIDE REPERTOIRE

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Introduction: IFN α , a cytokine produced during viral infections, is a major trigger of Autoimmune Thyroid Diseases (AITD). Our group showed that while IFN α upregulates thyroglobulin (Tg) gene transcription in genetically susceptible individuals it also accelerates lysosomal degradation of Tg protein. In vitro, Tg cleavage by cathepsin (CTS) L, a lysosomal protease, generates Tg.2098, a major T-cell epitope in AITD. **Objective:** To test the hypothesis that IFN α triggers AITD by altering Tg immunogenic peptide repertoire. **Methods:** We exposed ML-1 thyroid cells to IFN α and assessed the expression and activity of CTSL by western blot, immunofluorescence (IF) and enzymatic activity. We either knocked-down CTSL by siRNA or stably over-expressed it and analyzed Tg expression in ML-1 cells exposed to IFN α . We assessed CTSL role in generation of Tg.2098 in ML-1 cells treated with IFN α and CTSL-inhibitor (KPG94) by IF. To find the mechanisms by which IFN α controls CTSL in thyroid we employed pathway expression and inhibition assays in IFN α -treated thyrocytes. We developed a mouse model overexpressing IFN α in the thyroid (IFN α -TPO-Cre) and assessed the role IFN α -induced Tg degradation in experimental autoimmune thyroiditis (EAT). **Results:** IFN α triggered increased CTSL expression and activity in ML-1 cells. CTSL knock-down decreased and CTSL overexpression increased IFN α -induced Tg degradation in ML-1 cells. IF studies showed increased Tg.2098 levels in IFN α treated thyrocytes. CTSL-inhibitor treatment decreased IFN α -induced Tg.2098 levels in ML-1 cells. Analysis of the pathways controlling CTSL expression revealed activation of p38MAPK by IFN α . Inhibition of p38MAPK decreased IFN α -induced CTSL expression. IFN α -TPO-Cre mice showed decreased Tg and increased CTSL levels in the thyroid and developed Tg antibodies and T-cell responses after EAT induction. **Conclusion:** IFN α upregulates CTSL expression in thyroid, triggering Tg degradation into immunogenic peptides and development of EAT in genetically susceptible individuals. This represents a new mechanism of virally triggered AITD in predisposed individuals.

1112184 - INTEGRATED TRANSCRIPTOMIC AND EPIGENETIC PROFILING OF THYROCYTES IN AUTOIMMUNE THYROIDITIS VIA SINGLE CELL RNA-SEQ, BULK RNA-SEQ AND DNA METHYLATION PROFILING

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Introduction: Autoimmune thyroiditis (AIT) is characterized by immune cell infiltration and altered gene expression in thyrocytes. **Objective:** This study aimed to explore the transcriptomic and epigenetic landscapes of thyrocytes in AIT. **Methods:** We analyzed thyroid tissues from 20 AIT patients and 20 thyroid autoantibody-negative controls who underwent thyroidectomy. Single-cell RNA sequencing (scRNA-seq) was performed on tissues from 4 AIT patients and 4 controls. Thyrocytes from 16 AIT patients and 16 controls were isolated using Percoll gradients followed with primary culture, and validated by thyroglobulin staining to exclude immune cell contamination. Bulk RNA sequencing and DNA methylation profiling (Illumina 850K array) were conducted on these isolated thyrocytes. **Results:** scRNA-seq revealed that thyrocytes in AIT exhibited elevated expression of antigen-presenting genes (e.g., HLA-DQA1), chemokines and receptors (CXCR6, CXCL8, CXCL13, CCR2, CCL3, CCL4), adhesion molecules (ICAM2), and T-cell signaling genes (CD40LG, IRF1), suggesting an active immune-interacting role. Conversely, thyroid hormone production genes (PAX5, PAX8, TG, TPO, DUOX1) were downregulated. Upregulated genes were enriched in pathways linked to autoimmunity (e.g., T1DM, IBD, asthma). Bulk RNA-seq validated these findings, identifying 621 upregulated genes enriched in these pathways. DNA methylation profiling revealed 32,837 hypomethylated and 61,990 hypermethylated CpG sites, corresponding to 2,233 and 1,843 genes, respectively. Within the TSS500 region, hypomethylation correlated with increased expression of the previously mentioned immune-interacting genes, indicating epigenetic dysregulation. **Conclusion:** This study highlights the distinct transcriptomic and epigenetic profiles of thyrocytes in AIT, suggesting their potential role as unprofessional antigen-presenting cells. These findings provide new insights into thyrocyte-mediated autoimmunity and identify potential therapeutic targets.

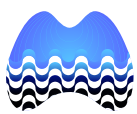
THYROID AUTOIMMUNITY

1112282 - RELATIONSHIP BETWEEN SERUM LEVELS OF SIROLIMUS (RAPAMYCIN) AND OUTCOME OF MODERATE-TO-SEVERE, ACTIVE GRAVES ORBITOPATHY

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Introduction: Sirolimus is an immunosuppressive drug with antiproliferative and antifibrotic properties. Treatment with sirolimus was recently found to be associated with a better outcome of moderate-to-severe, active Graves orbitopathy (GO) at 24 weeks compared to methylprednisolone. Here we investigated whether serum levels of sirolimus can predict the outcome of GO. **Methods:** Retrospective investigation in 30 patients [males: 4; females: 26; age 61.3 (9.62) yr] with moderate-to-severe, active GO treated with sirolimus (2 mg orally on the first day, followed by 0.5 mg per day for 12 weeks), given as second-line treatment. Eighteen were overall GO responders and 12 nonresponders at 24 weeks. Primary outcome: serum levels of sirolimus in overall GO responders vs nonresponders at 24 weeks. Secondary objective: to establish a cut-off value of sirolimus concentrations predictive of overall response to treatment at 24 weeks. **Results:** Serum levels of sirolimus at 12 weeks were higher in overall GO responders [4.6 (2.2) ng/mL] than in nonresponders at 24 weeks [2.8 (1.6) ng/mL; mean difference 1.7; 95% CI from 0.1 to 3.1; P=0.034]. Thus, a cut-off value of sirolimus concentrations at 3.5 ng/mL was established. Sirolimus levels ≥ 3.5 ng/mL were more frequent in overall GO responders than in nonresponders at 24 weeks [13/18 (72.2%) vs 3/12 (25%); OR: 7.8; 95% CI from 1.4 to 41.2; P=0.015], with a positive predictive value of 81.2% (95% CI from 60.9 to 92.3), a sensitivity of 72.2% (95% CI from 46.5 to 90.3), and a specificity of 75% (95% CI from 42.8 to 94.5). **Conclusions:** In patients with moderate-to-severe, active GO treated with sirolimus, the drug serum levels at 12 weeks are predictive of overall response at 24 weeks and suggest a direct dose-response relationship.



1112533 - SPECIFIC INTRA-ORBITAL FAT AND MUSCLE LYMPHOCYTE INFILTRATES ARE ASSOCIATED WITH DIFFERENT CLINICAL MANIFESTATIONS OF THYROID EYE DISEASE

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Introduction: Thyroid Eye Disease (TED) is usually characterized by an active inflammatory phase, assessed by clinical activity score (CAS) $\geq 3/7$, followed by an inactive fibrotic phase, which are treated with immunosuppressants (i.e. intravenous methylprednisolone, ivMP) and rehabilitative orbital surgery, respectively. Dysthyroid optic neuropathy (DON) is a severe TED complication requiring both emergency ivMP and surgery. **Objective:** We aimed to identify the phenotypes of orbital-infiltrating lymphocytes related to different clinical TED manifestations. **Methods:** Orbital surgery was performed in 20 DON and 35 inactive TED (TED-I) patients, of which 22 had never been treated with steroids (TED-I-Naïve), whereas 13 received ivMP 3.9 ± 4.4 (mean $\pm$ SD) years before surgery to inactivate TED (TED-I-MP). All DON patients had active disease and were treated with ivMP 0.4 ± 0.8 years before orbital decompression. Lymphocytes were derived from retroorbital tissues (both fat and extraocular muscles) and immunophenotyped by flow cytometry (21 surface/intracellular markers). **Results:** The degree of orbital lymphocytic infiltration positively correlated with CAS ($p < 0.005$), and negatively with disease duration ($p < 0.05$). DON and TED-I-MP patients showed significantly increased fat-infiltrating CD45+, B, T and T follicular helper (Tfh) lymphocytes, compared to TED-I-Naïve patients ($p < 0.05$). In DON patients lymphocyte infiltration (all subtypes) was markedly increased within muscles compared with fat ($p < 0.0005$). **Conclusion:** The degree of orbital lymphocyte infiltration correlated with TED activity and disease duration, supporting the indication to use immunosuppressants in the early phase of disease. Follicular responses (Tfh cells) seem crucially involved in the most severe TED forms. Interestingly, inactive TED patients who were treated years before with ivMP (TED-I-MP) showed orbital-fat lymphocytic infiltration different from those never treated (TED-I-Naïve), but similar to patients with active TED complicated with DON. Importantly, extraocular muscle infiltration was markedly increased especially in DON patients, with inflammatory muscle hypertrophy and enlargement leading to optic nerve compression.

THYROID AUTOIMMUNITY

1112363 - THERMOGRAPHIC ASSESSMENT OF THYROID EYE DISEASE IN RESPONSE TO STEROID THERAPY

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Introduction: Thyroid Eye Disease (TED) is an orbital condition linked to thyroid dysfunction, characterized by inflammation, vasodilation, and tissue remodeling, often resulting in localized temperature increases. Thermography, which detects infrared radiation emitted by tissues, has emerged as a promising tool for monitoring inflammatory activity and assessing therapeutic responses. **Objective:** This study aimed to evaluate the response to methylprednisolone pulse therapy in active TED using thermography. **Methods:** This prospective study included patients with TED, Clinical Activity Score (CAS) ≥ 3 , and moderate-to-severe TED as defined by the European Group on Graves Orbitopathy (EUGOGO). Patients underwent methylprednisolone therapy (500 mg weekly for six weeks), with external orbital temperatures assessed before, during, and after treatment. Thermal imaging was conducted using the PrediktaStation device in a controlled environment (24 °C, 50% humidity). Patients were acclimated for 10 minutes before imaging, and thermal images were captured at 30 cm, focusing on the eyes and cervical region. Orbital and periorbital regions of interest were analyzed with Python routines, extracting maximum and average temperatures. **Results:** A total of 23 patients were followed for six weeks. Thermal imaging revealed a progressive reduction in orbital temperatures during treatment, with an average decrease of 2.8 °C, representing a significant 9.1% reduction ($p < 0.05$). After the first pulse, 91.3% of patients showed a significant periorbital temperature drop of 1.35 °C below baseline ($p < 0.05$). Additionally, 86.9% experienced a continuous decline in orbital temperatures over the first three sessions, correlating with CAS score improvements. Later measurements showed slight temperature increases and stabilization, despite unchanged CAS scores. **Conclusion:** Thermography, as a non-invasive tool, offers valuable insights into the inflammatory processes of TED, often undetectable by conventional methods. The thermographic profiles observed highlight its potential for monitoring treatment responses and optimizing therapeutic strategies in TED management.

1113636 - ALK INHIBITION PROLONGS SURVIVAL IN A MOUSE MODEL OF ALK-POSITIVE ANAPLASTIC THYROID CANCER

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Introduction: Anaplastic thyroid cancer (ATC) is the most aggressive thyroid cancer with a median survival of about 6 months. So far, no therapies offering a survival benefit are established. Thus, new therapeutic approaches are urgently needed. In general, genetic alterations leading to ATC increase PI3K and MAPK/ERK signalling and include mutations in receptor tyrosine kinases and tumour suppressor genes. They often coincide with P53 loss, the most prevalent mutation in human ATC. Among such mutations are mutations and rearrangements of the anaplastic lymphoma kinase (ALK) gene. **Objective:** To investigate the role of ALK mutation and Trp53 in ATC development and assess potential therapeutic effects of ALK inhibition. **Methods:** We generated a mouse model with inducible thyrocyte-specific expression of constitutively active mutant ALKF1174L and homozygous deletion of Trp53 due to a Cre recombinase under control of the thyroglobulin promoter (Tg-CreERT2+/0;LSL-ALKF1174L/+;Trp53LoxP/LoxP mice, here referred to as Trp53KO/ALKF1174L mice). Moreover, we established primary thyroid cancer cell lines harbouring ALKF1174L and Trp53KO and examined the effects of ALK inhibition in vitro and in vivo. **Results:** Median survival of Trp53KO/ALKF1174L mice was severely reduced and the mice showed massively enlarged thyroids. Histopathology confirmed locally invasive and metastatic ATC. Treatment of primary Trp53KO/ALKF1174L ATC cells with the ALK inhibitor TAE-684 decreased AKT and ERK phosphorylation and induced dose-dependent cytotoxicity. Trp53KO/ALKF1174L mice treated with TAE-684 showed significantly extended median survival compared to the solvent group (66 days vs. 18 days, $p < 0.0001$). **Conclusion:** Our data demonstrate that the combination of ALKF1174L mutation with Trp53 drives ATC development. This study provides first functional data supporting ALK inhibitors in patients with ALK-driven ATC. Our novel ATC mouse model and derived cell lines offer valuable tools to explore the molecular characteristics of ATC, especially signalling pathway activation and tumour microenvironment, and to test novel therapeutics for advanced thyroid cancers.

THYROID CANCER BASIC

1112395 - DELIVERY OF MIR-485-5P AND MIR-495-3P VIA EXTRACELLULAR VESICLES IMPAIRS CELL MIGRATION AND INVASION IN THYROID CANCER CELLS

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Introduction: Extracellular Vesicles (EVs) have emerged as a promising delivery system for targeted therapy, including drugs, proteins and nucleic acids such as microRNAs (miRNAs). Despite their potential, the use of exosomal miRNAs as therapeutic targets in Thyroid cancer (TC) remains largely unexplored. We hypothesized that normal thyroid follicular cells (NThy-ORI) overexpressing miR-495-3p or miR-485-5p produce EVs enriched with these miRNAs, which can be delivered to tumor cells and potentially influences cancer-relevant biological processes. **Objective:** This study investigated the utility of EVs in delivering tumor-suppressor miRNAs to thyroid carcinoma cell lines. **Methods:** EVs from NThy-ORI cells overexpressing miR-485-5p or miR-495-3p were isolated using differential ultracentrifugation. Nanoparticle tracking analysis (NTA) and electron microscopy (EM) were employed to the EVs' characterization. In vitro cell proliferation and migration assays were conducted to explore the EV-mediated delivery and biological function of tumor suppressor miRNAs on three thyroid cancer cell lines (TPC-1, BCPAP and KTC-2). **Results:** We demonstrated that the miRNAs were released into the conditioned medium both naked and encapsulated within EVs. The uptake of these EVs by three cancer cell lines impaired cell proliferation and migration in vitro. **Conclusion:** So far, our results suggest that normal thyroid follicular cells can be engineered to produce EV-packed tumor suppressor miRNAs and impair cell proliferation and migration of thyroid cancer cells in vitro.

1112956 - EXPOSOMIC ANALYSIS OF THYROID CANCER: CORRELATING HISTOPATHOLOGICAL CHARACTERISTICS WITH PERSISTENT ENVIRONMENTAL ORGANIC POLLUTANTS

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Introduction: Preliminary data have shown elevated concentrations of ubiquitous environmental chemicals in differentiated thyroid cancer when compared to normal controls. **Objective:** This study sought to correlate the presence of persistent organic pollutants with histopathological characteristics in differentiated thyroid cancer. **Methods:** Retrospective review of de-identified human archived cryopreserved specimens of differentiated thyroid cancer (n=60, 20 per subtype, including Papillary Thyroid Carcinoma, Follicular Carcinoma, Follicular Variant of Papillary Thyroid Carcinoma). High-resolution exposomic analysis to quantify the amount of multiple environmental contaminants was performed using gas chromatography-mass spectrometry (GC-MS). Annotation of raw spectra was performed by mapping mass-to-charge ratios and retention times to an in-house library of pure chemical standards run on the same instrument. Annotated signals were only analyzed if they were detected in $\geq 70\%$ of samples. ANOVA and linear regression were used to assess the relationship between chemical abundance and histologic characteristics. **Results:** 288 unique chemicals were identified in the samples, and 73 had significant correlation with histopathologic characteristics. 33 contaminants were associated with tumor variant, 16 with number of tumors, 13 with lympho-vascular invasion (LVI), 12 with tumor size, 7 with extra-thyroidal extension (ETE), and 4 with multifocality. 8 chemicals were identified to have more than one significant correlation with histopathologic characteristics. The chemicals with the most associations were propylparaben (common preservative; LVI, ETE, size, number of tumors), 3-hydroxycarbofuran (pesticide; multifocality, size, number of tumors), and 4-aminobiphenyl-1 (discontinued color additive; LVI, size, number of tumors). **Conclusion:** Multiple environmental chemicals have been identified at higher concentrations in differentiated thyroid cancer cryopreserved specimens. More than a quarter, including common chemicals such as propylparaben, were found to correlate with histopathologic characteristics associated with more aggressive disease. More studies are needed to assess the role of these contaminants in thyroid carcinogenesis and tumor characteristics associated with these environmental organic pollutants.

THYROID CANCER BASIC

1112265 - HETEROGENEITY OF MYELOID CELLS IN ANAPLASTIC THYROID CANCER: WHEN “NICHES” MATTER

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1 - INSERM U1015, Gustave Roussy, Villejuif, France, F-94805; 2 - UMR 9019, Gustave Roussy, Villejuif, France, F-94805; 3 - Service d'Anatomopathologie, Département de Biopathologie, Gustave Roussy, Villejuif, France, F-94805; 4 - Sanofi Immuno-Oncology Research, Vitry-sur-Seine, France; 5 - Service d'Oncologie Endocrinienne, Département d'Imagerie, Gustave Roussy, Villejuif, France, F-94805

Introduction: Anaplastic thyroid cancer (ATC) is a very aggressive and ultrarare undifferentiated thyroid cancer with one of the poorest prognoses in oncology. Macrophages can constitute up to 70% of ATC tumor microenvironment, which may account for therapeutic resistance and aggressiveness. These findings underscore the potential critical role of myeloid cells in this disease. **Objective:** Our study investigates the spatial architecture of ATC tumors and the contribution of myeloid cells in the aggressive behavior of anaplastic tumor cells. **Methods:** We evaluated 16 thyroid tumors included in PRIMATHyC, a STING personalized medicine program (NCT04932525). ATC samples were reviewed and subtyped by an expert pathologist. Using spatial proteomics with MACSima technology, we identified specific subpopulations of myeloid cells previously described by single-cell RNA sequencing (Mulder *et al.*). **Results:** Compared to differentiated thyroid cancer characterized by a very low number of macrophages, we confirm that ATC tumors are highly enriched in tumor-associated macrophages. In fact, our analysis revealed distinct niches (areas of the tumor that share some common features) associated with specific macrophage subsets, providing new insights into the spatial organization and potential functional roles of myeloid cells in anaplastic tumors. These niches can be described according to pathology subtypes. Squamoid ATC niches, defined by squamous tumor cells, are highly infiltrated and enriched in CD206+ macrophages, interacting with tumor cells undergoing epithelial-to-mesenchymal transition. Fusiform ATC niches -defined by spindle-shaped tumor cells- are, on the contrary, highly infiltrated and enriched in CD163+ macrophages, interacting closely with exhausted CD8+ T cells and invasive tumor cells. **Conclusion:** This is a first step toward a better understanding of the immune spatial architecture of ATC tumors and how macrophages of each niche are contributing to tumor aggressiveness, either through immuno-suppression, promotion of invasion or resistance to treatment.

1112254 - HISTONE ACETYLTRANSFERASE LOSS-OF-FUNCTION PROMOTES THYROID CANCER PROGRESSION IN VIVO AND SENSITIZES HUMAN THYROID CANCER CELLS TO HIGHLY SPECIFIC PROTEIN DEGRADERS

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Introduction: Despite recent therapeutic advances, anaplastic thyroid cancer (ATC) remains a highly aggressive tumor with almost invariably fatal outcomes. Loss-of-function (LOF) alterations in histone acetyltransferase (HAT) genes, namely CREBBP and EP300, occur in 15%-20% of ATCs, but only in <1% of their well-differentiated counterparts. **Objective:** Here we aimed at understanding the biological consequences and therapeutic opportunities of HAT disruption in thyroid cancer progression. **Methods:** We tested our hypotheses by evaluating the effects of endogenous and CRISPR-edited LOF mutations of HAT genes, the generation of thyroid-specific genetically engineered mouse models of Crebbp and Ep300 loss (alone or in combination with BrafV600E) and by employing highly specific proteolysis-targeting chimera (PROTAC) compounds targeting HAT proteins. **Results:** Endogenous and CRISPR-generated CREBBP/EP300 LOF mutations in human thyroid cancer cell lines resulted in diminished global levels of their catalyzed histone acetyl marks, i.e., H3K27ac and H3K18ac. HAT silencing enhanced cell proliferation in murine thyroid cancer cell lines. Thyroid-specific mouse models of Crebbp and Ep300 disruption displayed enlarged thyroid glands at 30 weeks. Concomitant activation of BrafV600E and loss of Crebbp or Ep300 in mouse thyroids resulted in thyroid cancer progression, including histological changes, increased proliferation and occasional lung metastases. ChIPseq and RNAseq performed on both isogenic human thyroid cancer cells and mouse tumors identified specific superenhancer regions and expression programs impacted by HAT loss. CRISPR screens from the DepMap portal identified a mutual CREBBP/EP300-dependency of HAT-mutant human cancer cell models. We showed that these thyroid cancer cells with partial disruption of HAT function displayed an increased vulnerability to treatment with highly-specific PROTAC compounds targeting reciprocal HAT proteins for degradation, ultimately resulting in reduced cell viability compared to cells with intact HATs. **Conclusion:** Overall, our findings prove the direct role of HAT loss in thyroid cancer progression and support exploring synthetic lethality dependencies in CREBBP/EP300-mutant ATCs.

THYROID CANCER BASIC

1112387 - IN VIVO DETECTION OF THE MOLECULAR MECHANISMS OF CELL DEATH INDUCED BY CARBON ION THERAPY IN ANAPLASTIC THYROID CANCER

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Introduction: Despite new advancements for the treatment of anaplastic thyroid cancer, the way to find an effective and less toxic therapy is still challenging. **Objective:** The aim of this study was to identify the molecular mechanisms induced by the carbon ion therapy and to detect in vivo its efficacy by 18F-FDG PET/CT of chick chorio allantoic membrane (CAM) xenografts of human anaplastic thyroid cancer cells. **Methods:** Human anaplastic thyroid cancer (ATC) cells C643 and two patient-derived cells have been irradiated once with carbon ion (1-3 Gy). The next day, the cells were xenografted in CAM. After 6 days, the xenografts were injected systemically with 5 MBq of 18F-FDG. After 60 minutes, PET/CT was performed. The xenografts were stained for the proliferation marker Ki-67. Colony assay, cell viability and apoptotic assay were performed. DNA DSBs (double strand breaks) repair markers, apoptotic and autophagic markers were detected by Western blot and RT-qPCR. RFP-GFP-MAP1LC3B-C643 cells were monitored by confocal microscopy. **Results:** Carbon ion radiation reduced (>50%) the number of colonies, the cell viability but was not able to induce apoptosis. The active form of the DNA DSB repair kinase P-ATR was up-regulated as well as the transcript level of the autophagy and the cell cycle control markers. The maturation of the autophagy process was observed after irradiation. The irradiation reduced more than 50% the growth of the ATC xenografts. PET/CT evidenced a strong positive signal from the untreated xenografts. Instead, the irradiated xenografts were almost negative. The reduction of the proliferation rate after irradiation was confirmed by Ki-67 staining. **Conclusion:** The carbon ion irradiation induced autophagic death of ATC cells. FDG-PET/CT appears to be a functional tool for pre-clinical investigation of CAM xenograft derived from ATC cells. Immunohistochemical analysis confirmed the reduction of proliferation of the xenografts thus supporting the in vitro findings.

1112367 - METFOMIN REDUCES JAK/STAT PATHWAY ACTIVATION IN ANAPLASTIC THYROID CANCER IN MONOLAYER AND SPHEROID CELLS MODELS

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Introduction: Anaplastic carcinoma (ATC), although rare, is extremely aggressive (survival of 6-25 months). Multikinase and targeted therapies are the therapeutic options for ATC as tumors are radioiodine-refractory; however, most patients relapse or showed side effects. Thus, research for new antitumor/adjuvant drugs for advanced thyroid cancer is needed. Previous studies have shown metformins antitumor properties through AMPK activation and mTOR inhibition. The activation of the JAK/STAT pathway has been associated with cancer progression and metastasis but has not been widely explored in ATC. For testing drugs, the use of 3D models that mimic the characteristics of the tumor microenvironment is increasingly common. **Objective:** To assess whether the JAK/STAT pathway is involved in metformins antineoplastic activity in anaplastic thyroid cancer cells using monolayer (2D) and spheroid (3D) models. **Methods:** ATC cells (KTC2 and HTH83), HTH83 cells with deletion of STAT3 by CRISPR-CAS9 (H83S3del-1 and H83S3del2), and the non-tumor cell line (Nthy-Ori3.1) were used. Cell viability was assessed with the Presto Blue reagent in both 2D and 3D cultures. For the 3D models, the “hanging drop” technique was used, and morphological characterization was conducted. Western blot was used to evaluate the activation of STAT3 and AKT. **Results:** Metformin reduced cell viability in all cell lines, KTC2 and HTH83 were more sensitive than Nthy-Ori3.1 in 2D models. In 3D models, metformin reduced cell viability at higher concentrations, reduced spheroid size and increased cell dissemination. Metformin reduced the expression of p-STAT3 in KTC2 and HTH83 cells, while having no effect on p-AKT. In 2D culture, metformin failed to reduce cell viability in STAT3-knockout cells; likewise, metformin failed to alter spheroid characteristics. **Conclusion:** We confirmed the cytotoxic activity of metformin, an affordable and safe drug, in ATC cells through the JAK/STAT pathway in 2D and 3D models. These findings warrant further investigation of metformin for ATC

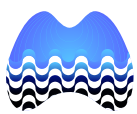
THYROID CANCER BASIC

1112399 - NIFUROXAZIDE ACTIVITY IN ANAPLASTIC THYROID CANCER: MODULATION OF CANCER STEM-LIKE CELL PROPERTIES AND THE INVOLVEMENT OF JAK/STAT3 PATHWAY

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Introduction: Anaplastic thyroid carcinoma (ATC) is the rarest but most aggressive thyroid cancer (TC), with survival of 6 - 25 months due to resistance acquisition and limited therapeutic options. Cancer stem cells (CSCs) have been related to cancer self-renewal and drug resistance. In ATC, JAK/STAT constitutive activation has been associated with progression and cancer stem-like cells properties. In some cancer models, nifuroxazide (NFZ) was able to inhibit JAK/STAT pathway and reduced viability. In melanoma, NFZ was bio-activated by ALDH1A3, a CSCs biomarker, suggesting NFZ selectivity towards CSCs population. **Objective:** To assess the activity of NFZ as an inhibitor of the JAK/STAT pathway to modulate ATC CSCs properties. **Methods:** ATC cell lines KTC-2, HTH83 and 8305c and the non-tumoral cell line Nthy-ori 3-1 were used. ALDH activity was monitored using ALDEFLUOR fluorophore by flow cytometry. Expression of CSCs markers (ALDH1A3, SOX2 and CD44) by real-time PCR and sphere formation assays were performed. The JAK/STAT3 pathway activation was evaluated by western blot. **Results:** In all ATC cell lines, higher expression of ALDH1A3 mRNA, number of ALDH-positive cells and ability to form spheres were observed compared to Nthy-ori 3-1. The NFZ treatment reduced the expression of ALDH1A3, SOX2 and CD44 in a dose-dependent manner in KTC-2, while CD44 expression was found decreased in HTH83 and 8305c. The NFZ treatment also reduced the number and size of spheres compared to control and the expression of p-STAT3 in HTH83. **Conclusion:** Our results show that ATC lineages are enriched with CSCs and NFZ activity appears to reduce CSCs properties through inhibition of JAK/STAT3 pathway. These results warrant further investigation of NFZ repositioning as a potential target therapeutic agent for advanced thyroid cancer.



1112561 - SERUM MICRORNA ANALYSIS FACILITATES THE DECISION BETWEEN ACTIVE SURVEILLANCE AND IMMEDIATE SURGERY OF THYROID MICROCARCINOMA

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Introduction: The identification of thyroid microcarcinoma (TMC) with aggressive behavior is a challenge for the implementation of active surveillance (AS). **Objective:** To elaborate a serum expression test of miRNAs to differentiate TMC with aggressive from indolent behavior to help recommend AS/surgery. **Methods:** This prospective observational study included patients with malignant thyroid nodules measuring 3 to 15 mm. Patients with low-risk TMC could opt for AS or surgery. Otherwise, they were referred for surgery. AS patients were followed up every 6 months for the first 2 years and annually thereafter and were referred for surgery in the occurrence of disease progression or at patient's request. Patients undergoing surgery were classified according to the risk of recurrence and/or persistence of ATA (RRP). We analyzed the serum expression of miR-146b-5p, miR-204, miR-221-3p, miR-222-3p and miR-21-5p. miR-16 was chosen as normalizer. The ROC curve was used to establish the cut-off value of miRNA expression able to differentiate the RRP into low or intermediate/high. **Results:** 51 patients were included, 30 in the AS and 21 in the surgery group. Five patients switched to surgery. Patients who preferred surgery or switched to surgery were younger ($p < 0.001$). The mean follow-up time in AS was 36.4 ± 25.8 months. No patient experienced disease progression during AS. Molecular analysis of surgery group revealed that upregulation of miR-146b-5p/miR-16 (≥ 0.1757) and downregulation of miR-204/miR-16 (< 0.02223) were associated with intermediate/high RRP ($p = 0.005$ and 0.006 respectively). The downregulation of miR-204/miR-16 presented sensitivity of 75% and NPV of 86.7% being considered a rule-out test. The combination of upregulation of miR-146b-5p/miR-16 with downregulation of miR-204/miR-16 had specificity and NPV of 100%, being a good rule-in test. The remaining miRNAs were excluded. **Conclusion:** The serum analysis of miR-146b and miR-204 can be used to classify TMC in terms of its prognosis, allowing a more precise indication of AS/surgery.

THYROID CANCER BASIC

1112284 - STUDY ON THE ROLE AND MECHANISM OF MIOX IN REGULATING FERROPTOSIS IN PAPILLARY THYROID CARCINOMA

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Introduction: Papillary thyroid carcinoma (PTC) is the most common subtype of thyroid cancer, accounting for about 80% of all thyroid cancer cases globally. Therefore, it is essential to identify biomarkers related to PTC, elucidate their roles and molecular mechanisms in the development and progression of PTC. **Methods:** Fresh papillary thyroid carcinoma and adjacent non-cancerous tissues were collected to detect the expression of MIOX and analyze its correlation with the clinicopathological features and prognosis of patients. Cell viability under ferroptotic stress was assessed using the CCK8 kit. Ferroptosis-related indicators were detected using C11-BODIPY staining, GSH assay kits, and MDA assays. Stable MIOX-overexpressing PTC cell lines were constructed and implanted subcutaneously in nude mice to establish xenograft tumor models. Immunoprecipitation (IP) combined with mass spectrometry was used to identify downstream binding proteins that co-regulate ferroptosis with MIOX. **Results:** In 90 pairs of PTC patients, MIOX was highly expressed in adjacent non-cancerous tissues. Overexpression of MIOX inhibited the proliferation, invasion, and migration abilities of PTC cell lines. Transmission electron microscopy showed that MIOX overexpression resulted in more ferroptosis-related morphological changes in PTC cells, exacerbating cell death under ferroptotic stress, increasing lipid ROS and MDA accumulation, and depleting GSH. In vivo, MIOX inhibited tumor growth and enhanced the antitumor effect of Erastin. Immunoprecipitation-mass spectrometry analysis identified PKM as a protein interacting with MIOX. Knockdown of PKM on the basis of MIOX overexpression further promoted ferroptosis. Co-immunoprecipitation experiments confirmed the specific binding of the two, which was more significant under ferroptotic stress. **Conclusion:** This study found that MIOX was significantly low-expressed in PTC tissues, and its low expression was significantly associated with larger tumor diameter, higher TNM stage, and poorer survival in PTC patients. MIOX and PKM formed a complex to co-regulate ferroptosis in PTC.

1112306 - TARGETING PI3K/AKT/MTOR SIGNALING AND INHIBITION OF BCR/ABL TYROSINE KINASE AND GLUCOSE UPTAKE OVERCOMES RESISTANCE TO LENVATINIB IN THYROID CANCER

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Introduction: Lenvatinib is an FDA-approved multi-kinase inhibitor used for therapy of metastatic progressive thyroid cancer (TC). The partial response to lenvatinib therapy is usually transient and subsequent progressive disease develops in most patients. The 10-year survival rate for patients with metastatic progressive TC non-responsive to standard therapy is only 10%. **Objectives:** The goal of this study was to characterize Lenvatinib resistant (LR) TC using in vitro models and to establish therapy candidates in LR-TC cell lines. **Methods:** LR was established in the Lenvatinib-sensitive (LS) TC cell lines (THJ29T, TPC1) through long-term treatment with escalating doses of the drug, resulting in the achieved fold resistance of >100. The LS and LR cells were phenotyped using unsupervised RNA sequencing, immunoblotting, and analysis of glucose metabolism by Seahorse assays. The MIPE6.0 library of 2800 compounds was used for screening of LR growth inhibition and the compounds with the highest Delta AUC (area under the curve) calculated from the TC growth curves by difference between AUC of LS and LR cells were selected for validation. **Results:** There was a significant upregulation of genes involved in mitochondrial respiration (OXPHOS), such as COX15 and COX20, increased glucose utilization via OXPHOS ($p < 0.001$) and activation of PI3K (phosphoinositide 3-kinases, $p < 0.01$) and mTOR (mammalian target of rapamycin, $p < 0.01$) signaling pathways in the LR as compared to LS cells. Consistently, PI3Ka and PI3Kb inhibitors (16 compounds) and mTORC1 inhibitors (7 compounds) were found to selectively decrease growth of LR model. Moreover, among the two most selective compounds were a glucose transporter 1 (GLUT1) inhibitor: BAY-876, and a Bcr-Abl kinase inhibitor (dasatinib) with a delta AUC of 178 and 166 respectively. **Conclusions:** Targeting PI3K/Akt/mTOR signaling, inhibition of BCR-Abl kinase and glucose uptake might be promising tools to overcome LR in TC that we plan to validate in in vivo models.

THYROID CANCER BASIC

1112572 - THE PHENOTYPE CORRELATED WITH NON CYSTEINE RET GERMLINE MUTATION IS CHARACTERIZED BY THE PRESENCE OF MEDULLARY THYROID CANCER ALONE

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Introduction: Genotype-phenotype correlations between RET mutations and clinical manifestations of MEN2 syndrome are well established. **Objective:** Aim of this study was to show that non-cysteine RET mutations are more likely not related to MEN2A but that are causative of hereditary MTC (hMTC) only. **Methods:** During the last 30 years, we identified 215 families with hMTC. Fifty-three families had a Cys634 mutation, 37 a Cysteine mutation in exon 10, 17 had the M918T mutation, 61 had a V804M/L mutation, 14 a S891A and 33 had other non-cysteine mutations. All patients were annually submitted to clinical and biochemical examinations to ascertain any parathyroid and adrenal gland involvement. **Results:** Five-hundred-fifteen subjects with non-cysteine RET mutation have been screened: 108 were index cases, 213 were RET gene carriers and 194 were not mutated. Only 3 families harboring the V804M mutation showed the presence of additional endocrine neoplasia. However, in one family there was only 1 subject with hyperparathyroidism that was cured with the surgical removal of one single parathyroid adenoma. In another family, a second germline mutation of TMEM127 was found correlating with the presence of pheochromocytoma even in family members without RET mutations. The third family showed several cases with both MTC and pheochromocytoma but the genetic analysis did not find any other gene alteration in genes commonly involved in familial pheochromocytoma. However, the genealogic tree clearly showed a strict segregation of MTC and pheochromocytoma in one branch of the family while the other had only MTC. **Conclusions:** These data strongly support that non cysteine RET mutations are specifically causative of hMTC syndromes without any other endocrine neoplasia. In these 3 families with MTC and non-cysteine germline mutations, MTC was incidentally associated with other endocrine neoplasia. There is no reason to screen gene carriers with cysteine RET mutations for pheochromocytoma and hyperparathyroidism.

1112601 - TRACING THE MOLECULAR ROUTE TO PROGRESSION IN DEFECTIVE MIRNA BIOGENESIS THYROID LESIONS

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Introduction: Alterations in DICER1 and DGCR8 drive benign thyroid manifestations, well-differentiated and recently reported in poorly-differentiated thyroid cancers. **Objective:** To determine the deregulated miRNAs involved in benign and malignant thyroid tumors associated with miRNA biogenesis defects and pinpoint key effectors in tumor progression. **Methods:** We performed multi-omic profiling of miRNA production impaired thyroid tumors. Combining newly identified cases with previous in-house cases, whole exome sequencing (WES) (N=18), miRNA profiling (N=38) were performed in benign and malignant DICER1-/DGCR8-mutated cases. Shared miRNA profiles of DICER1- and DGCR8-mutated cases were interrogated and profiles unique to benign or malignant samples were determined. The spatial transcriptome of 1 DICER1 and 1 DGCR8 case with different histological components was profiled. **Results:** WES of DICER1-/DGCR8-mutated samples denoted the classical mutually exclusive pattern with alterations in canonical thyroid cancer (TC) driver genes while demonstrating a putative mutational route to progression. Interrogation of miRNA expression profiles across DICER1-/DGCR8-mutated and control cases encompassing 5 histological subtypes revealed 36 differentially expressed (DE) miRNAs shared by DICER1-/DGCR8-mutated TCs and 2 DE miRNAs shared by benign thyroid lesions highlighting 34 miRNAs unique to the malignant status. Pathway analyses of the predicted miRNA targets of DICER1-/DGCR8-mutated TCs showed an association with known cancer signaling (MAPK, TGF- β) and cell cycle pathways. Spatial transcriptomics analysis showed how DICER1/DGCR8 tumors recapitulate the transcriptomic profile of follicular patterned thyroid cancers. Pathways associated with angiogenesis, dedifferentiation and Notch and Hedgehog signaling were upregulated in DICER1-PDTC stroma. The molecular profile of DGCR8 tumors exhibited an inflammatory component. **Conclusion:** The mutational landscape and miRNA profiling confirmed a linear model of progression in DICER1/DGCR8 tumors independent of the hereditary or sporadic origin of the disease. DICER1-/DGCR8-mutated TCs showed an effect on known TC signaling and cell cycle pathways. Integration of multi-omic molecular profiling has the potential to reveal prognostic biomarkers for these tumors.

THYROID CANCER CLINICAL

1112631 - ANALYTICAL VALIDATION OF A CUSTOMIZED TARGETED RNA NGS PANEL FOR DETECTING GENETIC ALTERATIONS IN 57 RECURRENT MUTATED GENES FOR DIAGNOSIS AND PROGNOSIS OF INDETERMINATE THYROID NODULES AND THYROID CANCER

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Introduction: Accurate diagnosis and prognosis of thyroid nodules are essential for treatment decisions. Targeted next generation sequencing (NGS) using customized panels has emerged as a preferred method for detecting multiple somatic alterations on a single platform. However, this approach presents significant challenges that underscore the need for rigorous analytical validation to guarantee consistent and high-quality results. **Objective:** To develop and perform the analytical validation of a targeted RNA NGS panel designed to enable molecular classification of thyroid samples across both pediatric and adult populations. **Methods:** We designed a custom RNA NGS panel to detect single nucleotide variants (SNVs), gene fusions, and gene expression in thyroid samples. To evaluate the panel's performance, we selected 90 well-characterized thyroid samples, including those with mutations in the targeted regions and appropriate controls. RNA quantity was measured using the Qubit RNA HS assay, and quality was assessed with the TapeStation RNA HS system. Libraries were prepared using 100 ng of RNA with the Illumina RNA Prep with Enrichment Kit and sequenced on the Illumina NextSeq 2000 system. Data analysis was performed with the DRAGEN RNA pipeline v4.3.7. **Results:** We developed and validated a comprehensive capture-based enrichment panel. Our panel (0.31 Mbp) included 4040 probes designed to detect gene fusions, SNVs and differential gene expression across 57 genes. Sequencing yielded over 500 million paired-end reads, with an average of 10 million mapped reads per sample. The positive percentage agreement for SNVs was 100%. For gene fusions, the agreement was 67%, likely due to intratumoral heterogeneity or incomplete probe coverage, which will be further assessed. We additionally identified gene fusions involving MET, THADA and SYN2 genes and SNVs that had not been previously detected in the reference samples. **Conclusion:** Our customized panel showcased high accuracy for detecting key variants and improving thyroid nodules diagnosis and prognosis.

1112329 - ASSESSMENT OF INTERNATIONAL MEDULLARY THYROID CARCINOMA GRADING SYSTEM PROGNOSIS IN PATIENTS WITH DISTANT METASTASES

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Introduction: The International Medullary Thyroid Carcinoma Grading System (IMTCGS), a two-tiered system with high-grade having a Ki-67 $\geq 5\%$, tumor necrosis or mitotic index ≥ 5 per 2 mm², has been recently shown to be a powerful prognostic tool for MTC whatever the stage. **Objectives:** To evaluate the prognostic power of the IMTCGS in metastatic MTC patients on survival outcomes from metastasis diagnosis. **Methods:** Monocentric retrospective study of 99 metastatic MTC patients treated at Gustave Roussy from 2000 to 2024 for whom IMTCGS evaluation on the primary tumour was available. **Results:** A IMTCGS low-grade was found in 32 patients (32.3%), while 67 (67.7%) showed a high-grade cancer. High-grade patients were older ($p=0.009$) and had larger primary tumours ($p<0.001$) compared to low-grade. Postoperative calcitonin, presence of symptoms, number of metastatic sites per patient, prevalence of synchronous metastases and RETM918T mutation were similar between the two groups. Median overall survival (OS) from distant metastases diagnosis was shorter in high-grade compared to low-grade (4.8 versus 13.9 years; $p=0.01$), as well as the time to systemic treatment initiation (TTI) (1.0 versus 4.8 years; $p<0.001$). RETM918T mutation was not associated with worse OS. A Ki67 $\geq 20\%$ was associated with worse OS (2.6 years) compared to cases with Ki67 $<5\%$ (10.5 years; HR: 4.68; $p=0.001$) and 5%-19% (6.5 years; HR: 2.54; $p=0.009$). At multivariate analysis, IMTCGS high-grade and presence of bone metastases resulted as independent predictors for worse OS and shorter TTI ($p<0.05$ in both determinations). Median OS from treatment initiation was similar between low-grade and high-grade (2.8 versus 3.9 years, respectively; $p=0.87$) in 75 patients. **Conclusion:** We confirmed the prognostic role of IMTCGS grade in metastatic MTC. We identified MTC patients with Ki67 index $\geq 20\%$ as a new category.

THYROID CANCER CLINICAL

1112623 - CHALLENGES IN DETERMINING THE OPTIMAL TIMING FOR THYROID REMOVAL IN YOUNG MEN2A PATIENTS: INSIGHTS FROM TWO BRAZILIAN REFERRAL CENTERS

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Introduction: Genetic screening of the RET gene can identify individuals at risk of developing hereditary medullary thyroid carcinoma. Although guidelines recommend prophylactic thyroidectomy for asymptomatic carriers, the ideal timing remains controversial. **Methods:** This study evaluated outcomes of MEN2A patients diagnosed at or before 20 years of age. **Results:** The study included 104 patients, 100 (96.2%) were diagnosed by genetic screening and four were index cases. The mean age at diagnosis was 11.2 ± 5.6 years, and 65.4% were female. Codon 634 was the most prevalent pathogenic variant (70.2%). A total of 87 patients underwent total thyroidectomy, 15 were under active surveillance, and two were scheduled for surgery. The mean age at surgery was 13.4 ± 5.0 years, with a median preoperative basal serum calcitonin (preCTN) level of 28.0 pg/mL (9.860.5). Follow-up data were available for 85 (97.7%) patients. After an average follow-up of 10.9 years, 75 (88.2%) patients showed excellent response, while 10 had persistent disease (4 biochemical and 6 structural disease). Factors linked to persistent disease included being an index case, age at diagnosis, age at surgery, preCTN levels, and the presence of lymph node or distant metastases. ROC curve analysis evaluated preCTN level as a predictor of lymph node metastasis and persistent disease, with optimal cutoff values of 28.5 pg/mL (100% sensitivity, 53% specificity) and 71.9 pg/mL (100% sensitivity, 88% specificity), respectively. Multivariate analysis identified preCTN level <71.9 pg/mL as an independent prognostic factor for achieving disease-free status (RR 1.688; CI 1.0872620; $p=0.020$). **Conclusions:** Long-term follow-up showed that most young MEN2A patients who underwent thyroidectomy later than current guidelines suggest achieved disease-free status, highlighting that delaying surgical treatment for certain RET mutation carriers with low serum CTN levels may be considered.

1112460 - CIRCULATING MICRORNAS IN THE FOLLOW-UP OF PATIENTS WITH PAPILLARY THYROID CARCINOMA

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Introduction: MicroRNAs (miRs) are non-coding RNAs that regulate posttranscriptional gene expression. Changes in their expression in pathological conditions, such as thyroid cancer, may be reflected in circulating miR profile. **Objective:** To identify circulating miRs in patients with papillary thyroid carcinoma (PTC) that correlate with disease extension and response to therapy. **Methods:** Plasma miR expression profiles of 70 PTC patients were prospectively evaluated, divided into a training (n=18) and a validation cohort (n=52). miR expression was assessed using qRT-PCR. In training cohort, plasma samples from 9 patients with metastatic PTC (lymph node metastases [LNM] and distant metastases [DM]), responsive and refractory to 131I therapy, and 9 patients with excellent response to therapy were screened for 754 miRs using the TaqMan Advanced miRNA Human Cards. Based on hierarchical analyses, differences in miR expression and biological plausibility, 14 miRs were selected to customize a validation panel. This panel was applied to 33 patients with structural incomplete response (14 LNM and 19 DM) and 19 with excellent response to therapy, and the differences in miR expression were assessed. **Results:** In the training cohort, the following miRs were differently expressed in metastatic PTC compared to patients with excellent response, and selected to the customized panel: miR-362-3p, miR-17-5p, miR-450a-5p, miR-337-5p, let-7c-5p, miR-484, miR-146b-5p, miR-487a-3p, miR-122-5p, miR-32-5p, miR-10a-5p, miR-106b-5p, miR-221-3p, and miR-222-3p. In the validation phase, 6 out 14 miRs were confirmed as differently expressed in patients with metastatic PTC compared to those with excellent response: let-7c-5p, miR-337-5p, miR-146b-5p, miR-484, miR-487a-3p, and miR-221-3p. In the comparison of miRs expression among metastatic PTC patients, miR-484 was overexpressed in DM compared to LNM. **Conclusion:** Patients with metastatic PTC have a distinct circulating miR expression profile compared to those with excellent response to therapy, particularly those with DM that show increased circulating miR484 compared to local recurrence.

THYROID CANCER CLINICAL

1112228 - IMMUNOMODULATORY EFFECTS OF LENVATINIB IN ADVANCED THYROID CARCINOMA

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Introduction: Aggressive thyroid cancers (TC) are densely infiltrated by immunosuppressive monocytes and macrophages, correlating with a poor prognosis. Preclinical studies indicate that Lenvatinib, a multi-target kinase inhibitor approved for treatment of TC, has immunomodulatory influences on myeloid cells from healthy donors that could contribute to its anti-tumoral effects. **Objective:** This study aims to comprehensively investigate the functional and metabolic signature of circulating myeloid cells in patients with TC treated with Lenvatinib. **Methods:** Whole blood was collected from 30 patients with advanced metastatic TC, of which 15 using Lenvatinib for a median of 2.8 months and 15 not treated with Lenvatinib. Monocytes were isolated and their cytokine production capacity was assessed after ex vivo stimulation with lipopolysaccharide (LPS) in the presence and absence of Lenvatinib. Cytokine and lactate concentrations were measured in supernatants. In healthy donors, functional exploratory experiments were performed including ROS assays and Seahorse metabolic assays. **Results:** Monocytes of patients using Lenvatinib had an increased production of the anti-tumor cytokine IL-1RA upon LPS stimulation compared with those from patients not receiving Lenvatinib. Patients with poorly differentiated tumors (n=6) showed a trend towards lower LPS-induced production of IL-1 β and IL-8. Ex vivo Lenvatinib exposure of treatment naïve patients monocytes highly attenuated their capacity to produce IL-1 β , IL-8, IL-6, IL-10 and TGF- β upon LPS stimulation. Moreover, ex vivo Lenvatinib exposure lowered lactate production in patient samples, consistent with reduced glycolysis rates in healthy donors monocytes. Finally, Lenvatinib increased cytotoxic ROS production. **Conclusion:** In patients with advanced TC, Lenvatinib treatment modulates anti-tumor immune responses by altering cytokine production capacity, potentially reversing some immunosuppressive properties of myeloid cells, and increasing their cytotoxic capacity. These immunomodulatory effects can potentiate the anti-tumoral effects of Lenvatinib and could be further explored therapeutically in future studies.

1112342 - IMPACT OF PHYSICAL ACTIVITY AND ITS MAINTENANCE IN THE EFFICACY AND SAFETY OF TYROSINE KINASE INHIBITORS IN ADVANCED THYROID CARCINOMA PATIENTS

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Introduction: Aim: Tyrosine kinase inhibitors (TKIs) display high efficacy in the treatment of advanced thyroid cancer (TC), though are burdened by multiple adverse events (AEs). **Objective:** This preliminary study aims to evaluate the impact of physical activity and its maintenance on the safety and efficacy of TKIs in advanced TC. **Methods:** We enrolled 28 patients: 14 Differentiated TC, 6 Poorly Differentiated TC, 8 Medullary TC, treated for an average time of 26 months with Lenvatinib (18), Vandetanib (4), Cabozantinib (2) and Selpercatinib (2). Three modified long-form International Physical Activity Questionnaires were administered for each patient at different time points (T0, before TKI treatment; T1, intermediate; T2, at last follow-up). Metabolic equivalents (METs) were calculated at each time point. AEs were graded according to the CTCAE v5.0. Tumour response was evaluated according to RECIST v 1.1. **Results:** PD occurred more frequently in basal inactive patients in comparison with mildly and highly active patients (43% vs. 14%, p 0.15). Basal inactive patients experienced more TKI interruptions both during T1 (85% vs. 30%, p 0.01) and T2 (85% vs. 47%, p 0.08). Patients who maintained their PA status throughout the FU had a better efficacy and safety profile in comparison with patients with a reduced PA status: presence of > 5 AEs (31% vs. 100%, p 0.006), Gr ≥ 3 AEs (38% vs. 100%, 0.01), hospitalization for an AE (66% vs. 8%, p 0.008) and PD during treatment (40% vs. 8%, p 0.09). **Conclusions:** Inactive patients at baseline show a worse PFS and physical activity maintenance is strongly associated with a milder toxicity profile and lower PD events during the entire follow-up. These are the first findings supporting the role of physical activity in TKIs-treated patients and could open the road to prehabilitation in this field.

THYROID CANCER CLINICAL

1114005 - LENVATINIB TREATMENT AS A NEOADJUVANT OPTION IN LOCALLY ADVANCED THYROID CANCER

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Introduction: Advanced thyroid cancer includes a group of patients with a worse prognosis. ITKs are a management option in those with unresectable primary tumors. **Objective:** To describe our experience with lenvatinib as neoadjuvant treatment for locally advanced thyroid carcinoma. **Methods:** Retrospective cohort study of patients with thyroid cancer treated with lenvatinib between 2022 and 2025 for locally advanced cancer in Medellín, Colombia. **Results:** 21 patients were included (20 papillary, 1 anaplastic), 52.4% men, average age 61 years (ED 16); the most frequent adverse events were arterial hypertension (71.4%), asthenia (28.6%), and weight loss (28.6%). 3 patients (15.8%) required permanent discontinuation of lenvatinib, 4 patients (21%) died during follow-up (1 anaplastic due to progression, 1 case due to undetected CNS metastases that presented convulsive status, 2 cases of ventilatory failure), 6 (28.6%) underwent surgery, all had papillary cancer, 5 with classic variant, 1 with tall columnar cells, the resection margin was R0 in 3 (50%), 2 R1 (33.3%) and 1 R2 (16.7%). The operated patients were considered candidates for management with I-131, 1 received radiotherapy. 2 patients are pending resection surgery. The median treatment time until surgery was 261 days (IQR 169-327). The median follow-up was 346 days (IQR 100-477), among the 12 who had control images, the response by RECIST 1.1 was 3 complete response (25%), 5 partial response (41.7%) and 4 stable disease (33.3%), which implies ORT of 66.7% and DCR of 100%. **Conclusion:** Management of patients with unresectable thyroid cancer with lenvatinib resulted in one in three being eligible for surgery, and half are still being managed.

1112385 - LESIONAL DOSIMETRY IN ¹³¹I REFRACTORY METASTATIC DIFFERENTIATED THYROID CANCER WITH BRAFP.V600E OR RAS MUTATION TREATED WITH TRAMETINIB +/- DABRAFENIB FOLLOWED BY HIGH ACTIVITY OF RADIOACTIVE IODINE

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Introduction: In the MERAIODE phase II prospective trial (NCT 03244956), patients with radioactive iodine refractory metastatic differentiated thyroid cancer (DTC) were treated with trametinib + dabrafenib in case of BRAFp.V600E mutation and by trametinib in case of RAS mutation, both followed by the administration of 5.5 GBq of ¹³¹I. A post-therapeutic dosimetry study was planned to assess the correlation between doses delivered to the lesions and morphologic response to treatment. **Methods:** Absorbed doses (AD) were calculated from images acquired 1, 2, 3 and 4 days after ¹³¹I administration. The volume of lesions was manually segmented on the diagnostic CT scans acquired prior ¹³¹I and after 3, 6 and 9 months of trametinib +/- dabrafenib and ¹³¹I administration. Lesions were categorized according to a 3D extrapolated RECIST 1.1 classification: Progressive Disease (PD) with a volume increase $\geq 73\%$, Partial Response (PR) with a decrease $\geq 65\%$ and standard Complete Response (CR) and Stable Disease (SD). **Results:** 25 lesions (19 lesions with BRAFp.V600E mutated DTC and 6 lesions with RAS mutated DTC) were selected. The median absorbed dose for the BRAFp.V600E mutated lesions was 393.5 Gy [range: 20.4 Gy - 2906.3 Gy] and was greater (p-value = 0.0005) than for RAS mutated lesions with a median absorbed dose of 35.3 Gy [range: 6.9- 76.0 Gy]. For patients with BRAFp.V600E mutated DTC, 58% of the lesions were in PR/CR at 6 months with a median AD of 896.4 Gy, significantly greater (p=0.006) than for SD/PD lesions with a median AD of 183.4 Gy. A response rate of 80% was achieved for lesions receiving an AD > 393 Gy. **Conclusion:** The median AD was significantly higher in the BRAFp.V600E mutated DTC lesions than in the RAS mutated DTC. BRAFp.V600E mutated DTC lesions with a partial and complete response received significant higher doses than other lesions.

THYROID CANCER CLINICAL

1112183 - LONG-TERM OUTCOME FOR PAPILLARY THYROID CARCINOMA WITH LUNG METASTASIS

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Introduction: Papillary thyroid carcinoma (PTC) with lung metastasis has a relatively favorable prognosis. Treatment has centered around radioactive iodine (RAI) therapy, but the advent of molecular targeted therapies have recently caused a paradigm shift in management. **Objective:** This study analyzes the prognostic factors for long-term outcomes of PTC with lung metastasis and investigates the characteristics of RAI-refractory cases. **Methods:** Among 1,538 patients who underwent initial surgery for PTC between 1993 and 2013, 196 (12.7%) had lung metastasis. Genetic analysis of the BRAF V600E mutation and TERT promoter mutation was conducted for 90 cases. Survival curves were estimated using the Kaplan-Meier method, with comparisons by log-rank test. Multivariate analysis was performed using the Cox proportional hazards model, and factors predicting RAI uptake were analyzed using logistic regression. **Results:** The maximum follow-up period was 26 years, with a median of 8 years. To date, 85 patients have died due to distant metastasis. Disease-specific mortality rate was 76.3% at 5 years, 57.8% at 10 years, and 39.0% at 20 years. Univariate analysis identified significant poor prognostic factors, including age ≥ 55 years, BRAF mutation, TERT promoter mutation, metastasis beyond the lungs, lung metastasis size ≥ 1 cm, lack of RAI uptake, thyroglobulin doubling time (Tg-DT) ≤ 2 years, and co-occurrence of local recurrence. In multivariate analysis, significant factors included lung metastasis size ≥ 1 cm, lack of RAI uptake, and Tg-DT ≤ 2 years. BRAF mutation was significantly correlated with lack of RAI uptake. Only 8.9% of BRAF-positive cases showed RAI uptake. **Conclusions:** Although PTC patients with lung metastasis have a high likelihood of disease-specific mortality, long-term survival can be expected in cases with small metastases and longer Tg-DT. Since the probability of RAI effectiveness is low in BRAF-positive cases, early initiation of molecular targeted therapy may be reasonable.

1112409 - PREDICTIVE FACTORS OF RADIOACTIVE IODINE-REFRACTORY EVOLUTION OF THYROID CANCER IN A PROSPECTIVE COHORT

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Introduction: Radioiodine refractory (RAIR) differentiated thyroid carcinomas (DTC) explain most of DTC mortality. Few studies have looked at risk factors for developing RAIR-DTC, especially using recent histological classifications, while early detection may improve management. **Objective:** The aim of this prospective study was to identify clinical and updated histopathological risk factors for RAIR disease. **Methods:** Prospective analyses of DTC patients operated in a tertiary center between 2009 and 2018 with a diagnosis of pT3, pT4 or M1 DTC according to the 2010 TNM classification and with more than one year of follow-up. Centralized histological review according to 2022 histological classification was realized in all cases. The 2015 American Thyroid Association (ATA) guidelines were used to define RAIR-DTC. Cox model exploring time to development of RAIR disease was used to identify risk factors for RAIR disease. **Results:** Among 253 patients, histopathological review identified 22 NIFTP, 6 UMPT and 225 DTC with a median follow-up of 8.3 years, 40 became RAIR-DTC (17.8%). Univariate analysis identified age, thyroglobulin at first RAI treatment, tumor size, pN stage, TERT promoter mutation (but not BRAF), unencapsulated tumor, adipose, muscular and vascular invasion, Ki67 index, tumor necrosis, number of mitoses, and high-grade follicular cell derived carcinomas (high-grade DTC and poorly differentiated carcinomas (HR 8.8 CI= 4.8-18.1; $p < 0.001$)) as risk factors for RAIR-DTC. Four risk factors were selected in the multivariate model which presented 91% AUC: age ≥ 55 years (HR=1.822; $p=0.093$), thyroglobulin ≥ 20 ng/mL at first RAI (HR=5.944; $p < 0.001$), TERT promoter mutation (HR=3.528; $p < 0.001$) and high-grade follicular cell-derived carcinomas (HR=6.162; $p < 0.001$). **Conclusion:** The recently created category of high-grade follicular cell-carcinomas, age, high thyroglobulin at first RAI and TERT promoter mutation were identified as major factors for early identification of patients at risk of progression to RAIR disease, while BRAF mutation was not.

THYROID CANCER CLINICAL

1112394 - PROGNOSTIC VALUE OF RET STATUS IN PATIENTS WITH UNRESECTABLE MEDULLARY THYROID CANCER TREATED BY VANDETANIB: THE PRONOMET STUDY

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Introduction: Vandetanib, a multikinase inhibitor targeting RET, VEGFR and EGFR, is indicated in unresectable advanced medullary thyroid cancers (uaMTC). If its efficacy is well documented in RET mutated patients (RETm), evidence lacks in RET wild-type (RETwt) patients, leading the European Medicine Agency to restrict its approval. **Objective:** Therefore, this study assessed the prognostic value of RET status in vandetanib-treated uaMTC patients. **Methods:** This retrospective study pooled data regarding vandetanib-treated uaMTC patients from (1) the international OBS14778 study (combining ZETA trial and observational data) and (2) the multicenter TUTHYREF registry collecting data of all French refractory thyroid cancers. Included patients had RETwt status confirmed by recent tumor next-generation sequencing. The endpoints were progression-free survival (PFS) and overall survival (OS), that were estimated using Kaplan-Meier estimator. Cox models were used to adjust on confounders. **Results:** 210 patients (128 from TUTHYREF, 82 from OBS14778) were included: 48 RETwt and 162 RETm. Overall, 27% were diagnosed before 2010, 74% were treatment-naïve and 76% had confirmed disease-progression before vandetanib. Median vandetanib duration was 14.8 months (IQR [4.3-30.9]). Except for age (median age 64.5 vs 56.9 years in RETwt and RETm respectively), patients had similar characteristics in the two groups. With a median follow-up of 39.5 months, median PFS were 13.8 months and 18.5 months in RETwt and RETm patients respectively ($p=0.24$). After adjustment on age, metastasis burden, time from diagnosis, confirmed progression and treatment-naïve status, the hazard ratio (HR) for PFS (RETm versus RETwt) was 0.87, 95%CI[0.58-1.3]. Median OS was 71.5 months for RETwt and 84.4 months for RETm patients ($p=0.07$). Due to high between-studies heterogeneity ($I^2=76.8\%$), HR for death was not estimated across studies. **Conclusions:** In this large cohort of uaMTC, we did not find any significant prognostic value of RET status in vandetanib-treated patients. This treatment may thus be reconsidered for RETwt patients.

THYROID CANCER CLINICAL

1112612 - SAFETY AND EFFICACY OF SELPERCATINIB TREATMENT IN ADVANCED MEDULLARY THYROID CANCER PATIENTS: A REAL-LIFE STUDY

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Introduction: The highly selective RET inhibitor selpercatinib has shown significant efficacy in advanced/metastatic RET-mutant medullary thyroid carcinoma (MTC) patients. This study describes the real-life experience with selpercatinib in treating advanced MTC. **Materials and Methods:** We evaluated the data and clinical outcome of 42 patients treated with selpercatinib (2020-2024) in our Unit. **Results:** Most of patients (40/42%-95.2%) had stage IV at the diagnosis with a median age of 47. Before starting selpercatinib 26/42 (62%) patients performed other surgeries/local treatments. One third (33.3%) received selpercatinib as first line systemic treatment, 21/42 (50%) inside clinical trials. In 78.6% RET mutation was somatic and M918T was the most common (24/33%-72.4%). Selpercatinib was started for progressive disease in 78.6%, the starting dose was 160 mg/BID in 88.1% and in 93% of the cases, more than 10 metastatic lesions were present. Best overall response was reached after a median of 2 months (stable disease 45%; partial response 55%). Dose reduction was experienced in 40.5% while drug temporarily withdrawal in 31%, due to AEs. Calcitonin and CEA significantly dropped down after 2 months and remained stable up to the data lock. After a median of 20 months only 2 progressive diseases, and all in patients previously treated with other MKI, were experienced. In 52.5% partial response and 42.5% stable disease was observed. **Conclusions:** This real-life experience confirmed the efficacy and safety of selpercatinib in treating RET-mutant MTC patients. Durability of response is still an open issue, but this seems to be longer in the naïve patients.

THYROID CANCER CLINICAL

1112424 - ULTRASOUND-GUIDED CRYOABLATION, LASER OR RADIOFREQUENCY ABLATION OF CERVICAL METASTASES FROM THYROID CARCINOMA: A PROSPECTIVE CLINICAL TRIAL

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Objective: To assess the efficacy and safety of cervical lymph node metastases (LNMs) from differentiated or medullary thyroid carcinoma (DTC or MTC) thermal ablation under ultrasound (US) guidance with laser (LA), radiofrequency (RF), or cryoablation (CA). **Materials and methods:** This prospective clinical trial obtained IRB approval. All subjects provided informed consent. Eligible subjects presented with up to six concurrent LNMs between 0.8-4.0 cm diameter. US examinations were conducted at baseline, 6, 12, and 24-months. Changes in tumor volume, technical success, complications, tumor markers and need for additional surgery were evaluated. **Results:** Eighty-four patients (n=165 tumors) were treated, 71 with DTC (84.5%) and 13 with MTC (15.5%). The median age was 55.5-year-old, 63 (75%) being women. Twenty-eight patients (131 LNMs) were randomly assigned for each ablation group. Fifteen patients (17.9%) who developed 34 new LNMs underwent ablation (CA) overtime (total treated LNMs: 165). Technical success was 98.8%. General baseline, 6-, 12- and 24-month LNM volume (mL) were: 1.20±3.14 cc (n=84); 0.33±1.60 cc (n=74); 0.15±0.73 cc (n=60); and 0.10±0.36 cc (n=45). LNMs VRR at 6-, 12-, and 24-months increased in all groups (P<0.05). One severe AE (1.2%) (1/84) - vocal cord palsy, prolonged hospitalization, pulmonary infection and death occurred in a patient with widely metastatic disease. No moderate AE was observed. Mild AE were transient hoarseness 9.5% (8/84), cutaneous fistula with spontaneous resolution 1.2% (1/84), and persistent hoarseness due to unilateral vocal cord palsy 1.2% (1/84). No subsequent therapies were required to the treated LNMs. **Conclusion:** Thermal ablation modalities (LA, RF, CA) were both feasible, effective, and safe for well-selected patients, providing adequate local control of LNMs. No significant differences among the three ablation methods regarding complications, side effects, and tolerability were observed. Thermal ablation is an alternative therapy for treating cervical LNMs from thyroid carcinoma.

1113739 - UNSTIMULATED POSTOPERATIVE THYROGLOBULIN IS HIGHLY ACCURATE IN PREDICTING TREATMENT RESPONSE IN HIGH-RISK DIFFERENTIATED THYROID CANCER PATIENTS - A RETROSPECTIVE COHORT STUDY

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Introduction: High-risk differentiated thyroid cancer (DTC) patients show variable outcomes, with approximately 30% achieving excellent responses at follow-up. While postoperative stimulated thyroglobulin (STg) is a recognized predictive marker, the prognostic significance of unstimulated thyroglobulin (UTg) obtained before radioiodine therapy (RIT) is still under-explored. **Objectives:** To assess whether postoperative UTg is a prognostic factor in high-risk DTC patients. **Methods:** This retrospective cohort study analyzed DTC patient records from two tertiary hospitals (2015-2024). Clinical, ultrasonographic, anatomopathological, and laboratory data from baseline, treatment, and one-year follow-up were evaluated. Response to treatment was categorized as favorable (excellent and indeterminate) or unfavorable (biochemical and structural incomplete), along with the development or absence of metastasis. Receiver Operating Characteristic (ROC) curves determined optimal cutoff values. Patients with positive anti-Tg antibodies were excluded. **Results:** 1,000 DTC patients were identified, of which 144 were high-risk. Fifty-seven patients met the inclusion criteria. Significant predictors of unfavorable outcomes included advanced age ($p=0.048$), larger tumor size ($p=0.002$), higher UTg ($p<0.001$), and STg ($p<0.001$). After multivariate logistic regression, UTg was an independent predictor for one-year outcomes (OR=0.008; 95% CI: 0.001–0.088; $p<0.001$). The UTg cutoff of 2.1 ng/mL distinguished outcomes ($p<0.001$) with high sensitivity (83.3%), specificity (96.0%), and accuracy (90.7%). A higher cutoff of 3.8 ng/mL identified metastases (sensitivity 86.4%, specificity 90.5%, accuracy 88.4%; $p<0.001$). UTg showed non-inferiority to STg in predicting outcomes, with larger areas under the curve for unfavorable responses (0.929 vs. 0.839; $p=0.964$) and metastases (0.926 vs. 0.876; $p=0.980$). **Conclusion:** Postoperative UTg is a robust prognostic indicator for high-risk DTC patients, providing a non-inferior alternative to STg with enhanced accessibility and fewer side effects. We recommend incorporating routine postoperative UTg measurements for high-risk patients. When UTg levels exceed 2.1 ng/mL, especially higher than 3.8 ng/mL, further investigation of potentially resectable metastatic foci should be considered before RIT. Prospective studies are needed to validate this clinical algorithm.

THYROID CANCER CLINICAL

1112312 - VALIDATION OF THE INTERNATIONAL MEDULLARY THYROID CANCER GRADING SYSTEM AND IDENTIFICATION OF EZH2 AS A PROGNOSTIC AND POTENTIAL THERAPEUTIC MARKER IN MEDULLARY THYROID CANCER PATIENTS

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Introduction: Medullary thyroid cancer (MTC) is a heterogenous and elusive disease. While the International MTC Grading System (IMTCGS) provides baseline risk stratification, it lacks therapeutic relevance. EZH2 overexpression harbors an adverse prognosis in various cancers, with several EZH2-inhibitors undergoing investigation. **Objective:** This study aimed to validate the IMTCGS in a cohort of MTC patients. In addition, we examined the prognostic value of EZH2, as well as several other biomarkers. **Methods:** Clinical data were collected and MTC specimens were retrospectively reviewed and morphologically assessed. Immunohistochemistry (IHC) of Ki-67 allowed IMTCGS validation. IHC of EZH2, PD-L1 and PSMA was evaluated on a tissue micro-array (TMA). **Results:** Primary tumors of 64 patients were included (48% female and 16% hereditary MTC). Median tumor size was 28 mm (IQR 15-40). Necrosis, ≥ 5 mitoses, and Ki-67 $\geq 5\%$ was seen in 19 (30%), 3 (5%) and 7 (11%) cases, respectively. Median Ki-67 was 0.9% (IQR 0.4-2.1). 43 (67%) and 21 (33%) were classified as low- and high-risk, respectively, according to the IMTCGS. High-risk tumors were associated with a lower distant metastasis-free survival (DMFS) (HR 5.651, $p=0.017$), locoregional recurrence-free survival (LRFS) (HR 18.323, $p<0.001$) and disease-specific survival (DSS) (HR 10.001, $p=0.002$), but not with overall survival (OS) (HR 2.109, $p=0.146$). EZH2 expression was identified in 39 of 46 (85%) cases available for assessment on the TMA. We identified $\geq 10\%$ EZH2 expression in 9/46 cases (20%), which was predictive for DMFS (HR 4.747, $p=0.030$), LRFS (HR 4.242, 0.039), DSS (HR 19.736, $p<0.001$) and OS (HR 8.386, $p=0.004$). PD-L1 and PSMA expression (present in 10/46 and 45/46 cases, respectively) had no prognostic value. **Conclusion:** This study confirms the prognostic value of the IMTCGS and identifies EZH2 as a novel prognostic biomarker in MTC patients. The therapeutic potential of EZH2 warrants further investigation in larger cohorts.

1112193 - VASCULAR INVASION AS A PREDICTOR OF DISTANT RECURRENCE IN FOLLICULAR CARCINOMAS: ARE THE DEFINITIONS OF "WIDELY INVASIVE FOLLICULAR CARCINOMA" AND "ENCAPSULATED ANGIOINVASIVE FOLLICULAR CARCINOMA" APPROPRIATE?

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Introduction: Follicular thyroid carcinoma (FTC) is subclassified into three categories; minimally invasive (mFTC) having minimal capsular invasion (CI) only; encapsulated angioinvasive (eaFTC) with vascular invasion (VI) with no or minimal CI; and widely invasive (wFTC) having extensive (gross) CI regardless of the presence of VI. **Objective:** In this study, we verified the appropriateness of these classifications using in our series. **Methods:** We enrolled 523 patients who underwent initial surgery at Kuma Hospital between 1998 and 2015. All were classified as FTC (N=446) or oncocytic carcinomas (N=77). We set two grades of VI; VI(1+) having < 4 VI foci, and VI(2+) with ≥4 VI foci. The median postoperative follow-up period was 132 months (12-277 months). Sixteen patients were classified as M1, and to date, 37 patients showed recurrences to distant organs. **Results:** For 507 M0 patients, VI was an independent prognostic factor for distant recurrence. Distant recurrence-free survival (DR-FS) of VI-positive patients was not uniform but became significantly poorer from VI(-) to VI(2+); VI(1+) vs. VI(-), p=0.011, and VI(2+) vs. VI(1+), p=0.014. However, DR-FS of wide CI did not significantly differ (p=0.494) from that of no or minimal CI. On multivariate analysis, other than VI(1+) (p=0.021, odds ratio [OR] 2.542) and VI(2+) (p< 0.001, OR 8.030), male sex (p=0.001, odds ratio [OR] 3.338), age≥55 years (p=0.001, OR 3.043), and non-oncocytic pathology (p=0.041, OR 8.000) independently predicted DR. The 20-year DR-FS of wFTC/VI(1+/2+) and eaFTC/VI(2+) was 69.1% and 71.4%, respectively, which were poorer than that of eaFTC/VI(1+), at 86.3% (p=0.001, and p=0.042, respectively). However, 20-year DR-FS of wFTC/VI(-) was excellent, at 97.0%, which was similar to that of mFTC, at 92.6% (p=0.124). **Conclusion:** Subclassification of VI and restricting wFTC to VI-positive cases might be better to keenly reflect patients prognoses. Revisiting the WHO classification should be necessary for accurate prediction of patients prognoses.

THYROID CELL BIOLOGY

1112619 - ANAPLASTIC THYROID CANCER UNDERGOES GENOMIC AND PHENOTYPIC PLASTICITY IN RESPONSE TO BRAF INHIBITOR TREATMENT

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Introduction: Anaplastic thyroid cancer (ATC) is a rare and aggressive dedifferentiated thyroid cancer. Approximately 40% of ATC cases harbor the BRAFV600E mutation, which constitutively activates the MAPK pathway, driving cancer progression. While BRAFV600E mutant ATCs are known to arise from differentiated thyroid cancers such as papillary thyroid cancer (PTC), the functional and microenvironmental changes underlying this transformation remain poorly understood. **Objective:** To investigate these dynamics, we developed a mouse model of BRAFV600E-driven thyroid cancer progression, incorporating a fluorescent tag to facilitate the isolation and analysis of tumor cells independent of the surrounding microenvironment. **Methods:** The model employs a tamoxifen-inducible, thyroid peroxidase promoter-driven cre-recombinase system, enabling thyroid-specific expression of BRAFV600E for PTC and concurrent p53 loss for ATC, with tdTomato expression marking tumor cells. **Results:** Our findings reveal that ATC undergoes significant genomic and phenotypic plasticity. All ATC tumors exhibited genomic instability, consistently showing chromosome 12 amplification. Interestingly, the majority of tumor cells in vivo expressed the thyroid lineage marker PAX8. However, in vitro culture led to the loss of PAX8 expression, acquisition of a mesenchymal phenotype, and selection against chromosome 12 amplification. When these cells were transplanted back into syngeneic mice, PAX8 expression was restored, and subclones favoring chromosome 12 amplification predominated. BRAF inhibitor treatment further highlighted ATC plasticity, inducing population restriction where persistent cells lacked PAX8 expression and exhibited a mesenchymal phenotype. Notably, this resistant population endured even after BRAF inhibitor withdrawal. **Conclusion:** These results demonstrate that ATC retains phenotypic plasticity rather than undergoing terminal dedifferentiation. The tumor microenvironment strongly influences ATC biology, promoting chromosome 12 amplification and PAX8 expression, and fostering plasticity that supports resistance to targeted therapies.

1113992 - DEHAL1 MODULATES OXIDATIVE STRESS INDUCED BY ENDOGENOUS AND ANTHROPOGENIC OXIDANTS

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Introduction: DEHAL1 recycles iodine in the thyroid by deiodination of iodotyrosines. The gland of Dehal1 KO mice shows increased expression of Nrf2-dependent antioxidant enzymes, suggesting compensation for intrinsic ROS excess. At present, the capacity of the enzyme to modulate reactive oxygen species (ROS) in thyroid, liver or kidney remains unexplored. **Objective:** To investigate DEHAL1's antioxidant capacity against endogenous and anthropogenic oxidants, and the signaling pathway involved. **Methods:** DEHAL1's promoter sequences were analyzed for antioxidant responsive elements (AREs, interacting with Nrf2) using USCS and Jasp. Dehal1 induction by the Nrf2-stimulator sulforaphane (SFN) was studied in HEK293 kidney cells by qPCR. Mouse hepatic (mHep) cells lacking Dehal1 expression were transfected with 50 ng hDEHAL1 cDNA or empty vector. Cells were exposed to H₂O₂ (1 mM, 1.5h) or TBBPA, (200 µM, 3h). ROS were quantified using two probes: DCFDA, detecting hydroxyl or peroxy radicals, and DHE detecting superoxide, and normalized by cell viability (MTT assay). **Results:** Four AREs were identified in DEHAL1 promoter and intron 1 (RS>0.8), suggesting NRF2-mediated transcription. Accordingly, SFN induced a 3.7±1.9-fold upregulation of DEHAL1 in HEK293 cells (p<0.005). mHep cells exposed to H₂O₂ increased 1.8±0.2 and 1.6±0.1-folds the DCFDA and DHE signals, respectively (p<0.005). TBBPA caused 5.5±0.4-fold increase in DCFDA and 1.6±0.1-fold in DHE signals (p<0.005), indicating potent ROS induction. In contrast, DEHAL1 restored the H₂O₂-induced ROS elevation to basal levels, representing 80% and 70% reduction of DCFDA (p<0.01) and DHE signals (p<0.005), respectively, and fully restoring cell viability (p<0.05). The elevation of ROS by TBBPA was also neutralized by DEHAL1, representing the clearance of 110% excess radicals (p<0.005) caused by the xenobiotic, suggesting an intrinsic ROS scavenging activity of DEHAL1. **Conclusion:** DEHAL1 is a novel antioxidant enzyme responsive to NRF2-stimuli, whose activity may mitigate the intrinsic oxidative burden of thyroid cells, and those derived from environmental pollutants in liver or kidney.

THYROID CELL BIOLOGY

1112372 - FUNCTIONAL ANALYSIS OF SLC5A5 GENE VARIANTS ASSOCIATED WITH CONGENITAL HYPOTHYROIDISM

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Introduction: Iodide transport defect is an uncommon cause of congenital hypothyroidism due to biallelic loss-of-function variants in the sodium iodide symporter (NIS)-coding gene SLC5A5. Next-generation sequencing-based studies have revealed SLC5A5 variants of uncertain significance in patients with congenital hypothyroidism. **Objective:** To investigate the pathogenicity of uncharacterized congenital hypothyroidism-associated SLC5A5 gene variants. **Methods:** Bibliographic compilation and bioinformatic analysis of novel SLC5A5 gene variants identified in patients with congenital hypothyroidism. Functional analysis was performed in HeLa cells, which do not endogenously express NIS, transiently transfected with expression vectors encoding wild-type NIS or its variants. **Results:** Bibliographic search revealed missense (p.G18R, p.L54P, p.D191G, p.G250V, p.Q265R, p.R273C, p.R273H, p.A320T, p.G341R, p.R376W and p.P560L) and nonsense (p.L336*, K388*, p.R516* & Q639*) SLC5A5 gene variants. Bioinformatic analysis using an NIS-specific variant classifier predicted p.A320T, p.R376W, and p.P560L to be benign, and the remainder to be pathogenic. Nonsense variants were classified as pathogenic because they eliminate essential elements for NIS plasma membrane expression. Functional assays revealed that the variants p.R273C, p.R273H, p.A320T, p.R376W and p.P560L retain over 70% of wild-type NIS activity, whereas p.G18R, p.L54P, p.D191G, p.G250V, p.Q265R and p.G341R show an 80% reduction. Immunofluorescence and immunoblot assays showed that p.G18R, p.D191G, p.R273C, p.R273H, p.A320T, p.R376W and p.P560L are properly expressed at the plasma membrane, whereas p.L54P, p.G250V, p.Q265R and p.G341R show reduced expression. **Conclusions:** Next-generation sequencing has expanded our understanding of genes involved in thyroid hormonogenesis, thus revealing molecular mechanisms of congenital hypothyroidism. However, our data highlight the importance of performing functional in vitro assays to underscore the pathogenicity of variants of uncertain significance.

1112374 - PATHOGENIC VARIANTS IN CONSERVED RESIDUES OF SLC5A FAMILY MEMBERS REVEALED KEY RESIDUES FOR NIS FUNCTION

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Introduction: Loss-of-function variants in the sodium iodide symporter (NIS)-coding gene SLC5A5 cause congenital hypothyroidism due to insufficient iodide availability for thyroid hormonogenesis. NIS belongs to the SLC5A family of sodium-dependent transporters that actively transport vitamins, minerals, and nutrients across the plasma membrane. Pathogenic variants in other SLC5A family members are also associated with human pathologies, including glucose-galactose malabsorption and renal glucosuria. **Objective:** To investigate the effect on NIS function of pathogenic variants located in conserved residues of other SLC5A family members. **Methods:** Pathogenic variants in conserved residues of the SLC5A family members were identified by bibliographic search and multiple sequence alignment. Functional analysis was conducted in HeLa cells, which do not endogenously express NIS, transiently transfected with expression vectors encoding wild-type NIS or its variants. **Results:** The pathogenic missense variants (p.D28N and p.L369S in SLC5A1, p.G484D in SLC5A2, and p.Y162C in SLC5A6) located in conserved residues along the SLC5A family members corresponding to p.D16N, p.L328S, p.Y150C, and p.G444D in NIS were identified. Bioinformatic analysis predicted the variant p.G444D as pathogenic and p.D16N, p.Y150C, and p.L328S as likely pathogenic. Iodide transport assays showed that all variants caused a ~50% reduction in activity compared to that of the wild-type NIS. In addition, immunofluorescence assays indicated that the variants p.D16N and p.Y150C are properly expressed at the plasma membrane, whereas the variants p.L328S and p.G444D show reduced plasma membrane expression. **Conclusion:** Novel residues required for NIS function have been revealed based on the study of pathogenic variants located in conserved residues of other SLC5A family members. These findings highlight the importance of conserved residues in the biology of the SLC5A family of transporters, shedding light on the molecular basis of congenital hypothyroidism-causing NIS variants.

THYROID EPIDEMIOLOGY

1112323 - TREATMENT PATTERNS AMONG METHIMAZOLE-TREATED PATIENTS WITH GRAVES' DISEASE

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Introduction: Antithyroid drugs (ATD) are the most common pharmacological treatment for hyperthyroidism due to Graves disease (GD) and are usually the first- and often second-line therapy, prior to thyroid ablation (i.e., thyroidectomy or radioactive iodine [RAI]). In the US, methimazole (MMI) is the most frequently prescribed ATD. **Objective:** To evaluate dosage and treatment patterns following MMI initiation among patients with GD. **Methods:** Data from the IQVIA open claims and PharMetrics Plus databases were utilized. Patients who had their first MMI prescription claim between November 2020 and October 2021 and a diagnosis of thyrotoxicosis (hyperthyroidism) within 3 years prior or 2 years after the index MMI claim were included. Patients were followed for 104 weeks from their first MMI prescription to evaluate treatment patterns. **Results:** Among 46,373 patients who met the study inclusion criteria, 41% initiated treatment with low-dose (0 to ≤5 mg/day) MMI therapy, while 34% initiated moderate-dose (>5 to ≤15 mg/day), 15% initiated moderate-to-high dose (>15 to ≤25 mg/day), and 10% initiated high-dose (>25 mg/day) MMI. Overall, 35% discontinued MMI within 56 weeks, including 17% and 8% who had thyroidectomy and RAI treatment, respectively. Another 25% of patients were on low-dose or off treatment by week 24 and were not on a dose >5 mg through week 104. The remaining 40% of patients were not therapeutically stable at the end of 56 weeks. Many patients cycled through large dose fluctuations and experienced failed trials of MMI, and ≈10% persistently remained on MMI doses >15 mg/day throughout 56 weeks. **Conclusion:** These findings highlight the variable and complicated dosing and treatment patterns following MMI therapy. The relatively high proportion of patients who either do not achieve therapeutic stability or remain on higher doses of MMI after a year of treatment underscore the need for alternative pharmacologic therapies for Graves hyperthyroidism.

1112503 - TWENTY-YEAR SECULAR TREND OF THYROTOXICOSIS AND THYROTOXIC PERIODIC PARALYSIS IN HONG KONG

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Introduction: Thyrotoxic periodic paralysis (TPP) is a rare complication of thyrotoxicosis characterized by hypokalemia, episodic muscle weakness/paralysis, which is potentially fatal when cardiopulmonary complications occur. Lack of large TPP cohorts hinders relevant epidemiology study. **Objectives:** To establish a population-based registry of thyrotoxicosis and TPP in Hong Kong, and to evaluate their secular trend during 2002-2021. **Methods:** Clinical data from the electronic medical database in Hong Kong, the Clinical Data Analysis and Reporting System (CDARS), was retrieved. One hundred potential cases of thyrotoxicosis (by ICD-9-CM: 242.xx) and TPP (by ICD-9-CM: 242.xx and 359.3, plus low potassium level) were randomly selected from CDARS, followed by reviewing clinical notes, examining laboratory test records, and deriving positive predictive value (PPV) of the clinical data. A population-based registry of thyrotoxicosis and TPP in Hong Kong was established. The standardized incidence rate of both thyrotoxicosis and TPP were computed with annual percentage change (APC) for trend analysis. **Results:** The PPV of clinical data in CDARS for thyrotoxicosis and TPP were 0.86 (95% CI: 0.79-0.93) and 0.97 (95% CI: 0.94-1), respectively. Population-based cohorts of thyrotoxicosis (n=83,184) and TPP (n=999) were established. The age- and sex-standardized incidence rate of thyrotoxicosis increased from 45.22 to 80.7 per 100,000 person-years from 2002 to 2021, with APC of 4.72% (95% CI: 2.02-8.05). Both sexes had increasing trend in age-standardized incidence rate of thyrotoxicosis. As TPP patients were predominantly male, the age-standardized incidence rate of TPP was stratified in both sexes. In 2002 and 2021, the incidence rate (per 100,000 person-years) in male was 1.48 and 1.28 respectively, while that in female was 0.11 and 0.13, without significant trend observed. **Conclusion:** This is the first study validating clinical data for TPP in electronic medical database. Its high PPV enabled establishment of the largest TPP cohort to-date, facilitating future epidemiology studies.

THYROID GENETICS

1112209 - CARDIAC COMPLICATIONS IN PATIENTS WITH RESISTANCE TO THYROID HORMONE DUE TO THYROID HORMONE RECEPTOR BETA GENE MUTATIONS (RTHβ)

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Introduction: Resistance to thyroid hormone beta (RTHβ), caused by mutations in the thyroid hormone receptor beta (THRβ) gene, is associated with cardiac symptoms such as palpitations, tachycardia, and atrial fibrillation (Af). However, comprehensive data on cardiac complications remain limited. **Objective:** This study aimed to elucidate the clinical characteristics and cardiac complications in Japanese patients with RTHβ. **Methods:** A retrospective analysis of 43 patients from 37 families diagnosed with RTHβ at Ito Hospital (2005-2023) was performed. THRβ mutations were confirmed in all cases. Data on clinical symptoms, arrhythmias, comorbidities, and treatments were analyzed. **Results:** The median diagnostic age was 36 years (range: 14-78); 30 females and 13 males. Comorbidities included Hashimoto's disease (8 patients) and Graves disease (2 patients). Pre-diagnosis treatments included antithyroid drugs (14 patients), radioactive iodine (1 patient), and thyroid surgery (3 patients). Palpitations occurred in 65.1% (28/43) of patients, tachycardia in 14.0% (6/43), with 72.1% (31/43) experiencing either symptom. Arrhythmias were observed in 23.2% (10/43), including Af in 20.9% (9/43). Of these, 5 were persistent and 4 paroxysmal (median onset age: 58 years). Beta-blockers or calcium channel blockers were used in 11 patients without arrhythmias. Patients with Af (n=9) were significantly older at diagnosis (median age: 53 vs. 31 years, p=0.0327). Thyroid function tests and THRβ mutations showed no significant differences between groups. **Conclusions:** Cardiac complications, especially Af (20.9%) and palpitations, are common in RTHβ. Regular monitoring and early management are critical to reduce cardiac risks.

1112624 - MOLECULAR CHARACTERIZATION OF A LARGE SERIES OF SUBCENTIMETRIC PAPILLARY THYROID CARCINOMAS

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Introduction: Thyroid cancer incidence has been increasing. This increase results, in part, from the overdiagnosis of subcentimetric (<10 mm) papillary thyroid carcinomas (SPTC). SPTC cases are usually indolent, leading to patient overtreatment. However, a few can be highly aggressive and metastatic. This has created the need to study these SPTC and try to clarify which tumors may be surveilled only, and which tumors require intervention. **Objective:** To progress in the identification of more aggressive cases we gathered a database in which 1027 SPTCs were included. Clinicopathological data and surgical tissue samples are being collected from Hospital São João, Porto, Portugal. **Methods:** Molecular characterization of the samples is ongoing. At this moment, we have completed the clinicopathological and molecular analysis of 189 cases. Cases were screened for BRAF, NRAS and TERTp mutation. Mutations were detected and validated by Sanger sequencing. **Results:** For the 189 cases, mean age was 50.3 years $\pm$ 14.1. Mean tumor size was 6.6 $\pm$ 2.3 mm. BRAF mutation was present in 25.4%, NRAS mutation in 8.5% and TERTp mutation in 14.3% of all cases. Six cases (3.2%) presented BRAF and TERTp mutation. Molecular analysis showed that in BRAF mutated tumors, patients tended to be younger (30.7% < 55 years vs. 17.3% $\geq$ 55 years, $p=0.039$), tumors presented most frequently with poorly defined limits (16.9% well defined limits vs 41.5% poorly defined limits, $p<0.001$), infiltrative/mixed growth (17.0% expansive growth vs 32.7% infiltrative/mixed growth, $p=0.014$), positive resection margins (23.5% negative vs 83.3% positive, $p=0.002$). TERTp mutated tumors had less frequently inflammatory infiltrate when compared to TERTp WT tumors (18.3% absent vs 6.3% present, $p=0.027$). **Conclusions:** In the present series we found that BRAF mutated SPTC are associated with younger patient age and invasive growth. A larger series using molecular data is necessary to progress in distinguishing between indolent and aggressive SPTCs.

THYROID GENETICS

1112208 - THE ROLE OF THYROID HORMONE IN SUSCEPTIBILITY TO TYPE 2 DIABETES IN OFFSPRING: REGULATORY MECHANISMS OF THE PLACENTAL GENOMIC IMPRINT AT THE DLK1-DIO3 LOCUS IN WOMEN WITH HYPOTHYROIDISM

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Introduction: The regulation of metabolism, vital from fetal development to adulthood, is intrinsically linked to thyroid hormones. During pregnancy, dysregulations that impact epigenetic control can predispose to metabolic diseases, including type 2 Diabetes Mellitus (DM2). Despite theories about reduced expression of deiodinase 3 (D3) and changes in DNA methylation patterns at the DLK1-DIO3 locus associated with glucose intolerance in T2DM, the intricate mechanisms connecting thyroid and pancreas remain unclear. Studies indicate a significant increase in the methylation of MEG3-DMR zones in pancreatic beta cells from diabetic patients, resulting in decreased expression of microRNAs. Therefore, we investigated whether hypothyroidism acts as a deregulator in placental imprinting mechanisms. **Objective:** To evaluate the epigenetic control mechanisms responsible for imprinting the DLK1-DIO3 locus in placentas from hypothyroid mothers. **Methods:** Two groups with 12 pregnant women were selected: Healthy group and Group with hypothyroidism and TSH value (greater than or equal to 4.5 IU/mL in the first trimester of pregnancy). A comparative study of the placental DNA methylation profile was carried out by post-bisulfite pyrosequencing of zones I MEG3-DMR, IG-DMR-1 and IG-DMR2. We used the Tukey Kramer statistical test with a significance level of 5%. **Results:** In the MEG3-DMR region, a statistically significant difference ($p<0.05$) was found in the average methylation profiles of the hypothyroid group in relation to the healthy group, highlighting the epigenetic control mechanisms responsible for imprinting the DLK1-DIO3 locus. **Conclusion:** The described hypermethylation of the region responsible for DIO3 expression in the placentas of hypothyroid mothers reveals an epigenetic mechanism linking maternal hypothyroidism to offspring metabolic outcomes. These findings underscore the critical importance of maintaining normal thyroid hormone levels in hypothyroid pregnant patients to ensure optimal fetal development and metabolic health.

1112321 - FUNCTIONAL TESTING OF POTENTIAL NOVEL THYROID HORMONE TRANSPORTERS INFORMED BY A LARGE SCALE THYROID FUNCTION GENOME-WIDE ASSOCIATION STUDY

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Introduction: Thyroid hormone transporters are crucial for cellular uptake of thyroid hormones. Mutations in monocarboxylate transporter 8 (MCT8) cause a severe neurodevelopmental and metabolic disorder, highlighting their clinical significance. Although ~25 transporters are known to transport thyroid hormones, it is unknown whether all thyroid hormone transporters have been identified yet. **Objective:** To identify novel thyroid hormone transporters. **Methods:** Genetic look-up and colocalization analyses were performed using GWAS-data to assess the correlation of thyroid function tests and genes encoding all 436 solute carrier (SLC) and 48 ATP-binding cassette (ABC) transporters. Genes encoding transporters localized at the cell membrane and not already investigated for thyroid hormone uptake in literature were selected for functional testing. The candidate transporters were transiently expressed in COS-1 cells and incubated for 10 minutes with 1 nM radio-labeled thyroxine (T₄), triiodothyronine (T₃), reverse T₃ (rT₃) or 3,3-diiodothyronine (T₂) in the presence of μ -crystallin (CRYM). **Results:** The genetic look-up and colocalization analysis was performed in 271,040 euthyroid individuals across 46 cohorts from the ThyroidOmics Consortium. This revealed a significant association with 60 transporters genes (including known transporters like MCT8 and SLC17A4) of which 32 were never tested before. We performed functional testing for 28 transporters, of which 27 showed no uptake of T₄, T₃, T₂ or rT₃. Only SLC17A1 showed a non-significant 1.5 fold uptake of T₄, although poor membrane expression was observed. **Conclusion:** In this study, screening for novel thyroid hormone transporters utilizing a GWAS-based genetic look-up, none of the 28 selected candidates showed significant uptake of thyroid hormones. The T₄ uptake by SLC17A1, of which the expression is currently optimized, might prove relevant in the future. Further studies, including testing the remaining 4 transporters and other iodothyronine metabolites, may reveal whether or not the transporter genes identified in the GWAS are bona fide thyroid hormone transporters.

THYROID HORMONE ACTION

1112598 - TRIIODOTHYRONINE MODULATES DENDRITIC CELL-DERIVED EXTRACELLULAR VESICLES AND THEIR ROLE IN IMMUNE RESPONSE REGULATION

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Introduction: T₃ activates dendritic cells (DCs), promotes pro-inflammatory adaptive responses, and increases antigen-specific cytotoxic responses, improving antitumor responses, as largely demonstrated by our group. Nonetheless, the cellular mechanisms involved in T₃'s effects are unknown. **Objective:** Due to the role of DCs-derived extracellular vesicles (DCs-EVs) in cell-to-cell communication and their ability to directly and indirectly impact immune responses, we aimed to investigate T₃ effects on DCs-EVs and EV-depleted conditioned medium (CM). **Methods:** Therefore, murine (C57BL/6) DCs were cultured (18h) with T₃ (10nM) (DCs-T₃) or without (DCs-Ct). CM was collected and processed by differential ultracentrifugation to obtain DCs-EVs (10K-EVs and 100K-EVs, following 10,000 g and 100,000 g ultracentrifugation for 40' and 90', respectively), and EV-depleted CM. EVs were quantified by NTA and Bradford, and characterized by WB and electron microscopy. DCs-EVs and EV-depleted CM were co-cultured with syngeneic DCs, for EV uptake and DCs activation analyses by FACs. Additionally, DCs-EVs and EV-depleted CM were co-cultured with Balb/c mice splenocytes, for T cell activation marker analysis by FACs. Statistical analyses considered p $\leq$ 0.05 significant. **Results:** Significant increase in 10K-EVs concentration, and a tendency of increase of 100K-EVs was found in DCs-T₃ (vs DCs-Ct) by NTA (paired t-test), though not by Bradford. WB revealed decreased expression of syntenin in DCs-T₃-derived EVs (vs DCs-Ct-derived EVs), indicating that T₃ may alter EV cargo. Preliminary results using CFSE-labeled EVs suggest an uptake of both EVs by DCs. DCs-T₃-derived EVs and EV-depleted CM of DCs-T₃ significantly increased %CD86high DCs (Tukey test), indicating syngeneic DCs activation. Preliminary results showed no significant differences in CD25 expression when splenocytes were cultured with either EVs or EV-depleted CM, indicating no major allogeneic T cell activation. **Conclusion:** In conclusion, T₃ increases the release of EVs and soluble mediators (possible proteins) by DCs, which can activate syngeneic DCs, potentially impacting immune responses, though they do not appear to induce direct T cell activation.

1112587 - CLINICAL IMPLICATIONS FOR OBESITY MANAGEMENT: BARIATRIC SURGERY-INDUCED CHANGES IN TSH AND ITS CORRELATION WITH THE NEW MODEL OF OBESITY CLASSIFICATION PROPOSAL BY SBEM/ABESO, A CROSS SECTIONAL STUDY

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Introduction: Thyroid-stimulating hormone (TSH) plays a crucial role in energy metabolism and adipogenesis, with elevated levels often observed in individuals with obesity. While obesity is commonly associated with normal thyroid hormone levels, the relationship between TSH and obesity severity remains debated. This study evaluates the impact of bariatric surgery on TSH levels in euthyroid obese patients and explores correlations with body mass index (BMI) changes. **Objectives:** To assess the changes in TSH levels following bariatric surgery and their association with BMI reduction in euthyroid obese individuals. **Methods:** This retrospective observational study included 96 euthyroid obese patients who underwent bariatric surgery at a specialized obesity clinic. Pre - and postoperative data, including BMI, TSH, and free thyroxine (T₄) levels, were analyzed. Patients were classified according to the World Health Organization (WHO) BMI criteria and a novel obesity classification by SBEM/ABESO, which incorporates weight loss percentages. **Results:** Preoperatively, a positive correlation was observed between BMI and TSH levels ($r=0.291$, $p<0.01$), supporting the hypothesis of TSH as a marker of energy imbalance. Post-surgery, BMI reductions were significant, with 47.9% of patients transitioning out of Class III obesity ($BMI \geq 40 \text{ kg/m}^2$). Concurrently, TSH levels decreased significantly in all BMI categories (2.48 ± 0.2 to $1.81 \pm 0.25 \text{ mU/L}$, $p<0.001$), with the largest reductions in patients achieving greater weight loss. No significant changes in T₄ levels were observed. TSH changes were not significantly associated with the percentage of weight loss, as suggested by the classification of SBEM/ABESO. **Conclusion:** Bariatric surgery not only improves anthropometric and metabolic profiles but also reduces TSH levels in euthyroid obese patients. These findings suggest that TSH may serve as a dynamic marker of metabolic adaptation and weight reduction, highlighting its relevance in managing obesity and related thyroid dysfunctions.

THYROID HORMONE METABOLISM

1112276 - NEW INSIGHTS INTO THYROID HORMONE METABOLISM AND AMMONIA DETOXIFICATION IN MASLD USING N-ACETYLCYSTEINE (NAC) AND L-ORNITHINE L-ASPARTATE (LOLA)

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Introduction: Thyroid hormones (THs) are fundamental to various aspects of liver physiology. Research indicates that TH dysfunction, particularly due to alterations in deiodinase enzymes such as D3, plays a critical role in the progression of metabolic dysfunction-associated steatotic liver disease (MASLD). This condition affects approximately 38% of the global adult population and is characterized by fat accumulation in the liver, resulting in a series of alterations. In MASLD, the Urea Cycle and Krebs Cycle shift their enzymes to alternative pathways for ammonia detoxification, disrupting normal energy metabolism. Although the exact mechanisms remain partially understood, THs are involved. **Methods:** In our study, adult male Sprague Dawley rats were randomly assigned to several groups: a control group on a standard diet (2.93 kcal/g, $n=10$) and an intervention group on a high-fat diet deficient in choline (MASLD, HDCE, 4.3 kcal/g, $n=10$), along with two treatment groups, MASLD+NAC ($n=12$) and MASLD+LOLA ($n=12$), over a period of 16 weeks. **Results:** We observed alterations in redox parameters that were improved with both treatments. In the MASLD group, there was an increase in the expression of D3, colocalized with M1 macrophages and TRbeta protein levels, while MCT8 levels remained unchanged. Additionally, mitochondrial respiration decreased, and no effects were observed with treatments. Furthermore, Glutamate Dehydrogenase (GDH) activity diminished, whereas α -Ketoglutarate Dehydrogenase (α -KGDH) activity increased. It was also determined that Grp78 (decreased by 74%) and Grp75 (increased by 60%) are regulated by T3 and are endoplasmic reticulum (ER) chaperones meaning ER stress. **Conclusion:** Our study corroborates the interaction between TH metabolism and the compensatory mechanisms that counteract elevated ammonia levels, as well as the enzymes regulating this process in MASLD. Both NAC and LOLA demonstrated potential in correcting TH metabolism and enhancing ammonia detoxification in MASLD, which may help alleviate symptoms or slow the progression of the disease.

THYROID HORMONE METABOLISM

1112274 - TYPE 3 DEIODINASE IS ACTIVATED IN THE BRAIN OF AN ANIMAL MODEL OF METABOLIC ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

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Introduction: Thyroid hormone plays a crucial role in regulating brain cell maintenance, plasticity, and energy production. The conversion of T4 to its active form, T3, in the brain relies on the enzyme type 2 deiodinase (D2), while type 3 deiodinase (D3) inactivates T3. Several factors can lead to oxidative stress and an imbalance in D3 function due to disease. However, the response of D3 in adult brain tissue under different disease conditions is not well understood. **Objective:** In this study, we evaluated the induction of D3 and its effects on the brain in a metabolic dysfunction-associated steatotic liver disease (MASLD) animal model. **Methods:** Adult male Sprague Dawley rats (n=20) were randomly assigned to either a control group (standard diet at 2.93 kcal/g) or a choline-deficient high-fat diet (HFCD at 4.3 kcal/g). **Results:** After 18 weeks on an ad libitum diet, the rats developed MASLD. Following this period, the animals were sacrificed, and we assessed various parameters, including oxidative stress, D3 expression and protein levels, T3-controlled genes, endoplasmic reticulum (ER) stress, and mitochondrial function. Notably, blood ammonia levels were elevated in the MASLD group. Brain tissue analysis from the MASLD group revealed increased carbonyl and TBARS levels (P<0.001) and decreased sulfhydryl and glutathione levels (P<0.001). Furthermore, D3 was induced (P<0.0001) in the MASLD group through the ERK signaling pathway, while T3-controlled genes decreased, indicating reduced T3 levels in the brain. We also observed increased endoplasmic reticulum stress and decreased mitochondrial biogenesis (P=0.001). Mitochondrial respiration was reduced, likely reflecting the impact of elevated ammonia. **Conclusion:** The increased inactivation of T3 by dysfunctional D3 in the MASLD brain leads to a series of cellular disruptions. These changes may partially explain the worsening neurological symptoms seen in patients with liver disease.

THYROID NODULE

1112644 - DEFINING A CUTOFF FOR CALCITONIN LEVELS IN FINE-NEEDLE ASPIRATION WASHOUT FLUID TO EXCLUDE MEDULLARY THYROID CARCINOMA DIAGNOSIS

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Introduction: Given that active surveillance is an option for the follow-up of benign, indeterminate thyroid nodules and papillary microcarcinomas, excluding the presence of medullary thyroid carcinoma (MTC) is crucial in these cases. However, cytology of thyroid nodules can fail to diagnose MTC in up to 50% of cases, and serum calcitonin is useful for early diagnosis but has limited sensitivity and positive predictive value. On the other hand, measuring calcitonin in fine-needle aspiration (CT-FNA) washout fluid from the same sample used for FNA may improve diagnostic accuracy. **Objective:** To evaluate the accuracy of CT-FNA measurement for excluding MTC. **Methods:** The study assessed CT-FNA measurements of 377 thyroid nodules from 278 patients who underwent ultrasound-guided FNA between 2017 and 2024, using an electrochemiluminescence assay. **Results:** Of the 377 nodules, 368 (96.6%) had CT-FNA values up to 9.8pg/mL, with all presenting benign, indeterminate, or papillary thyroid carcinoma (PTC) cytology. Nine nodules had CT-FNA greater than 9.8 pg/mL. One showed benign cytology, and four were suggestive of PTC. The highest CT-FNA value without MTC or C-cell hyperplasia was 29.3 pg/mL. Three nodules confirmed as MTC had CT-FNA values of 493 pg/mL, 137,096 pg/mL, and > 200,000 pg/mL. Interestingly, one patient presented a borderline elevated CT-FNA of 99.81 pg/mL with PTC. The histological specimen was reevaluated, revealing C-cell hyperplasia adjacent to a micropapillary thyroid carcinoma. The ROC curve identified a cut-off value of 64.5 pg/mL, with 100% sensitivity and 99.7% specificity. **Discussion:** Currently, the literature reports varying cut-off values for CT-FNA measurement, ranging from 8.5 pg/mL to 39.6 pg/mL, with one report citing values as high as 220 pg/mL. **Conclusion:** The highest CT-FNA value without MTC or C-cell hyperplasia was 29.31 pg/mL, while a CT-FNA cut-off of 64.5 pg/mL demonstrated excellent sensitivity and specificity for diagnosing MTC. These results could be utilized to exclude MTC in patients under follow-up for thyroid nodules.

1112390 - ENHANCED ALGORITHM FOR THYROID NODULE CLASSIFICATION: PERFORMANCE COMPARISON OF MIR-THYPE V1 AND V2

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Introduction: Cytologically indeterminate thyroid nodules (Bethesda III/IV) are common, often leading to unnecessary diagnostic surgeries. In 2018, the mir-THYPE full test algorithm (v1) based on microRNA analysis was introduced for classifying these nodules. Recently, an enhanced algorithm version (v2) was developed incorporating machine learning, and integrating DNA mutation analysis to improve diagnostic accuracy. **Objective:** To simulate and evaluate the performance of the v2 algorithm in classifying the same samples previously analyzed with v1. **Methods:** The cohort comprised 1,718 thyroid nodules (945 Bethesda III; 773 Bethesda IV) from 1687 patients who underwent molecular testing, the microRNA and DNA data were extracted from fine-needle aspiration (FNA) smear slides of the nodules. Initially, nodules were classified with v1 algorithm in routine clinical settings. The v2 algorithm was applied to re-analyze these same samples utilizing microRNA profiling and DNA mutation detection (BRAF V600E, TERT C228T and C250T). Anatomopathological data from 329 nodules (112 benign; 217 malignant) served as reference to evaluate v2 algorithms performance. To address the unrealistically high disease prevalence of 66.0%, an adjusted real-world prevalence of 32% was calculated using Bayes theorem. **Results:** Comparing algorithms, v2 increased the Benign Call Rate (BCR) from 57.0% to 68.4%, classifying 1175 nodules as benign versus 979 with v1. Furthermore, v2 identified 543 samples as positive for malignancy vs 739 samples by v1. In this simulation, v2s projected real-world performance metrics are: sensitivity of 94.5%, specificity of 75.9%, positive predictive value (PPV) of 64.8%, negative predictive value (NPV) of 96.7% and accuracy of 81.8%. **Conclusion:** The v2 algorithm demonstrates a marked improvement in BCR and overall diagnostic performance, increasing the number of patients who could benefit from the test in reducing unnecessary diagnostic surgeries. The high PPV and NPV suggest optimized performance for future clinical applications.

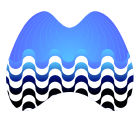
THYROID NODULE

1112391 - PREOPERATIVE MIR-146B EXPRESSION AS A PREDICTOR OF AGGRESSIVE OUTCOMES IN DIFFERENTIATED THYROID CARCINOMAS

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Introduction: Thyroid cancer ranks as the ninth most prevalent cancer globally, and often with a favorable prognosis. However, some cases exhibit aggressive features. Elevated expression levels of microRNA-146b (miR-146b) in differentiated thyroid carcinomas (DTC) has been associated with worse clinical features, including lymph node metastasis (LNM), extrathyroidal invasion (EI), and the presence of BRAF V600E mutation. These findings highlight miR-146b as a potential biomarker of disease progression and worse prognosis. **Objective:** This study aimed to assess miR-146b expression levels as a prognostic biomarker for predicting aggressive clinical-pathological phenotypes in DTC, using fine-needle aspiration (FNA) smear slides to aid in earlier identification and optimized patient management. **Methods:** A cohort of 204 preoperative FNA smear slides from DTC nodules was analyzed for miR-146b expression (normalized) and the presence of the BRAF V600E mutation by qPCR using TaqMan assays. Histopathological data were reviewed to identify LNM, EI, vascular invasion (VI) and ATA recurrence risk (RR). Receiver Operating Characteristic (ROC) curves established miR-146b expression cut-offs, creating three risk zones: low, moderate, and high. **Results:** Elevated expression of miR-146b was proportionally correlated with aggressive features, and the probability of developing these features in each miR-146b expression zones was: Presence of LNM - 12.0% (low), 34.5% (moderate), 75.0% (high); probability of classification into ATA intermediate/high RR categories - 16.0% (low), 46.2% (moderate), 66.7% (high); and presence of BRAF V600E mutation - 6.1% (low), 71.4% (moderate), 94.7% (high). No correlation was found between miR-146b and EI or VI, suggesting that these features may be driven by distinct molecular pathways requiring further investigation. **Conclusion:** The assessment of miR-146b expression levels may serve as a valuable preoperative tool for predicting aggressive features in DTC, enabling enhanced early risk stratification, leading to tailored treatments and improved resource allocation in healthcare.



1112275 - RADIOFREQUENCY ABLATION VERSUS ETHANOL ABLATION FOR BENIGN THYROID NODULES TREATMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Radiofrequency ablation (RFA) is a well-established therapy for thyroid nodules. Ethanol Ablation (EA) is cheaper and widely used in practice for benign thyroid cysts. Less is known about the efficacy of RFA compared to EA in the treatment of benign thyroid nodules. **Objective:** This systematic review and meta-analysis was performed and reported in accordance with the Cochrane Collaboration Handbook of Systematic Review of Interventions and the Preferred Reporting Items of Systematic Reviews and Meta-Analysis (PRISMA) guidelines. We compared the effectiveness of RFA versus EA in benign thyroid nodules. **Methods:** Embase, Cochrane Central Register of Controlled Trials and PubMed database were searched for randomized trials or observational studies that compared Radiofrequency Ablation and Ethanol Ablation as single approach to benign thyroid nodule treatment and reported the outcomes of (1) binary therapeutic success rate; (2) nodule volume reduction; (3) cosmetic score rate; and (4) improvement of symptoms. Heterogeneity was examined with I^2 statistics. **Results:** We included 5 studies, 2 randomized controlled trials and 3 non-randomized cohorts, with a total of 292 patients. A total of 136 (47%) patients received Radiofrequency Ablation and 156 (53%) received Ethanol Ablation. In those receiving RFA, there was an overall trend towards achieving binary therapeutic success rate (0.96% vs 0.87%; OR 4.55; 95% CI 1.21-17.18; $p=0.020$; $I^2=0$) but no significant difference in nodule volume reduction between RFA and EA groups (MD -0.02; 95% CI -2.7-2.65; $p=0.99$). There was no significant difference between groups when it comes to cosmetic score rate (MD -0.18; 95% CI -0.46-0.09; $p=0.20$) or improvement of symptoms (MD -0.07; 95% CI -0.51-0.37; $p=0.77$). **Conclusion:** These findings indicate that RFA demonstrates superior efficacy over EA in terms of binary therapeutic success rates. However, EA remains a viable and cost-effective option for treating benign thyroid nodules, particularly in resource-limited healthcare settings.

THYROID NODULE

1112455 - REDEFINING BETHESDA III: THE VALUE OF BINARY STRATIFICATION IN PREDICTING THYROID MALIGNANCY

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Introduction: The 3rd edition of the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) proposes a binary subcategorization for Bethesda III (BIII) based on nuclear atypia. It distinguishes aspirates with nuclear atypia (AUS-N) from other types of atypia (AUS-O), highlighting a higher risk of malignancy (ROM) in AUS-N. **Objective:** To assess the performance of binary stratification in estimating ROM in BIII nodules. **Methods:** Retrospective study of BIII fine-needle aspirates performed at our institution between 2011-2024. Demographic characteristics were collected. Aspirates were classified as AUS-N or AUS-O according to TBSRTC 3rd edition. AUS-O was subdivided into architectural, oncocytic, or lymphoid atypia as suggested by TBSRTC 2nd edition. Outcomes were defined as malignant (histological confirmation) or benign (histopathology, benign re-aspirate, or stable clinical/sonographic follow-up). Statistical methods included Fishers exact or chi-square tests. **Results:** Of 2,160 satisfactory aspirations, 84 (3.9%) were BIII. Median age of the population was 54 years, 89.3% women; median nodule size 26 mm; 31.2% had Hashimoto's thyroiditis. AUS-O was identified in 57 cases (67.9%), and AUS-N in 27 (32.1%). Among AUS-O, 84.2% were subclassified as architectural atypia, 10.5% oncocytic, and 5.3% lymphoid atypia. Final outcomes were available for 73.8% of cases (median follow-up: 30 months). Surgery was performed in 28 patients (73.6% AUS-N vs. 32.5% AUS-O, $p=0.003$). The overall ROM for the category was 22.6%: 12 papillary carcinomas (all AUS-N) and 2 primary thyroid lymphomas. ROM was significantly higher in AUS-N than in AUS-O (63.1% vs. 4.6%, $p<0.0001$). AUS-N showed 85.7% sensitivity and 85.4% specificity for diagnosing malignancy. Within AUS-O, no malignancies were observed in architectural or oncocytic atypia, but 2/3 lymphoid atypia cases were lymphomas ($p<0.01$). **Conclusions:** Binary stratification effectively identifies AUS-N as a high-ROM group. Subclassifying AUS-O remains critical to distinguish negligible-risk cases from lymphoid atypia, which require tailored management.

1114103 - THE GENOMIC LANDSCAPE OF 250,000+ THYROID NODULES UNDERGOING EXOME-ENRICHED RNA SEQUENCING

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Introduction: In 2021, genomic analysis of 50,000+ consecutive thyroid tumors with Bethesda III-VI (BIII-VI) cytology assessed by the Afirma Genomic Sequencing Classifier (GSC) was published. **Objective:** To analyze an expanded Afirma cohort of over 250,000 samples, including optional TERT promoter testing (TERTp) data. **Methods:** Cytologic and molecular differences were assessed in 252,510 consecutive thyroid tumors with BIII-VI cytology undergoing Afirma GSC testing from 2018-2024. TERTp was assessed in 8,627 samples from 2023-2024. **Results:** Median age was 59.3 years, 76.5% were female, and median nodule size was 2.2 cm. Among BIII/IV nodules, 163,992 (69%) were classified as GSC-(B)enign. In BIII-VI non-GSC-B nodules, expressed variants were detected in 35.9%, 43.6%, 55%, and 78.9%, respectively. BRAFV600E was most frequent, particularly in BV/VI (44.9%/76.4%). NRAS was the most prevalent RAS variant, most common in BIII/IV nodules (13%/17.3%). TERT mutations, alone (n=932, 10.8%) or co-occurring with BRAFV600E (n=828, 9.6%), were most common in BVI. Fusions were identified in 6% of non-GSC-B nodules, most often in BV (9.3%). Most prevalent fusions involved RET, more commonly seen in Bethesda V/VI than III/IV nodules (3.6% of all samples vs. 0.7% of GSC-(S)uspicious samples), and PPARγ, which was primarily detected in Bethesda III/VI nodules (2.5% vs. 0.6% in V/VI). Nodules with more than one variant or fusion were rare (<1.2% in each Bethesda category). Over the last 7 years, the rate of GSC-S in BIII declined significantly from 32.6% in 2018 to 26.1% in 2021 and then rose to 31.8% by 2024 (p<0.01). Similar trends were seen in BIV (44.7% → 40.9% → 45.4%) over the same time. **Conclusion:** This large study describes the molecular landscape of nodules sent for Afirma GSC testing and highlights the molecular alterations seen in different Bethesda categories, including TERTp mutations. Temporal shifts in GSC-S rates are of interest and warrant further investigation.

THYROID NODULE

1112599 - ULTRASONOGRAPHIC-HISTOLOGICAL CORRELATION OF THYROID NODULES IN A CHILEAN CENTER AND PERFORMANCE OF ACR-TIRADS VARIABLES

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Introduction: Thyroid nodules are common, and the majority are benign, which raises concerns about identifying ultrasonographic predictors that could suggest malignancy. **Objective:** To evaluate the ultrasonographic-histological correlation of thyroid nodules using the ACR-TIRADS criteria and biopsy results according to the Bethesda system. **Methods:** Observational, descriptive, and prospective study. Patients over 18 years old with fine-needle aspiration (FNA) biopsies performed between June 2023 and October 2024 were included. Biopsies without a diagnosis (Bethesda I) were excluded. Demographic and ultrasonographic characteristics, ACR-TIRADS score, and biopsy results were recorded. Likelihood Ratio (LR (+)) for ultrasonographic variables and negative predictive value (NPV) and positive predictive value (PPV) for different ACR-TIRADS groups were calculated, excluding Bethesda III-IV results. **Results:** A total of 1162 thyroid nodules were analyzed, with 46 Bethesda I nodules excluded. Of the remaining nodules, 44.6% were Bethesda II and 26.8% Bethesda V-VI. ACR-TIRADS 3 nodules showed 69.1% Bethesda II results, while ACR-TIRADS 5 nodules showed 61% Bethesda V-VI. 85.5% of the patients were female, with an average age of 51 years and a mean BMI of 28 kg/m². ACR-TIRADS 3 nodules had an NPV of 83% for predicting Bethesda II biopsies, while the PPV for ACR-TIRADS 4 and 5 nodules was 19% and 70%, respectively, for Bethesda V-VI results. The LR (+) values for ultrasonographic variables were: hypoechoic nodule (1.2), microcalcifications (3.4), irregular borders (4.6), taller-than-wide shape (5.1) and very hypoechoic (13.5). **Conclusion:** This study emphasizes the usefulness of ultrasonographic characteristics in improving the accuracy of biopsy indications, the application of simplified models, and their potential as inputs for artificial intelligence in thyroid nodule evaluation within our population. The PPV and NPV of ACR-TIRADS in our context are also reported.

1112186 - IDENTIFYING PREDICTORS OF PERMANENT HYPOPARATHYROIDISM AFTER THYROID CANCER SURGERY - A COMPREHENSIVE REAL-LIFE RETROSPECTIVE ANALYSIS

Rossella Melcarne¹; Giorgio Grani¹; Fabrizio Consorti¹; Tal Deborah Engel¹; Eva Iannuzzi¹; Giuseppe de Ruggieri¹; Laura Giacomelli¹; Cosimo Durante¹; Marco Biffoni¹

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Introduction: Postoperative hypoparathyroidism (POH) is a common complication of total thyroidectomy, leading to low serum calcium levels due to insufficient parathyroid hormone secretion and has a significant impact on patients quality of life, often requiring lifelong medication and follow-up. The possibility of a post operation permanent POH (p-POH) after thyroid surgery, especially in department dedicated to endocrine surgery is expected to be around 2.2%, yet in real-life, the numbers are significantly higher. Identifying predictors of p-POH remains a critical unmet need in clinical practice. **Objective:** This study aims to identify potential predictive factors for developing p-POH in patients undergoing thyroid cancer surgery, and improving preoperative planning, surgical techniques, and patient outcomes. **Methods:** We conducted a retrospective analysis of 522 patients selected from the X of the X of X database, that underwent thyroid surgery for differentiated thyroid cancer with a follow-up of 12 months. The primary outcome was the incidence of p-POH, defined as the requirement for calcium and/or vitamin D supplementation beyond 12 months post-surgery. Statistical analyses were performed to assess associations between clinical and surgical variables, such as histology, lymph node metastases, central/lateral compartment neck dissection, and response to therapy, with the occurrence of p-POH. **Results:** Among the 522 patients analyzed, 60 (11.5%) developed p-POH. Strong predictors of p-POH included the extent of neck dissection, the presence of lymph node metastases, total thyroidectomy compared to lobectomy, American Thyroid Association (ATA) risk stratification, and the number of lymph nodes removed. Conversely, tumor size, radioiodine therapy, and one-year treatment response were not significant predictors. **Conclusion:** This study identifies the primary predictive factors for p-POH following thyroid cancer surgery. Our findings highlight the importance of a multidisciplinary approach involving both endocrinologists and surgeons, as well as the need for tailored surgical techniques and preoperative planning to reduce the risk of p-POH and prevent adding chronic conditions to treated patients.

THYROID SURGERY

1112242 - INTRAOPERATIVE USE OF FLUORESCENCE WITH INDOCYANINE GREEN TO PREDICT POSTOPERATIVE HYPOPARATHYROIDISM

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Introduction: Parathyroid fluorescence with indocyanine green (ICG) might prevent and predict postoperative hypoparathyroidism (hypoPT) after total thyroidectomy (TT). We aimed to evaluate parathyroid gland vascularization with ICG during TT. Further, we aimed to evaluate safety of ICG fluorescence and to correlate changes in PTH with postoperative hypoPT after TT. **Methods:** From May 2021 to June 2023, consecutive patients underwent TT and parathyroid fluorescence with ICG. Each visible parathyroid gland was scored 0, 1 or 2 depending on fluorescence intensity. Patients with at least one gland score of 2 were compared to those without. We measured PTH before and after TT, changes in calcium, creatinine and alanine transaminase (ALAT), postoperative alfacalcidol requirements, and adverse events of ICG use. **Results:** We operated 124 patients and a gland score of 2 reduced the need for alfacalcidol at discharge (8% vs. 38%, $p = 0.004$), but did not exclude hypoPT. Patients classified with permanent hypoPT had PTH decrease $> 83\%$ during TT and needed alfacalcidol treatment after 12 months. Creatinine increased in permanent hypoPT patients compared to others ($p = 0.01$). We saw no ALAT increase or adverse events after ICG use. **Conclusion:** ICG-based parathyroid fluorescence during TT was safe and predicted immediate postoperative hypoPT. However, in this series, a gland score of 2 could not exclude development of hypoPT. We found the grading system limited by its reliance on subjective assessments. Further, the identified creatinine increase in hypoPT may arise from lack of PTH.

1112305 - LARYNGEAL ULTRASOUND PERFORMANCE FOR THE DIAGNOSIS OF VOCAL CORD PARALYSIS POST-THYROIDECTOMY: A MULTICENTER DIAGNOSTIC TEST STUDY IN MEDELLIN, COLOMBIA

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Introduction: Assessment of vocal cords using laryngeal ultrasound represents a non-invasive and readily accessible alternative. **Objective:** This study aims to evaluate the diagnostic performance of this method in hands of head and neck surgeons, in identifying post-thyroidectomy vocal cord paralysis. **Methods:** Cross-sectional diagnostic test study. Laryngeal ultrasounds were performed immediately post-surgery following thyroidectomy. Results were compared with laryngoscopy conducted by the anesthesiologist during extubation or nasolaryngoscopy within the first week post-surgery. The number of vocal cords evaluated was recorded based on the number of nerves at risk during each surgery. Sensitivity analyses were conducted under best and worst-case scenarios for cases where ultrasound did not provide adequate acoustic window. This study was approved by institutional ethics committees. **Results:** A total of 146 patients were included, undergoing 95 total thyroidectomies and 51 partial thyroidectomies. Two patients required oncologic resection of a recurrent laryngeal nerve, thus only the contralateral cord was included in the analysis, totaling 239 vocal cords evaluated. Five cases of vocal cord paralysis were identified (2.1%). In 7 patients (4.9%) with 12 nerves at risk, adequate acoustic window was not achieved. Sensitivity was calculated at 80%, specificity was 97% (94.4%-99.6%), positive predictive value was 52.5% (25%-80%), and negative predictive value was 99.6%. **Conclusions:** Laryngeal ultrasound demonstrates good performance in assessing vocal cords with a notable ability to rule out vocal cord paralysis, potentially reducing the need for unnecessary invasive studies.

THYROID SURGERY

1112476 - REVOLUTIONIZING BENIGN NODULE TREATMENT: THE IMPACT OF RADIOFREQUENCY ABLATION

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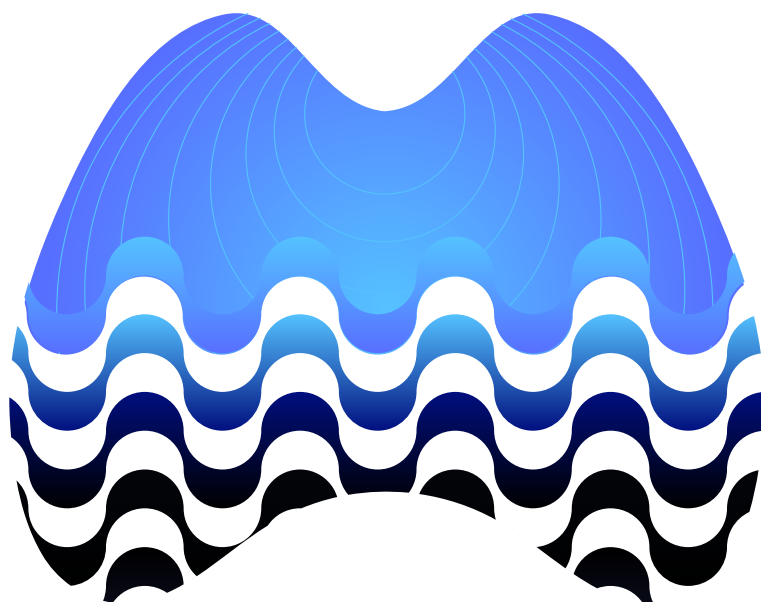
Introduction: Radiofrequency ablation (RFA) has emerged as a minimally invasive alternative to surgery for managing benign thyroid nodules, offering promising outcomes for suitable candidates. We present our experience in a single center of benign nodules. This technique serves as a less invasive alternative to traditional surgical options such as thyroidectomy or lobectomy. **Methods:** We performed a retrospective study based on prospective data, involving 119 patients treated with ablative techniques between November 2021 and December 2024. The inclusion criteria were benign thyroid nodules, confirmed as benign (Bethesda II) with two fine-needle aspiration. The patients were divided into two groups based on whether their volume was greater than or less than 15 ml. In this study, the percentage of volume reduction was evaluated at 3, 6 and 12 months. **Results:** We analyzed a total of 119 patients from November 2021 to December 2024. Of these patients 80,6% were female, with an average age of 55 years. Of 111 patients were evaluated at 3 months, 90 patients at 6 months, and 71 patients were followed up for more than one year. Regarding laboratory tests, none of our patients presented modifications on their thyroid function (100%) on their follow-up. We presented 3 cases (2.5%) of temporary dysphonia (with complete resolution before the third month), 1 case of Claude Bernard-Horner syndrome (0,84%), and 1 case of ecchymosis (0.84%). **Conclusion:** Our study demonstrates that RFA is an effective and safe alternative to surgery for the treatment of benign thyroid nodules. Demonstrated that the greatest benefit is achieved one year after ablation It was observed that nodules smaller than 15 ml showed a greater tendency to decrease in size. These findings support the use of RFA as a minimally invasive providing a valuable alternative to invasive surgical.

1112527 - TRANSFORMING PARATHYROID SURGERY: THE ROLE OF RADIOFREQUENCY ABLATION IN TREATING ADENOMAS

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Introduction: This study aims to present the initial experience at a single center using radiofrequency ablation (RFA) for treating primary hyperparathyroidism (PHPT). The focus is on outlining the criteria for patient selection, details of the procedure, short-term complications, and both biochemical and ultrasound outcomes. **Methods:** The patients included fulfilled both the clinical and imaging criteria. All were either deemed unsuitable for surgery or chose not to undergo it. A total of 35 patients with PHPT were included between June 2022 and December 2024. All participants had imaging findings consistent with a single parathyroid adenoma. Follow-up evaluations took place at 3, 6, 12, and 24 months, and included ultrasound assessments as well as laboratory tests. **Results:** We evaluated 35 patients between June 2022 and December 2024. 91% were female (33/35), with an average age of 60 years (3878 years). Seven patients (17%) had a history of previous cervical interventions, including six surgeries and one radiofrequency ablation. The average preoperative PTH level was 111 pg/dL (67213 pg/dL), and the average total calcium level was 9.8 mg/dL (9.312.5 mg/dL). 26 patients (74%) normalization of both PTH and calcium levels. Partial resolution was noted in two patients (6%), where PTH levels remained elevated, but calcium levels were normal, which were still considered biochemically adequate responses. Four patients (12.5%) did not normalization of either PTH or calcium levels. Four patients experienced transient dysphonia following the procedure. All cases of dysphonia resolved within two months. **Conclusion:** RFA shows promising results as a minimally invasive treatment for PHPT in patients who are unsuitable for surgery or choose not to undergo it. It was well-tolerated with minimal, transient complications. RFA offers a viable alternative to surgery, but further research is needed to assess long-term outcomes and refine patient selection.



17th

International **Thyroid** Congress

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POSTER PRESENTATION

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112563 - CAUSAL LINK BETWEEN THYROID FUNCTION AND FEMALE-SPECIFIC CANCERS: A BIDIRECTIONAL TWO-SAMPLE AND MEDIATION MENDELIAN RANDOMIZATION STUDY

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Introduction: Observational studies have demonstrated an association between thyroid function (free thyroxine, thyroid stimulating hormone, hyperthyroidism, and hypothyroidism) and female-specific cancers, including breast, ovarian, endometrial, and cervical cancers. However, the causal relationship between them remains elusive. **Objective:** We aimed to explore the causal relationship between thyroid function and female-specific cancers, while also investigating the role of sex hormones (total testosterone and estradiol) as potential mediators in this association. **Methods:** Initially, we investigated the causal relationship between thyroid function and female-specific cancers through bidirectional two-sample (T-S) Mendelian randomization (MR) study using Genome-Wide Association Study (GWAS) data. Subsequently, we employed mediation MR analysis to assess the potential role of sex hormones as intermediaries in this relationship. The robustness of our findings was further validated through a series of sensitivity analyses. Finally, we conducted bioinformatics analyses to explore underlying mechanisms, leveraging potentially relevant genes. **Results:** Bidirectional T-S MR analyses indicated that hypothyroidism reduces the risk of endometrial cancer (OR = 0.33, 95% CI: 0.160.66, P = 0.002) and breast cancer (OR = 0.48, 95% CI: 0.360.64, P < 0.001). Mediation MR analyses further suggested that hypothyroidism may lower the risk of both endometrial and breast cancers by decreasing levels of total testosterone. **Conclusion:** In this study, we established the causal relationship between thyroid function and female-specific cancers, offering novel perspectives for the early prevention and intervention of endometrial and breast cancer. Furthermore, we investigated the mediating role of sex hormones in the association between hypothyroidism and these cancers, providing valuable insights for future mechanistic research.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1114169 - CHEMICALLY INDUCED HYPOTHYROIDISM DISRUPTS NEURONAL MIGRATION, PARVALBUMIN-POSITIVE INTERNEURONS AND OLIGODENDROCYTE-ASTROCYTE DIFFERENTIATION IN THE DEVELOPING RAT BRAIN

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Introduction: Thyroid hormone (TH) system disrupting chemicals can interfere with TH-signaling and disrupt brain development. To protect humans from exposure to such chemicals it is critical that the regulatory system can identify adverse effects mediated by disruption of TH-signaling in toxicity studies. However, current test methods are not sufficiently sensitive, and new methods and endpoints of TH system disruption in the developing brain are urgently needed. **Objectives:** To identify dose-dependent adverse effects of chemically induced thyroperoxidase (TPO) inhibition in the developing brain. **Methods:** Pregnant and lactating Sprague-Dawley rat dams were exposed to vehicle control (corn oil), the antithyroid drug methimazole (MMI; 8 or 16 mg/kg bodyweight (bw)/day), or the pesticide amitrole (25 or 50 mg/kg bw/day) from gestational day (GD) 7 to pup day (PD) 16 (n = 11-12). Brains from PD16 male pups were analyzed with immunohistochemistry and in situ hybridization with RNAscope. Periventricular heterotopia, parvalbumin expression (protein and mRNA) and oligodendrocytes and astrocyte numbers in the corpus callosum were quantified. **Results:** Exposure to the TPO inhibitors MMI and amitrole induced neuronal migration errors, manifested as large periventricular heterotopia in the corpus callosum of the offspring's brain. In the cortex and hippocampus, parvalbumin protein and mRNA expression levels in parvalbumin expressing GABAergic interneurons were reduced. Additionally, in the corpus callosum, MMI and amitrole exposure altered the oligodendrocyte-to-astrocyte ratio, with a reduction in oligodendrocytes (Mag+-cells) and an increase in astrocytes (Gfap+-cells). **Conclusion:** Our study shows how exposure to TPO-inhibiting chemicals adversely affects critical processes in the developing brain. These analyses can help improve identification of TH system disrupting chemicals to protect humans from harmful chemical exposures.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1113944 - EFFECTS OF POLYSTYRENE NANOPLASTICS ON ENDOCRINE AND THYROID DISRUPTION: ANSWERS FROM IN VITRO AND IN VIVO MODELS

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Introduction: Increasing worldwide plastic pollution presents an emerging threat for human health. Micro and nanoplastics (NP) have been encountered in food, water and air. Moreover, recent evidence of presence in human tissues highlights the need for evaluating their potential effects, particularly as endocrine disruptors. **Objective:** This study aimed at elucidating the cellular biokinetics and molecular mechanisms of action of NP as thyroid disruptors in thyroid-derived PCCL3 cells and the zebrafish embryo (ZF) model. Effects on cardiology, morphology and behavior were also evaluated. **Methods:** Models were exposed to 30 nm polystyrene NP (PSNP). Thyroid hormone (TH) metabolism related gene/protein expression was studied through RTPCR and Western Blot; hormone levels by ELISA; cardiology, morphology, and behavior using a Leica Stereoscope and the Daniovision system. In addition, confocal microscopy was used to evaluate cellular absorption and elimination of plastic particles and intracellular localization. **Results:** PSNP were rapidly absorbed but only partially eliminated. Cellular localization was mainly in lysosomes and the endoplasmic reticulum to a lesser degree. No nuclear accumulation was observed. PSNP exposure rapidly and significantly altered the expression of genes critical for TH metabolism in both thyroid cells and ZF larvae. While downregulation was the dominant response, some genes exhibited upregulation or concentration-dependent shifts in expression patterns. In cells, MCT8 and NIS protein expression were also downregulated, and NIS function was affected. In larvae, TH levels were decreased and these thyroid disrupting effects caused developmental, cardiac, and behavioral abnormalities. **Conclusion:** PSNP exposure caused cellular accumulation and affected TH metabolism at multiple levels, with effects on gene and protein expression, systemic TH levels and development. Even at low concentrations, this correlated to morphological, cardiac and behavioral abnormalities in ZF larvae, reinforcing the endocrine disrupting potential of nanoplastics and highlighting the potential risk on thyroid function and human health.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112628 - ENDOCRINE-DISRUPTING CHEMICAL AND THYROID CANCER: INSIGHTS INTO MOLECULAR PATHWAYS AND TUMORIGENESIS

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Introduction: Thyroid cancer is the seventh most prevalent cancer worldwide, with its incidence rising through the decades, particularly among women. While early detection through advanced imaging contributes to this trend, exposure to endocrine-disrupting chemicals (EDCs) has emerged as a potential contributing factor to increased thyroid cancer rates. **Methods:** This study explores the molecular mechanisms by which EDCs, including heavy metals, phthalates, and phenols, influence thyroid carcinogenesis. **Results:** Heavy metals such as lead, cadmium, and mercury have been associated with increased thyroid cancer risk, particularly in populations with chronic environmental exposure. Studies show that these metals activate the ERK1/2 signaling pathway, promoting the proliferation of thyroid stem/precursor cells. Phthalates, including DEHP and MEHP, further enhance thyroid tumorigenesis through HDAC6 upregulation, PTEN inhibition, and activation of the PI3K/AKT pathway, leading to increasing cellular proliferation and migration in both normal and malignant thyroid cells. Long-term exposure to high doses of phthalates in animal models also induces thyroid hyperplasia, as confirmed by increased Ki-67 expression and inflammatory responses. Phenols such as bisphenol A, interact with estrogen receptors, particularly ERα, leading to activation of the MAPK and PI3K/AKT pathways. It also can induce AKT/mTOR activation in thyroid cancer cells and this activation culminates in increased proliferation, migration, and expression of cell cycle proteins, as well as the facilitation of epithelial-mesenchymal transition via ERK/Cox2 signaling. **Conclusion:** Overall, these mechanistic findings underscore the interplay between EDCs and the molecular mechanisms that drives thyroid carcinogenesis. Clarifying the influence of EDCs on tumor-initiating and tumor-promoting pathways remains crucial for developing effective public health measures, alternative molecules, and even inspire novel, pathway-targeted therapeutic interventions.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1114171 - GESTATIONAL AND LACTATIONAL EXPOSURE TO THYROPEROXIDASE-INHIBITING COMPOUNDS DISRUPTS THE DEVELOPING THYROID GLAND TRANSCRIPTOME

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Introduction: Thyroid hormone system-disrupting compounds can cause developmental hypothyroidism, adversely affecting thyroid hormone-dependent processes, including brain development. Inhibition of thyroperoxidase (TPO) in the thyroid gland is a key mechanism leading to such adverse effects, but the direct impact on the developing thyroid gland remains insufficiently characterized, not least at the transcriptional level. **Objective:** To investigate the effects of TPO-inhibiting compounds on the transcriptome and morphology of the developing thyroid gland. **Methods:** Pregnant and lactating Sprague-Dawley rat dams were exposed to vehicle control (corn oil), the antithyroid drug methimazole (MMI; 8 or 16 mg/kg bodyweight (bw)/day), or the pesticide amitrole (25 or 50 mg/kg bw/day) from gestational day (GD) 7 to pup day (PD) 16. Bulk RNA sequencing was conducted on thyroid glands from male fetuses (GD21) and pups (PD3, 6 and 16) (96 samples total, n = 6-10). Morphological analysis of PD16 thyroid glands complemented transcriptomic data. **Results:** Morphologic analysis of thyroid glands from 16 days old male pups exposed to MMI and amitrole showed signs of thyroid stimulating hormone (TSH) stimulation and increased activity with irregularly shaped follicles containing little colloid. There were tendencies for increased thyroid follicular epithelial cell height and increased numbers of proliferating cells (NKX2-1+/KI67+-cells). Transcriptomic analysis revealed underlying molecular changes with 923 differentially expressed genes (DEGs) clustered into 20 developmental stage- and exposure-specific patterns. While differences existed between exposure groups and ages, substantial overlap occurred between MMI and amitrole effects. Functional enrichment analysis highlighted mitotic cell cycle activity in fetuses and activation and development processes in postnatal pups, including angiogenesis, cell migration, extracellular space, and hormone secretion. **Conclusion:** This study reveals transcriptional and morphological changes in thyroid glands due to TPO-inhibitor exposure during development. The data provide insights into the potential link between thyroid hormone system disruption and later-life thyroid diseases.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1113684 - HEAVY METALS, TSH AND THYROID HORMONE LEVELS ASSOCIATION IN MATERNAL AND CORD BLOOD PLASMA AT URBAN POPULATIONS FROM RIO DE JANEIRO (THE PIPA STUDY)

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Introduction: Heavy metals, such as lead, mercury, cadmium and arsenic, are considered endocrine-disrupting chemicals of global concern due to their toxic effects on human health and the environment, including affecting the thyroid gland and potentially causing thyroid disorders. **Objective:** Evaluate the relationship between in utero exposure to the heavy metals (lead, mercury, cadmium and arsenic) with thyrotropin (TSH) and thyroid hormones (TH) at birth. **Methods:** The study population consisted of 99 mother-infant pairs from the birth cohort of the Childhood and Environmental Pollutants Project (PIPA-UFRJ), recruited between June 2021 and July 2022. Metals were analyzed using inductively coupled plasma mass spectrometry (ICP-MS). Hormones in maternal plasma and umbilical cord blood were measured using ELISA or Multiplex Assay. A descriptive analysis of the population's characteristics was performed, including birth anthropometric profile and weight gain up to one year of age. Spearman's correlation was used to evaluate the relationship between metal and hormone. Linear regression analysis was performed to assess the association between metal exposure, hormone levels, and weight gain. **Results:** The detection rates of metals in umbilical cord blood samples were lead (100%), mercury (93.8%), arsenic (59.2%), and cadmium (13.3%). Arsenic concentration in umbilical cord blood showed a positive correlation with TSH levels ($r=0.39$, $p=0.001$). No significant correlations were observed between the other metals and hormone levels in the cord blood as well as in the maternal plasma. Lead concentration was associated with higher weight at 12 months ($r=0.287$, $p=0.007$) and greater weight gain from the 3rd to 12th month ($r=0.305$, $p=0.006$). Conversely, Arsenic showed a negative correlation with weight gain from the 6th to the 12th month ($r=-0.238$, $p=0.042$). **Conclusion:** Prenatal arsenic exposure may be associated with TSH alterations in newborns. Both lead and arsenic induce changes in weight gain during the first year of life.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1114083 - IMPACTS OF MATERNAL EXPOSURE TO BISPHENOL F AND AF ON THYROID FUNCTION IN WISTAR RATS: EFFECTS DURING LACTATION AND ADULTHOOD

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Introduction: Endocrine-disrupting chemicals (EDCs), particularly bisphenol A (BPA) and its analogs bisphenol F (BPF) and bisphenol AF (BPAF), interfere with thyroid function and may lead to metabolic programming during critical developmental periods. **Objective:** This study evaluated the effects of maternal exposure to BPF and BPAF during lactation and adulthood. **Methods:** Evaluated the effects of maternal exposure to BPF and BPAF (10 or 50 µg/kg) during lactation on thyroid function parameters in Wistar rat dams and their offspring (CEUA/UERJ/031/2022). **Results:** Dams exposed to BPF10 showed an increase in DUOX activity (+87%, $p < 0.05$), while BPAF10-exposed dams exhibited an elevation in plasma T4 levels (+181%, $p < 0.05$), although thyroid mass and gene expression (DUOX, NIS, TSH-R, TPO, NOX2) remained unchanged. In offspring at weaning, BPF10-exposed males displayed an increase in DUOX activity (+57%, $p < 0.05$), whereas females showed a significant reduction of this enzyme activity (BPF10: -55%; BPF50: -49%). In adulthood, male offspring from BPAF groups exhibited >50% decreases in DUOX and TPO expression ($p < 0.05$), as well as elevated oxidative stress (TBARS for BPF50: +185%; TBARS for BPAF50: +132%; $p < 0.05$). All groups showed an increase in catalase and hormonal disturbances (+62% TSH in BPF50; +109% and +114% of T4 in BPF50 and BPAF groups, $p < 0.05$). Female offspring presented reduced DUOX expression (59%-66% for BPAF groups, $p < 0.05$) and diminished catalase activity, despite unchanged plasma thyroid hormones. Importantly, thyroid mass remained unaltered in all groups. **Conclusion:** These findings demonstrate that early life BPF and BPAF exposure induces sex- and age-specific thyroid dysfunction, with low-dose effects persisting into adulthood. The sustained oxidative stress (reduced catalase, elevated TBARS) and hormonal imbalances suggest metabolic programming of thyroid dysfunction. These results challenge the presumed safety of BPA alternatives and emphasize the need for rigorous assessment of their developmental impacts.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1113828 - PYRIPROXYFEN AS AN ENDOCRINE-DISRUPTING CHEMICAL: EFFECTS ON THE HYPOTHALAMUS-PITUITARY-THYROID AXIS IN ZEBRAFISH

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Introduction: Pyriproxyfen (PPF) is a juvenile hormone analog pesticide used to control *Aedes aegypti*, but its potential endocrine-disrupting effects in non-target organisms remain underexplored. Its structural similarity to thyroid hormones suggests it could impact the hypothalamus-pituitary-thyroid (HHT) axis. **Objective:** To investigate the subacute effects of PPF on the HHT axis in zebrafish females. **Methods:** Adult *Danio rerio* females were exposed for 14 days to 1, 10, or 100 µg/L of PPF, alongside a control group treated with 0.4% DMSO. RNA extraction, qPCR, and histological analyses of thyroid follicles were conducted to assess gene expression related to thyroid hormone synthesis and morphological alterations. **Results:** Histological evaluation revealed that exposure to 10 and 100 µg/L of PPF induced significant morphological alterations in thyroid follicles, including reduced colloid area, increased epithelial area, and a higher epithelial-to-colloid area ratio, with no evidence of ectopic follicles. These changes were accompanied by decreased colloid eosinophilia and epithelial stratification, suggesting follicular activation and potential impairment in thyroglobulin iodination. Gene expression analysis showed consistent increases in *nis* and *TPO* mRNA levels at 10 µg/L. *TG* expression was reduced in the group exposed to 10 µg/L. The same group also exhibited upregulation of *pax8* and *nkx2.1*, indicating enhanced transcriptional activity associated with thyroid development, along with increased expression of the TSH receptor in the thyroid. The hepatic expression of *dio1* and *dio2* appeared unchanged following exposure to PPF. In the brain, both TRH and its receptor were upregulated at 10 µg/L. **Conclusion:** The histological and molecular alterations support the hypothesis that PPF interferes with thyroid homeostasis, displaying features consistent with an endocrine disruptor.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112359 - ROUNDUP HERBICIDE HAS IMPORTANT DIFFERENTIAL EFFECTS ON THE MIGRATION OF THYROID CANCER CELLS

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Introduction: Glyphosate, the main ingredient of the most widely used herbicide worldwide, is considered a probable human carcinogen by the International Agency for Research on Cancer (IARC). We have previously demonstrated that Roundup® Original DI presents a nonmonotonic dual toxic and proliferative dose-response curve. Low concentrations of the pesticide, including doses considered acceptable by regulatory agencies, cause significant cell death, but also have an important proliferative effect, especially in TPC-1 cells. **Methods:** To investigate whether roundup could also affect the cellular aggressiveness of different thyroid cells, we evaluated the effect of five concentrations (ranging from 6.5 to 6,500 µg/L), including the acceptable occupational exposure limit (160 µg/L) and the acceptable daily intake (830 µg/L) on the migration of a control thyroid lineage (Nthy-ori 3-1), two papillary-derived (TPC-1 and BCPAP), and an anaplastic (8505C) cell line. Migration was evaluated by the wound healing assay at 0, 16, 24, and 48 h of exposure. **Results:** Roundup® had no effect on the migration rates of Nthy-ori 3-1 and TPC-1 cells but decreased by 16% the migration rate of BCPAP cells exposed to 6,500 µg/L for 48h (p=0.0030). In contrast, 8505C cells increased the migration rate by 14% after 48h of exposure to 6.5 µg/L and by 17% after 48h of exposure to 830 µg/L. **Conclusion:** We conclude that Roundup® influences cell migration in a variable manner, with important opposite effects on papillary-derived cancer cells harboring the BRAF V600E mutation and on an anaplastic cell line bearing p53 gene mutations. We suggest that these effects may be related to the present epidemiology of thyroid tumors, and since they occur at low doses, we propose that regulatory agencies reevaluate the safety of this herbicide.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1112496 - THE EFFECTS OF THE SWEETENER SUCRALOSE ON THYROID PARAMETERS IN VIVO AND IN VITRO

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Introduction: Since obesity is increasing worldwide, predisposing to comorbidities such as high blood pressure and diabetes, many patients replace sugar with a sweetener, aiming to reduce caloric intake. Despite that, obesity prevalence is still increasing, thus suggesting a possible effect of sweeteners as endocrine disruptors. **Objective:** Since thyroid hormones (TH) are the main regulators of basal metabolic rate, we aimed to evaluate the impact of sucralose and stevia on thyroid parameters. **Methods:** Adult male Wistar rats were fed a regular or high-fat diet, associated or not to sucrose, sucralose, and stevioside for 30 days. TH serum levels and thyroid DuOx activity were assessed. Non-tumor thyroid cell line PCCL3 was cultured in the presence or absence of sucralose at 1×10^{-5} µg/mL or 5×10^{-3} µg/mL, for 48 and 72 hours and mRNA levels of thyroid markers were evaluated. **Results:** In vivo, serum levels of T3 and T4 in the non-obese sucralose group were lower than in the control group (T3: C: $0,603 \pm 0,0798$; Su: $0,292 \pm 0,0368^*$; T4: C: $5,780 \pm 0,2485$; Su: $4,597 \pm 0,2869^*$). In addition, DuOx activity (C: $1,561 \pm 0,6069$; Es: $0,1546 \pm 0,08597$) and T4 levels were reduced in the stevioside group ((C: $5,780 \pm 0,2485$; ES: $4,539 \pm 0,3435^*$ µg/dL), thus suggesting that the consumption of sweeteners, whether natural or artificial, can lead to thyroid dysfunction. In the obese group, a tendency towards a decrease in T4 was observed (p=0.052). In PCCL3, NIS (C: $0,8400 \pm 0,1668$; 5×10^{-3} µg/mL: $0,3633 \pm 0,09397$), DuOx2 (C: $0,9150 \pm 0,1735$; 5×10^{-3} µg/mL: $0,4883 \pm 0,08522$) and TPO (C: $1,038 \pm 0,1469$; 5×10^{-3} µg/mL: $0,4183 \pm 0,1013$) mRNA levels were decreased after exposure to 5×10^{-3} µg/mL sucralose for 72h. Since they are key to the biosynthesis of thyroid hormones, our data suggest that sucralose could decrease serum T3 and T4 due to the reduction in gene expression of these proteins. **Conclusion:** Therefore, sucralose and stevia consumption could cause thyroid disruption, thus affecting basal metabolic rate and metabolism homeostasis, possibly predisposed to weight gain.

ENDOCRINE DISRUPTORS AND THYROID FUNCTION

1113812 - THE IMPACT OF THYROID DYSFUNCTION ON THE RED BLOOD CELL PARAMETERS

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Introduction: Thyroid hormones play a crucial role in metabolism and the proliferation of blood cells. Therefore, thyroid hormones directly affect hematological parameters by stimulating erythrocyte precursors and indirectly through the enhancement of erythropoietin production. **Objectives:** This study evaluated the differences in complete blood count (CBC) parameters among healthy controls, patients with Hashimoto's thyroiditis, and Graves' disease. **Methods:** This cross-sectional study included 158 participants (male 9, female 149), categorized into three groups: healthy controls, hypothyroidism (Hashimoto's thyroiditis), and hyperthyroidism (Graves' disease) in the outpatient clinic of the first central hospital in Ulaanbaatar, Mongolia for 2 years. **Results:** The study population included 60 patients with hypothyroidism (mean age: 47.3±14.33 years), 60 patients with hyperthyroidism (mean age: 39.05±13.46 years), and 38 healthy controls (mean age: 43.20±12.69 years). The majority of among participants were female (94.3%). Autoimmune thyroid disorders were associated with elevated thyroid-stimulating hormone (TSH) and thyroid autoantibody levels. Patients with hypothyroidism exhibited significantly higher levels of anti-thyroglobulin (Anti-TG: 1130 IU/L) and anti-thyroid peroxidase (Anti-TPO: 483.4 IU/mL) compared to controls and hyperthyroid patients. RDW levels were significantly elevated in both hypothyroid and hyperthyroid groups ($p<0.001$) and demonstrated a positive correlation with TSH levels ($p<0.05$). Additionally, red blood cells including MCV, MCH, and MCHC, indicated significant differences between groups ($p<0.05$). **Conclusion:** Red blood cell parameters, particularly elevated RDW levels were potential markers for inflammation and abnormal thyroid function. That suggested complete blood count may be one of the potential markers for autoimmune thyroid disorders in clinical practice.

HYPERTHYROIDISM

1112327 - A RARE CASE REPORT: GRAVES DISEASE WITH TR AB NEGATIVE, ANTI-TPO POSITIVE

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Introduction: Abstract: A few cases of severe Hashimoto's thyroiditis (HT) associated orbitopathy with negative TRAb are reported to date. Thyroid associated orbitopathy are detect immune inflammatory process at extraocular muscles in patients Graves disease. **Case Report:** Women 53 years presented with headache, palpebral edema, also proptosis. That year our patients was treatment with dexametason for 2 weeks after allergy problems TSH = 2,3 fT3 = 29 fT4 = 22 anti TPO < 970 and TRAb was negative level. She was post menopause from three years. MRI orbitopathy result with edema oculare for extraocular muscles. Periorbital muscles were inflammationed. We treatment these case with selenium for 10 days before methylprednisolon cycle. Hepatic function and Hemogram was normal without trombocitopenia. During MRI control we didn't find edema oculare other inflammation periorbital. Campus visual was normal. **Conclusion:** High level Anti-TPO is a very rare in women with Graves Disease without TRAb. Treatment was successful with methylprednisolone. It will be better to control our patients before treatment for Graves and anti-TPO.

HYPERTHYROIDISM

1112659 - ASSESSMENT OF URINARY SELENIUM CONCENTRATION IN PATIENTS WITH GRAVES DISEASE OF A UNIVERSITY HOSPITAL: PRELIMINARY RESULTS

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Introduction: Studies suggest an association between selenium and autoimmunity. Data regarding selenium supplementation for patients with Graves disease (GD), and/or ophthalmopathy, in areas without insufficiency are scarce. **Objective:** To determine urinary selenium concentration (USC) in GD patients in an area where selenium status is unknown and its impact on therapeutic response. **Methods:** Cohort comprising GD patients referred to a university hospital and a control group (CG) without GD. Therapeutic failure (TF) was defined in the absence of remission after antithyroid drug therapy, requirement for definitive treatment or relapse after documented remission. **Results:** A group of 81 GD and 13 CG were evaluated. Sustained remission (SR) was observed in 54.3% and TF was detected in 19 that relapsed after remission and 18 patients that underwent definitive treatment or did not remit. An adequate USC (10-110 mcg/L) was found in the entire group (median 40.9 mcg/L), but 25.5% had excessive (>110 mcg/L) and 8.5% insufficient USC (<10 mcg/L). Despite adequate median USC, it was lower in patients with GD (33.3 vs 60.8 mcg/L; $p<0.01$) and higher in those with TF (56.4 vs 27.3 mcg/L with SR; $p=0.016$). TF group less frequently had already previous selenium use prescription (PSUP) (17 vs 49%; $p<0.01$). Excessive USC tended to be more frequent (40.1 vs 26.8%; $p=0.10$) in patients with PSUP and was associated with higher frequency of abnormal serum glycaemia (SG) (84.2 vs 57.4%; $p=0.03$) even among those without diabetes (78.6 vs 47.5%; $p=0.04$). SG was higher in patients with PSUP (102.9 vs 89 mg/dL; $p<0.01$) even after excluding diabetics and in those in antidiabetic use (163 vs 98 mg/dL; $p=0.04$). **Conclusion:** Preliminary results suggest sufficiency of selenium in the sample where its supplementation was associated with abnormal SG, especially if leading to excessive USC. Despite sufficient, lower levels of USC were related to the presence of GD in comparison to CG.

HYPERTHYROIDISM

1112227 - B SYMPTOMS AND AN ENLARGED THYMUS A RED HERRING EXPLAINED BY GRAVES DISEASE

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Case Presentation: A 38-year-old female patient was investigated for weight loss (-15 kg), night sweats, and hyperthermia. Believed to reflect B symptoms, a CT of the chest and abdomen for the search of malignancy was performed, and it revealed an enlarged thymus of 6.7 x 6.2 x 4.5 cm thought to be suspicious for thymoma. The patient was referred to oncology. A FDG PET-CT showed homogenous hypermetabolism (SUV max 3.5) without suspicious findings, but a biopsy was planned. Fortuitously, the biochemical workup showed a suppressed TSH of < 0.005 mU/L (0.27-4.2), and the patient was evaluated by endocrinology. Clinically, she had classic manifestations of hyperthyroidism. FT4 was > 100 pmol/L (11.2-24.1), FT3 48.7 pmol/L (3.1-6.8), and the TSH-receptor antibodies were elevated at 22.1 U/L (<1.75). Ultrasound showed an enlarged thyroid with heterogeneous hypervascularized parenchyma. Oncology was advised to postpone the biopsy because thymic hyperplasia was considered to be a manifestation of Graves disease. Therapy was initiated with Carbimazole and Atenolol. An MRI performed 6 months later showed significant regression of the thymic hyperplasia to 2.7 x 2.1 cm. Eighteen months after the initial presentation thyroid function tests had fully normalized, and the MRI showed further regression of the thymus to 2.2 x 1.4 cm. **Discussion:** Thymic hyperplasia in patients with Graves disease has been recognized over 100 years ago but many clinicians are not aware of the association. The exact prevalence and pathophysiological mechanism are not known. In most cases, the thymic hyperplasia shows rapid regression with successful treatment of hyperthyroidism. **Final Comments:** The association between Graves disease and thymic hyperplasia must be known to avoid unnecessary procedures and patient distress. The condition usually improves with treatment and biopsy should only be considered if initial imaging studies show suspicious findings and/or if there is no regression after control of hyperthyroidism.

HYPERTHYROIDISM

1114343 - CARDIAC REMODELING LINKED TO GRAVES DISEASE AND SECONDARY HYPERTENSION IN A PATIENT WITH RHEUMATOLOGICAL SYMPTOMS

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Case Presentation: A 38-year-old female presented to the emergency department with a complaint of migratory painful polyarthritides accompanied by signs of inflammation. She had a lesion on her elbow, with no prior history of illnesses. During her hospitalization laboratory investigations showed a fine speckled nuclear pattern on antinuclear antibody testing, along with elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (PCR) levels. An electrocardiogram revealed signs of overload in both the left atrium and ventricle. Additionally, there were notable fluctuations in her blood pressure. The patient reported a history of tremors from a young age, insomnia, difficulty in gaining weight, and engaging in intense physical exercise. Hormonal assays indicated suppressed TSH, elevated free T4, and raised anti-TSH receptor antibodies, confirming a diagnosis of Graves' disease. She was started on treatment with propranolol and methimazole, leading to clinical improvement and subsequent discharge. **Discussion:** Graves Disease is the predominant cause of hyperthyroidism and can induce widespread systemic effects, including on the cardiovascular system. Thyroid hormones have a direct effect on the heart by increasing the heart rate and contractility, which can result in systolic hypertension, atrial fibrillation, and cardiac remodeling when excessively elevated. In this case, the patient experienced cardiac overload and secondary hypertension, which were further exacerbated by a possible underlying inflammatory rheumatological condition. The concurrent autoimmune processes suggest a complex interplay between Graves' disease and rheumatological diseases, underscoring the need for careful and thorough clinical monitoring. **Final Comments:** This case underscores the critical importance of a comprehensive evaluation in patients presenting with nonspecific symptoms and the early assessment of thyroid function when cardiovascular and inflammatory abnormalities are present. The co-occurrence of Graves Disease, secondary hypertension, and cardiac remodeling illustrates a potentially severe and preventable clinical outcome that can be addressed with prompt diagnosis and appropriate management

HYPERTHYROIDISM

1113973 - CAROTID DISSECTION SECONDARY TO PRIMARY HYPERTHYROIDISM: CASE PRESENTATION AND LITERATURE REVIEW

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Case Presentation: A 42-year-old mestiza woman, with no family or personal cardiovascular risk factors, presented with sudden-onset motor aphasia and right-sided hemiparesis. She was afebrile, with a blood pressure of 140/85 mmHg and a heart rate of 112 beats per minute. Neurological examination: Right central facial paralysis, right-sided hemiplegia, Glasgow Coma Scale score of 12 (eye opening: 4, verbal response: 2, motor response: 6), and NIHSS score of 17 (level of consciousness: 4, conjugate gaze: 1, facial paresis: 2, right hemi body limb paresis: 3+3, language: 2, dysarthria: 2). Electrocardiogram: Sinus tachycardia. Brain CT scan: Infarction in the left middle cerebral artery territory. Angiography: Tandem occlusion with thrombosis of the left internal carotid artery, extracranial and intracranial dissection, threadlike flow in the A1 and M1 segments, and absence of posterior flow. Laboratory findings: Positive anti-TSHR antibodies, thyroid profile showing elevated free T4 (10.5 ng/dL) and suppressed TSH (0.001 uIU/mL). The patient was started on synthetic antithyroid therapy and remains stable, attending neurophysiology consultations for neurological recovery. **Discussion:** Spontaneous carotid artery dissection results from blood extravasation into the tunica media due to an intimal tear. It is associated with fibromuscular dysplasia, connective tissue disorders, trauma, and mechanical strain, particularly in patients with underlying arthropathy. Although it can occur at any age, it is one of the leading causes of stroke in young adults. Despite the effects of thyroid hormones on the vascular bed and coagulation factors, carotid dissection has only been reported in three patients with hyperthyroidism. **Final Comments:** Spontaneous carotid artery dissection is a common cause of stroke in young patients and is associated with high morbidity and mortality. Its association with hyperthyroidism is rare, but awareness of this possibility is crucial for timely diagnosis and treatment to prevent severe complications.

HYPERTHYROIDISM

1112522 - CASE REPORT: TRIIODOTHYRONINE-PREDOMINANT GRAVES DISEASE

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Introduction: Clinical Presentation: A 72-year-old female patient was diagnosed with Graves disease during an episode of atrial fibrillation. Thyroid ultrasound revealed diffuse enlargement of the thyroid gland without any focal nodules. Her laboratory findings showed a thyroid-stimulating hormone (TSH) level of $< 0.01 \mu\text{IU/mL}$ ($0.274.2 \mu\text{IU/mL}$), a free T4 level of 3.84 ng/dL ($0.71.48 \text{ ng/dL}$), and a T3 level of $> 400 \text{ ng/dL}$ (35193 ng/dL). The TSH receptor autoantibody (TRAb) and anti-thyroid peroxidase titer were significantly elevated at 30.6 IU/L ($< 0.55 \text{ IU/L}$) and > 900 ($< 9 \text{ U/mL}$), respectively. Treatment with methimazole 30 mg/day was started and adjusted according to free T4 levels. After six months, free T4 levels had decreased, but TSH remained undetectable. A subsequent measurement of T3 showed a level of 351, confirming the diagnosis of T3 predominant Graves disease. Despite 18 months of regular treatment with methimazole, elevated T3 and TRAb levels persisted. She was referred for total thyroidectomy. **Discussion:** T3-predominant Graves disease is characterized by high serum T3, normal T4 levels, and a T3/T4 ratio > 20 (versus 410 in classical Graves disease). Unique TPO enzyme activity and increased type 1 (D1) and type 2 (D2) iodothyronine deiodinases activity leads to elevated T3. Antithyroid drugs (ATD) therapy reduces T4 which prolongs D2 activity, and in combination with increased D1 activity, results in an increase in T3 levels. These patients also have poorer responses to RAI therapy and often require higher I-131 doses once they have rapid iodine turnover. **Final Comments:** Given the poor prognosis with ATDs and the limited efficacy of standard-dose RAI therapy, thyroidectomy or tailored, higher-dose RAI protocols may be necessary for definitive treatment of T3-predominant Graves disease.

HYPERTHYROIDISM

1112643 - DOXYCYCLINE FOR THYROID EYE DISEASE: A SYSTEMATIC REVIEW

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Introduction: Thyroid eye disease (TED) is a significant complication of Graves' disease (GD). It is characterized by inflammation and tissue remodeling around the eyes, leading to symptoms such as proptosis, diplopia, and vision impairment, interfering with quality of life. Doxycycline is an antibiotic, and in addition to its antimicrobial properties, it establishes an anti-inflammatory and immunomodulatory action. It suggests potential benefits in TED management. **Objective:** This systematic review aimed to evaluate the efficacy and safety of Doxycycline in preventing the incidence and/or progression of TED in patients with GD. **Methods:** A comprehensive systematic literature search was conducted across multiple databases, including PubMed, Embase, and the Cochrane Library, up to November 2024. Randomized controlled trials (RCTs) and observational studies assessing the impact of Doxycycline on TED incidence, progression, symptom improvement, quality of life (QoL), clinical activity score (CAS), and safety in GD patients were included. The review model was based on PRISMA for systematic review. **Results:** 3 studies, encompassing a total of patients, were included in the analysis. Doxycycline therapy was associated with a significant reduction in the proptosis and diplopia. Patients treated with doxycycline experienced notable improvements in TED symptoms, including reduced eyelid aperture, and reported better QoL and CAS scores. Importantly, the use of doxycycline has reported adverse effects such as gastrointestinal symptoms, compared to controls. **Conclusion:** The use of doxycycline is a promising therapy in the management and progression of thyroid eye disease. Their beneficial effects on symptom improvement and quality of life, together with the few reported adverse effects, support the potential role of doxycycline in the treatment of TED. Further large-scale RCTs are needed to confirm these findings and elucidate the underlying mechanisms of doxycycline's benefits in TED as an alternative therapy.

HYPERTHYROIDISM

1112206 - EVALUATING RADIOACTIVE IODINE-131 AS A SAFE AND EFFECTIVE TREATMENT FOR GRAVES' DISEASE IN MONGOLIA

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Introduction: Graves' disease, an autoimmune thyroid disorder, can be managed with antithyroid drugs, surgery, or radioactive Iodine-131 (RAI). If untreated or improperly managed, Graves' disease can lead to serious complications, including cardiovascular problems, osteoporosis, and reproductive issues. Radioactive iodine-131 is an effective, cost-efficient alternative that offers the benefits of low radiation risk and minimal toxicity and avoids the need for hospitalization, surgery, or anesthesia. **Objective:** Therefore, this study aimed to evaluate the effectiveness of radioactive iodine-131 treatment in patients with Graves' disease. **Methods:** A retrospective review of four years of medical records was conducted for 109 patients diagnosed with Graves disease, aged 20 to 60, who received RAI-131 treatment at the Department of Radiology, First Central Hospital Mongolia. Data on patient demographics, treatment doses, and outcomes were analyzed. **Results:** The mean age of patients treated with RAI-131 was 44.3 ± 11.5 years, with a predominance of patients aged 30-59 years (61.5% female), with the highest proportion (18.3%) of women aged 30-39 years. Most patients (67.9%) administered an average dose (8.04 ± 0.27 mCi) over the study period. 73.4% of patients received a fixed dose, while 26.6% received an individual dose. The majority of patients (55.9%) who received regular doses (7-9 mCi) were women. The average time to reach the target thyroid-stimulating hormone (TSH) levels was 180 days after RAI treatment. **Conclusion:** Radioactive iodine (RAI) is an effective treatment for Graves' disease, with an average treatment dose of 8.17 ± 1.47 mCi. Most patients received a fixed moderate dose of 7-9 mCi, and the average time to reach target thyroid-stimulating hormone (TSH) levels was 180 days. These findings suggest that RAI is a reliable, non-invasive alternative for managing hyperthyroidism in Graves' disease, with minimal risks and complications.

HYPERTHYROIDISM

1112562 - EVALUATING THE IMPACT OF DIFFERENT CUMULATIVE DOSES OF INTRAVENOUS GLUCOCORTICOIDS IN GRAVES ORBITOPATHY: SAFETY, CLINICAL OUTCOMES, AND ADDITIONAL THERAPY REQUIREMENTS

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Introduction: Graves' orbitopathy (GO) in its inflammatory phase is commonly treated with intravenous glucocorticoids (IVGC), but recent guidelines recommend avoiding cumulative doses over 7.5 grams of methylprednisolone due to adverse effects (AEs). Second-line treatments include additional IVGC courses, radiotherapy (RT), and immunosuppressives. The safety and efficacy of various IVGC doses need further exploration to guide clinical practice. **Objective:** This study aims to evaluate the AEs, safety, and impact on clinical manifestations of GO patients treated with different cumulative IVGC doses, as well as common additional therapies. **Methods:** A retrospective cohort study of GO patients with confirmed inflammatory activity treated with IVGC. Patients were divided into three groups: classical dose (CD, up to 4.5 grams/year), intermediate dose (ID, 4.5 to 7.5 grams/year), and high dose (HD, > 7.5 grams/year). Additional therapies were also assessed. **Results:** Seventy patients were included: 23 in CD, 18 in ID, and 29 in HD. Preliminary data suggests that diplopia increased with dose (42.9%, 88.2%, and 96%, respectively). The HD group had more optic nerve impairment and higher exophthalmos (25.5 mm). Orbit decompression was less common in CD. RT was used in 93.1% of HD and 66.7% of ID patients (vs 9.7% in CD). Diplopia resolved in 55.6% of patients overall and in 42.9% of those receiving RT. Diplopia resolution rates were 73.3% for ID and 39.1% for HD groups. Common AEs included high blood pressure (40.7% vs 2.6%, $p < 0.05$) and hyperglycemia (37% vs 12.8%, $p = 0.02$) in patients receiving > 7.5 grams versus ≤ 7.5 grams. Fever/infections were more frequent in HD. No hepatitis cases were reported, but increased intraocular pressure and glaucoma were noted, although most patients had these conditions prior to infusion. **Conclusion:** IVGCs show potential benefits on some features of GO presentation, particularly when combined with other therapies. Close monitoring is essential due to potential AEs.

HYPERTHYROIDISM

1112550 - EVALUATION OF CHILDREN AND ADOLESCENTS WITH GRAVES' DISEASE IN A TERTIARY SERVICE

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Introduction: Graves' disease (GD) is an autoimmune disease characterized by the presence of an anti-thyroid hormone receptor antibody (TRAb). This antibody causes an overactive thyroid and ocular and dermatological abnormalities. In childhood, GD is the leading cause of hyperthyroidism, but it is considered relatively rare in the pediatric population. **Objective:** This study aimed to evaluate the profile of pediatric patients with GD and treatment preferences considering the manifestations in this age group. **Methods:** This was a retrospective descriptive analysis of the medical records of pediatric patients with GD in a tertiary service from 2005 to 2024. The study evaluated chronological age, clinical and laboratory data, associated complications, and treatments applied. **Results:** We had 48 children and adolescents with GD in our service, 34 females and 14 males, with a mean (SD) age at diagnosis of 9.5 (3.9) years. The antithyroid drugs (ATDs) used were methimazole (87.2%) and propylthiouracil. There were only 6 cases in which ATDs were used in low doses (< 10 mg), with doses of more than 10mg prevailing in the other cases and with an average treatment time of 25 months. Radioiodine therapy was chosen in 66.7% of the cases, 87.5% of which developed hypothyroidism. Only three patients underwent total thyroidectomy. Ten patients had orbitopathy, and ten had another autoimmune disease (alopecia, atopic dermatitis, diabetes mellitus 1 (DM1), celiac disease, psoriasis, lupus anticoagulant). Of the comorbidities, there are reports of Down's Syndrome (4), obesity (4), and 1 case of TI-RADS 3 thyroid nodule. **Conclusion:** As expected GD is more frequent in female patients, but in this cohort, the diagnosis was made at a younger age. The use of low doses of methimazole was less common, making it necessary to select the definitive treatment. Radioiodine therapy was the most frequent definitive treatment, with high rates of hypothyroidism.

HYPERTHYROIDISM

1112444 - EXOGENOUS T3 INTOXICATION IN A PATIENT WHO DENIED USE: CASE REPORT

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Case Presentation: Woman, 70 years old, attends her first consultation for hyperthyroidism treatment. She had been using methimazole 5 mg for 1 year, however, without improvement in the initial complaints that led to the investigation (loss of 8 kg in 14 months, fatigue and insomnia). Other comorbidities included systemic arterial hypertension and depression, treated with losartan and fluoxetine; she persistently denied the use of other medications. Initial screening tests revealed TSH < 0.01 (reference range: 0.45-8 mIU/mL), free T4 0.41 (reference range: 0.61-1.2 ng/dL), and total T3 426 (reference range: 80-200 ng/dL). Repeat tests confirmed the findings, showing TSH < 0.01, free T4 < 0.25, total T3 398, and thyroglobulin 1.6 (reference range: 3.577 ng/dL), supporting the initial suspicion of exogenous T3 intoxication. A new inquiry into medication use was conducted, but she denied it again. Consequently, family members were involved to assist with home treatment adjustments and to emphasize the importance of adhering to prescribed medications (methimazole was discontinued). The patient returned after 2 months showing improvement in symptoms, a 4 kg weight gain, and lab results indicating TSH 3.59, free T4 0.69, total T3 6.3, and thyroglobulin 12.3. **Discussion:** Factitious thyrotoxicosis is a form of thyrotoxicosis caused by accidental or deliberate ingestion of thyroid hormones (often for weight loss or improved athletic performance). Symptoms are similar to other forms of thyrotoxicosis but do not involve pain, exophthalmos, or goiter. Diagnosis is supported by low thyroglobulin levels due to suppression of endogenous thyroid production. **Final Comments:** Exogenous thyroid hormone administration is an important cause of hyperthyroidism and morbidity. Due to its rarity, this diagnosis is often not considered initially, leading to inadequate treatment and prolonged symptoms. Because of its association with psychiatric comorbidities, family involvement is often necessary.

HYPERTHYROIDISM

1114198 - GRAVES' DISEASE ASSOCIATED WITH CONGENITAL GENERALIZED LIPODYSTROPHY (BERARDINELLI-SEIP SYNDROME): A RARE CASE REPORT

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Case Presentation: We report a rare case of a 21-year-old female diagnosed with congenital generalized lipodystrophy (CGL) associated with Graves' disease (GD). She presented with poorly controlled diabetes and exhibited an atypical phenotype, including near-total lack of body fat, body mass index of 13.31 kg/m², phlebomegaly, umbilical protrusion, a large goiter (95 cm³), and orbitopathy compatible with GD. Laboratory tests confirmed hyperthyroidism secondary to GD (TSH <0.01 uIU/mL; FT4 4.81 ng/dL; TRAb 40 IU/L). Despite high insulin dose (8 IU/kg/day), the diabetes was still poorly controlled [Fasting glycemia 380 mg/dL; HbA1c 11.7%; C-peptide 3.59 ng/mL (1.0-4.4 ng/mL); anti-GAD < 5 IU/mL (up to 10 IU/mL)]. The serum leptin was low (0.42 ng/mL - normal values: 3.7-11.1 ng/mL), compatible with CGL diagnosis. Genetic testing showed a mutation in AGPAT2 (located at position chr9:136.676.051-136.677.087, with a partial deletion of exon 3 and a complete deletion of exon 4, in homozygosity), confirming the diagnosis of CGL type 1. The patient underwent total thyroidectomy, which improved glycemic control. However, due to the underlying condition, she remained dependent on high doses of insulin (7 IU/kg/day). She is currently waiting for metreleptin therapy. **Discussion:** To our knowledge, this is the first reported case of CGL associated with GD. Autoimmune diseases are frequently associated with acquired generalized lipodystrophy, but not with CGL. Some CGL patients develop thyroid diseases (nodules, hypothyroidism), but hyperthyroidism is not described. Hyperthyroidism in a patient with severe insulin resistance and difficult control diabetes can be more challenging. Both preoperative and postoperative management required a rigorous strategy to optimize metabolic and cardiovascular control. **Final Comments:** The severity of the clinical manifestations and the variable response to conventional treatments reinforce the importance of early diagnosis and a multidisciplinary clinical approach to promote overall health.

HYPERTHYROIDISM

1112432 - GRAVES DISEASE INDUCED BY ALEMTUZUMAB TREATMENT IN RELAPSING-REMITTING MULTIPLE SCLEROSIS: CASE REPORT

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Case Presentation: J.A.J., a 23-year-old female patient diagnosed with relapsing-remitting multiple sclerosis (RRMS) in July 2021, began treatment with alemtuzumab in August 2022. In November 2024, thyroid function tests revealed significant abnormalities: TSH 0.002 mIU/mL (reference range: 0.45.8 mIU/mL), free T4 4.67 ng/dL (reference range: 0.611.12 ng/dL), total T3 201 ng/dL (reference range: 87178 ng/dL), and TRAb 43.2 IU/L (reference range: > 3.1 IU/L). It presented, among the signs and symptoms of hyperthyroidism, only a mild tachycardia. Thyroid scintigraphy with technetium showed diffuse uptake throughout the gland. Treatment with methimazole 30 mg once daily and beta-blockers for heart rate control was initiated, leading to favorable clinical outcomes. **Discussion:** Autoimmune thyroid diseases (AITDs) are the most common adverse effects observed in RRMS patients treated with alemtuzumab. Among these, Graves disease (GD) is the most prevalent, with an estimated prevalence ranging from 16% to 41%. This phenomenon is attributed to immune reconstitution triggered by alemtuzumab, which renders the TSH receptor an autoantigen. In a retrospective cohort study involving 60 patients, thyroid disorders occurred in 47% of cases, with GD being the most frequent (35%). An atypical course of GD was reported in 67% of cases, where 44% experienced fluctuations between hyperthyroidism and hypothyroidism, and TRAb positivity was observed in 77%. The first episode of thyroid dysfunction typically manifests within the first year of treatment, with a progressive increase in prevalence over the first three years (from 4.6% to 16.1%), followed by a decline in subsequent years. **Conclusion:** Early recognition of this condition is crucial, as the remission rate after treatment with antithyroid drugs (ATDs) is high, suggesting a less aggressive disease course. ATDs are considered the first-line therapy for these cases.

HYPERTHYROIDISM

1113724 - HOW T3 AND T4 AFFECT THE QUALITY OF LIFE IN GRAVES' DISEASE PATIENTS

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Introduction: Graves' disease (GD) is the primary cause of hyperthyroidism, with severe impact on quality of life even in the euthyroid state. Current literature provides scarce data explaining how these patients' quality of life (QoL) is affected. **Objective:** The study's objective was to evaluate the long-term effect of the serum TT3/TT4 ratio on the QoL of GD patients. **Methods:** The study evaluated the quality of life, thy-PRO 39 questionnaire was applied to 119 patients with GD. **Results:** The initial characteristics were: Female (88%), smoking (8%), mean age 55 ± 14 , treatment type, antithyroid drugs (52%), radioiodine (28%), and 20% were in remission. Mean treatment time was months for the antithyroid group and the mean follow up was 67.45 ± 59.35 months for all patients. Groups 1-4 were divided according T3/T4 ratio quartile. Group 1 and 4 had more severe symptoms, regarding daily life compromise ($p < 0.005$), and Group 4 had more severe symptoms regarding anxiety ($p < 0.005$). Using the Spearman correlation test, there was a positive correlation between the increase in TT3/TT4 ratio and the severity of symptoms regarding depression, daily life compromise and general quality of life ($p < 0.005$). These findings were independent of age, gender, type of treatment (anti-thyroid drugs or radioiodine). **Conclusion:** Our results indicate that the effect of the TT3/TT4 on QoL in GD appears to be a long term outcome, with a positive correlation between the severity of symptoms and the increase in the ratio, regarding depression, daily life compromise and general quality of life even in the euthyroid state.

1112634 - HYPERTHYROIDISM AND HOBNAIL VARIANT OF PAPILLARY THYROID CARCINOMA: A CASE REPORT

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Case Presentation: A 20-year-old woman presenting with elevated thyroid hormones, mildly positive anti-thyroperoxidase and anti-thyroglobulin antibodies, negative anti-TSH receptor antibody and without goiter was diagnosed with hyperthyroidism and treated with tapazole. Despite no changes in gland palpation, a thyroid ultrasonography (US) was performed and showed a nodule with suspicious characteristics. Cervical US was also performed and no atypical lymph nodes were found. After a better hyperthyroidism control, a biopsy was done and was positive for papillary thyroid carcinoma (PTC) with extension to level VI cervical lymph node. Surgery was indicated and pathology confirmed infiltrative follicular papillary carcinoma and Hobnail pattern areas located in the right lobe with extrathyroidal extension to adjacent fibroadipose tissue with involvement of the parathyroid gland. Metastasis was detected in 10 lymph nodes out of 14 isolates at right level VI and in 3 lymph nodes out of 13 isolates at left level VI. After the procedure the thyroglobulin measurement was negative but due to the aggressive nature of the lesion, radioiodine therapy was indicated. Post-treatment cervical US and iodine 131 whole body scanning were performed and both were negative for metastases. **Discussion:** The Hobnail variant of PTC is a rare and aggressive form, representing between 1.08% and 1.69% of PTC cases, characterized by a high rate of lymphovascular invasion and extrathyroidal extension, in addition to iodine resistance. The association between hyperthyroidism and thyroid cancer varies from 0.5% to 15%, with a higher risk in patients with Graves' disease and nodules. **Final Comments:** It was described an unusual case of PTC in a patient without goiter or clinical nodule with aggressive characteristics. In patients with hyperthyroidism without goiter, US is not routinely indicated but this case shows the importance of careful evaluation of gland function and anatomy to confirm or exclude malignance.

HYPERTHYROIDISM

1112595 - IS IT SAFE AND EFFICIENT TO TREAT PATIENTS WITH AUTONOMOUSLY FUNCTIONING THYROID NODULE WITH A SINGLE SESSION OF 30 MCI OF RADIOIODINE? EXPERIENCE OF A SINGLE UNIVERSITY CENTER

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Introduction: Autonomously functioning thyroid nodule (AFTN) produces thyroid hormones independently of TSH leading to subclinical to overt hyperthyroidism. At radioactive iodine (RAI) uptake imaging, it appears as a hot nodule. Treatment of hyperthyroidism is indicated to reduce clinical risks. RAI treatment is a safe option compared to surgery and radiofrequency ablation. **Objectives:** To evaluate clinical and imaging data of patients with AFTN treated with one single dose of 30 mCi ¹³¹I at a single university center. **Methods:** From 2011-2024, patients with AFTN were evaluated retrospectively because of hot nodule at RAI uptake and technetium scintigraphy imaging. Thyroid ultrasound (US) characteristics (size, volume, composition, echogenicity and calcifications), thyroid function, RAI uptake at 24 hours without antithyroid drugs (ATD) were retrospectively evaluated before and after RAI treatment with 30 mCi ¹³¹I given in one session. Patients with previous surgery and RAI treatment, and nondominant thyroid nodule(s) >1.5 cm were excluded. Thyroid function was defined as euthyroidism, hyperthyroidism, hypothyroidism, subclinical hyper or hypothyroidism according to normal reference ranges using commercial kits. **Results:** From 77 patients with AFTN, 41 were selected with mean age of 50.9±16.7 years-old (21-79.9), being 90% females. Scintigraphy showed hot nodule located in the right lobe in half of patients with mean 24 hours RAI uptake 43% (normal range < 32%). All but 1 patient had hyperthyroidism nearby treatment. At US, 71% were solid-cystic with mean size 3.5 cm (1.4-6.3) and calcification was present in 22% of nodules. Other nodules were detected in 61%. After 2-4 months, 42% had normal thyroid function with no ATD. At 4-8 months, only 1 patient had overt hyperthyroidism. After 12 months, only 1 patient still showed subclinical hyperthyroidism. None developed thyroid autoimmunity. **Conclusion:** One single session of 30 mCi ¹³¹I therapy is an effective and safe choice to treat hyperthyroidism due to AFTN.

HYPERTHYROIDISM

1112212 - LONG-TERM FOLLOW-UP OF HYPERTHYROID PATIENTS AFTER DOSE-CALCULATED RADIOIODINE THERAPY

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Introduction: Radioiodine treatment can be an optimal solution for the long-term management of hyperthyroidism. However, its effects are unpredictable: hyperthyroidism may persist or recur, or hypothyroidism often develops as well. **Objective:** Our study analyzed the long-term impact of RAI treatment with dose calculation in a single endocrine center. **Methods:** Data of 449 patients who received RAI treatment between 01.01.2010. and 31.12.2014. was evaluated. The statistical analysis was performed with SPSS version 28. The precise origin of hyperthyroidism could be established in 443 cases: 182 patients were treated for Graves disease (GD), 174 for toxic adenoma (TA), and 87 for toxic multinodular goiter (TMG). At the time of diagnosis and treatment, patients with GD were significantly younger than those in the other two groups, with ages of 47 vs. 60 and 63 years, respectively. The median follow-up duration was 72 months. The median RAI dose was 323 MBq in GBD, 315 MBq in TA, and 409 MBq in TMG, with the latter being significantly higher. Additional RAI treatments were required in 21% of GD, 9% of TA, and 16% of TMG cases. **Results:** At the end of the follow-up, normal thyroid function was achieved in 51% of the patients, hypothyroidism developed in 41%, and 4.2% required further therapy for persistent hyperthyroidism. However, the outcome differed across patient groups. The rate of euthyroidism was significantly higher in non-autoimmune hyperthyroidism cases, with TA at 71%, TMG at 75%, and GD at 20% (p<0.001). Most GD patients (77%) developed hypothyroidism, which occurred earlier in GD at 5 months vs. 17 months and 50 months in TA and TMG, respectively. Hypothyroid patients received levothyroxine for thyroid replacement, with a median dose of 75 micrograms in GD and TA, and 25 micrograms in TMG. **Conclusion:** The dose-calculated RAI treatment successfully eliminated hyperthyroidism in 96% of our patients.

HYPERTHYROIDISM

1112341 - LONG-TERM TREATMENT WITH METHIMAZOLE OF OLDER ADULTS WITH AUTONOMOUS NODULAR GOITER AND SUBCLINICAL HYPERTHYROIDISM. RETROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Definitive treatment of toxic nodular goiter is usually obtained with surgery or radioiodine. However, in the elderly population, long-term Methimazole (MMI) poses an alternative to patients who are unfit for surgery or opposed to radioiodine. **Objective:** The study aimed to compare the efficacy of achieving euthyroidism with long-term MMI treatment versus definitive therapies in older adults with subclinical hyperthyroidism. **Methods:** This retrospective study evaluated 42 patients older than 60 with subclinical hyperthyroidism defined by serum TSH <0.3 mU/L and FT4 0.8-1.9 ng/dL with toxic nodules in scintigraphy. The patients were divided according to the treatment alternative: MMI more than 18 months after the initial diagnosis and the control group treated with surgery or radioiodine. Thyroid function status was recorded at baseline, 24, 36, and ≥48 months of follow-up. CHI2 and logistic regression were used to compare Euthyroidism between the two groups at each treatment period. **Results:** The MMI group (n=25) had (x±SD) 81±9.5 years, and 84% were females. The TSH levels at diagnosis were 0.28±0.5 mU/L, and FT4 1.57±0.3 ng/dL. The initial dose of MMI was 10±5.7 mg, which was reduced progressively to 5±2 mg at ≥48 months of follow-up. In the control group (n=17), 6 patients received RAI, and 11 were referred to surgery; age was 73±6.6 years, 94% were females, TSH at diagnosis was 0.18±0.1 mU/L and FT4 1.82±1.4 ng/dL. The proportion of Euthyroidism in the MMI group compared to the control group was similar: 76 vs 82%, 76 vs 87.5%, and 72 vs 100% (all p>0.5) at 24, 36, and ≥60 months. Adjustment for age did not modify the results. **Conclusion:** Treatment of thyrotoxic older adults with long-term MMI normalized thyroid function tests in most patients during the follow-up period. The efficacy was similar to that of conventional therapy with RAI or surgery.

HYPERTHYROIDISM

1112310 - MARKED REDUCTION IN TRAB ANTIBODIES AND THYROID EYE DISEASE AFTER THYROIDECTOMY IN GRAVES' DISEASE

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Introduction: Thyroid Eye Disease (TED) is a feared, disabling and difficult-to-treat complication commonly described in patients with Graves' disease (GD). Antibodies targeting the thyrotropin receptor (TRAb) are essential for the development of both GD and TED. The best GD treatment strategy to reduce TRAb and protect against TED is unknown. **Methods:** We conducted a retrospective cohort study including consecutive patients operated for GD with total thyroidectomy (TT) from 2017-21 with a long follow-up of more than two years. We included preoperative TRAb and values from the postoperative years. Pre- and postoperative evaluation of TED was included. **Results:** We operated 107 GD patients with a TT in the 5-year period. Median (Range) follow-up was 57 (33-90) months after TT. At baseline the median (Range) level of TRAb was 11 IU/L (1.5-369). A post-operative TRAb measurement was available in 74% of the patients. Following the TT, the level of TRAb was reduced by a median of 75% and in a majority the level normalized. Sixty % of the observed reduction in TRAb was seen after one year and 91% within two years. TED symptoms was present in 33 patients (31%) at baseline and improved in 97% after TT. **Conclusion:** In this retrospective study of patients with GD, operation with TT was followed by a marked reduction in the levels of TRAb and improvement in TED-symptoms. Accordingly, TT might be considered not only to control thyrotoxicosis but also when TED is present or when normalization of TRAb is desired, e.g. in fertile women.

HYPERTHYROIDISM

1114164 - METACHRONOUS THYROID CARCINOMA AND STRUMOSIS PERITONEAL: A RARE CASE OF MULTIFOCAL THYROID TISSUE INVOLVEMENT

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Case Presentation: A 42-years old woman, presented for thyroid nodules evaluation, first diagnosed 6 years ago. She had a fine needle aspiration (FNA) that was benign. She never had symptoms of hyper or hypothyroidism and never used thyroid drugs but was feeling difficulty swallowing. She had been diagnosed with endometriosis 4 years ago, had 3 miscarriages and undergone a left oophorectomy in May/2023 due to a cyst thought to be an endometrioma. Anatomic-pathological examination revealed *struma ovarii* (SO) and strumosis peritoneal (SP). On physical examination an enlarged thyroid was found. The patient was assessed by thyroid ultrasound, which showed 8 solid, isoechoic nodules (TIRADS 3), ranging from 0,5 to 1.9 cm. FNA of the largest nodule was classified as Bethesda 2. Chest RX, abdomino-pelvic MRI, thyroid function and antibodies, thyroglobulin, CEA, CA125 and CA19-9 were normal. She was referred for total thyroidectomy and a papillary microcarcinoma follicular variant was found in the right lobe. The patient was given a 7,4 GBq radioiodine dose, stimulated thyroglobulin was elevated and post-dose whole body scan showed anterior cervical and pelvic uptake. **Discussion:** SO is a rare monodermal subgroup that represents less than 1.3% of all ovarian tumors. Mature thyroid tissue implants in the peritoneum mainly occur if SO is malignant. Synchronous thyroid cancer and SO was described for the first time in 2023. Our patient had thyroid cancer diagnosed 17 months after SO surgery but had already been diagnosed with thyroid nodules for a long time. Currently, SO treatment lacks consensus due to its rarity, but the combination of surgery and radioiodine therapy has been used. **Final Comments:** This is the first description of metachronous thyroid cancer with SO and PS and follow-up will be essential to understand the disease and the prognosis.

HYPERTHYROIDISM

1112178 - MOYAMOYA SYNDROME: AN UNCOMMON ASSOCIATION WITH GRAVES DISEASE

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Case Presentation: A 21-year-old Chinese man was diagnosed with Graves disease (GD) during an initial evaluation for secondary causes of hypertension. He was started on carbimazole and euthyroidism achieved within 6 months. However, he defaulted follow-up and presented a year later with left hand clumsiness and slurring of speech. At presentation he was thyrotoxic: free T4 52 (NR: 8-16 pmol/L), free T3 21.3 (NR: 3.5-6 pmol/L), TSH < 0.01 (NR: 0.45-4.5 mIU/L), TRAb 14.6 (NR: 0-1 IU/L). MRI brain: acute infarcts in the right precentral/middle frontal gyrus and corona radiata. CT angiogram (CTA): long segment stenosis in bilateral internal carotid arteries (ICA) with a moyamoya pattern of angiopathy. SPECT scan: decreased right sided cerebral perfusion. Diagnosis: Moyamoya syndrome (MMS) associated with GD. Statins and single antiplatelet agent was started. He declined bypass surgery. Carbimazole was reinitiated and euthyroidism restored within 3 months. Repeat CTA 2 years later: Stable stenosis of bilateral ICA. He remained symptom free on carbimazole 5 mg daily. He declined radioactive iodine or thyroidectomy. **Discussion:** Postulated mechanisms of Graves and MMS include a) Sympathetic vasoconstriction of the intracranial arteries in thyrotoxicosis leading to the development of artery stenosis b) Hyperhomocysteinemia resulting in premature atherosclerosis c) Cross reaction between TSH receptor antibodies and cerebral artery antigens leading to autoimmune-mediated vasculitis Reports have observed a higher probability of occurrence and progression of MMS in thyrotoxic compared to euthyroid patients hence it is imperative to restore euthyroidism early. One needs to be careful of the risk of bleeding with antiplatelet therapy in MMS. Surgical revascularisation may reduce the risk of subsequent morbidity. **Final comments:** It is important to consider the rare association between Graves disease and MMS. As the natural history of MMS tends to be progressive, serial surveillance testing is needed to evaluate for evidence of disease progression.

HYPERTHYROIDISM

1112472 - NEONATAL HYPERTHYROIDISM SECONDARY TO MATERNAL GRAVES DISEASE: CASE REPORT AND MANAGEMENT INSIGHTS

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Case Presentation: Female patient, gestational age of 33 weeks + 1 day, delivered by cesarean section due to fetal distress, birth weight of 1,380g, Apgar scores of 7/8. She was transferred to the neonatal ICU due to prematurity and respiratory distress. The mother had a previous diagnosis of Graves disease with poor treatment adherence, requiring hospitalization for a thyrotoxic crisis at 17 weeks, with free T4 of 1.99 ng/dL (0.931.7 ng/dL), total T3 of 3.81 ng/mL (0.702.04 ng/mL), and TRAb >50 IU/L (<3.1 IU/L). She was discharged on Methimazole 20 mg/day and Propranolol 80 mg/day. Obstetric ultrasound at 26 weeks showed fetal heartbeats of 150 bpm, no goiter, but intrauterine growth restriction. At birth, the neonate was tachycardic with TSH 0.01 μ IU/mL (1.709.10 μ IU/mL), free T4 2.04 ng/dL (0.751.49 ng/dL), and TRAb 25.19 IU/L. Methimazole at 0.5 mg/kg/day was prescribed. At two months, TRAb levels decreased to 2.46 IU/L, TSH to 2.13 μ IU/mL, and free T4 to 1.12 ng/dL, indicating remission, and medication was discontinued. At 11 months of age, the infant remains euthyroid. **Discussion:** Hyperthyroidism is a rare thyroid disorder in neonates, with a prevalence of 0.10.4% of pregnancies worldwide. Maternal Graves disease accounts for 90% of cases, with transplacental passage of TSH receptor-stimulating antibodies (TRAb) occurring in 15% of these pregnancies. Poor maternal treatment adherence significantly increases risks of fetal and neonatal hyperthyroidism, heart disease, prematurity, fetal hydrops, and death. **Final Comments:** Maternal treatment with antithyroid drugs and regular follow-up of Graves disease significantly reduces the risk of neonatal disease. Detecting signs of neonatal hyperthyroidism and performing thyroid function and TRAb testing are essential for early diagnosis and appropriate treatment.

HYPERTHYROIDISM

1113938 - PHENOTYPE-WIDE ANALYSIS IN IDENTIFICATION OF FACTORS ASSOCIATED WITH THYROTOXIC PERIODIC PARALYSIS: A MALE POPULATION-BASED COHORT STUDY IN HONG KONG

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Introduction: Thyrotoxic periodic paralysis (TPP) is a rare but potentially lethal complication of thyrotoxicosis, characterized by hypokalemia, acute muscle weakness/paralysis. Yet, only one-third of patients had exposure to known precipitating factors. **Objective:** We aimed to examine whether prior medication or medical history may play a role in TPP development. **Methods:** Due to the prevalence of TPP in male, this is a population-based cohort study focusing on male, comprising male adults with TPP (n=895), or thyrotoxicosis without TPP (n=17,177) from 2002 to 2021 identified from a representative electronic medical database in Hong Kong. All drug prescription and diagnosis within 1 year prior to incident thyrotoxicosis or TPP, in addition to age and index year, were included as potential factors that affected TPP development. Stepwise selection for firth logistic regression (Stepwise) and elastic net regression (ElasticNet) analyses were conducted. Only those selected by both methods were considered TPP-associated factors. **Results:** A total of 102 medications and 23 diseases were initially examined. Our study replicated the association of a known protective factor of TPP, the beta-adrenoceptor blocking drugs (Stepwise: OR=0.54, 95% CI: 0.42-0.69; ElasticNet: OR=0.57; 95% CI: 0.44-0.73), which was an alternative treatment to reverse paralysis among patients with TPP. We also replicated the association of a known risk factor of TPP, the disorders of fluid, electrolyte, and acid-base balance (Stepwise: OR=7.28, 95% CI: 3.62-14.07; ElasticNet: OR=8.16; 95% CI: 3.85-16.75). Notably, novel protective and risk factors of TPP were identified, including drugs for nausea and vertigo (Stepwise: OR=0.49, 95% CI: 0.34-0.71; ElasticNet: OR=0.62; 95% CI: 0.4-0.92), and other forms of chronic ischemic heart disease (Stepwise: OR=10.23; 95% CI: 2.96-29.63; ElasticNet: OR=15.28; 95% CI: 3.6-54.36). **Conclusion:** Adopting a hypothesis-free approach, this study identified novel protective and risk factors of TPP. Awareness of the risk factors among male thyrotoxic patients may facilitate prevention of TPP.

HYPERTHYROIDISM

1112592 - PLASMAPHERESIS IN THE TREATMENT OF THYROTOXICOSIS

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Introduction: Therapeutic plasma Exchange (Plasmapheresis) is an alternative method for the treatment of thyrotoxicosis when antithyroid drugs cannot be used due to their side effects or ineffectiveness or in cases requiring rapid effect, such as thyroid storms. **Objectives:** This article aimed to evaluate the characteristics of our hyperthyroid patients treated with plasmapheresis. **Methods:** Plasmapheresis was performed on 12 thyrotoxic patients whose characteristics were obtained from our clinic's records. Twelve patients with a median age of 41 years were evaluated. **Results:** Of the 12 patients 11 (92%) were diagnosed as Graves disease. The other cause of thyrotoxicosis was amiodarone-induced thyrotoxicosis (n=1). Plasmapheresis was decided for five patients due to unresponsiveness to medical treatment, four due to drug-related hepatotoxicity, two due to skin side effects, and one due to vasculitis. Patients required plasmapheresis an average of 4 times. The mean fT3 value of the patients before plasmapheresis was 10.6 pg/mL and the mean fT4 value was 4.9 ng/dL. At the end of the procedure, the mean fT3 value of the patients was 4.6 pg/mL and the mean fT4 value was 1.9 ng/dL. In a patient who was unresponsive to medical treatment plasmapheresis was tried two times but could not be completed due to urticarial rash during plasma exchange and the patient was referred to surgery after being euthyroid with Lugol solution. During the procedure, 4 patients needed a central catheter insertion due to vascular access problems. **Conclusion:** Plasmapheresis is an effective alternative treatment option in preparation for ablative treatment for patients with side effects or ineffectiveness of antithyroid drugs. Considering the urticarial rash that developed in one patient and the need for catheterization in four patients in our series, we recommend plasmapheresis to be applied in selected patients.

HYPERTHYROIDISM

1114095 - PROPYLTHIOURACIL-INDUCED HEPATOTOXICITY IN A PATIENT WITH GRAVES' DISEASE: A CASE REPORT

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Case Presentation: A 39-year-old Haitian male with Graves' disease (diagnosed Oct 2024) presented with anorexia, 17 kg weight loss, choloria, jaundice, and right upper quadrant pain. He had been on propylthiouracil (PTU) 800 mg/day and propranolol 40 mg/day for three months prior to hospital admission. On admission, he was tachycardic (118 bpm) with tremors and marked jaundice. His Burch-Wartofsky score (35) suggested thyroid storm. Labs showed severe hyperthyroidism (TSH <0.005 μ IU/mL, free T4 3.4 ng/dL), TRAb >30 UI/L, liver enzyme elevation (AST 1536 U/L, ALT 1578 U/L), hyperbilirubinemia (24 mg/dL), and INR prolongation (1.56). Viral hepatitis serologies were negative. Abdominal CT revealed biliary sludge and nephrolithiasis. PTU-induced hepatotoxicity was suspected, leading to PTU discontinuation, methimazole initiation, and increased propranolol. Autoimmune hepatitis was ruled out (negative antibodies, biopsy). Despite medication adjustment, the patient showed no improvement after seven days, leading to radioactive iodine (RAI) therapy. Pre-RAI thyroid tests showed persistent hyperthyroidism (free T4 >7.7 ng/dL). After 50 days, liver function improved (AST 93 U/L, ALT 92 U/L), but TSH remained <0.005 μ IU/mL with free T4 at 7.7 ng/dL. The patient was informed about monthly further monitoring and the possible need for additional RAI due to high TRAb titers. **Discussion:** PTU is an antithyroid drug commonly used in the management of Graves' disease. Although effective, PTU carries a risk of severe hepatotoxicity, but can manifest as acute liver failure. The primary treatment involves drug discontinuation, monitoring, and consideration of alternative definitive therapy. In this case, RAI was a successful approach to avoid further hepatotoxic risk. **Final Comments:** Clinicians should consider PTU-induced hepatotoxicity in patients with jaundice and elevated liver enzymes. Early cessation of PTU and possible RAI therapy are critical to preventing liver damage.

HYPERTHYROIDISM

1112353 - QUALITY LIFE IN GRAVES' DISEASE: THE IMPACT OF AGE, GENDER, AND ETHNICITY

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Introduction: Graves disease is the leading cause of hyperthyroidism in the adult population, with different clinical presentations in different populations. Current literature provides scarce data about how the quality of life of these patients is affected at different ages, genders, and ethnicities. **Objective:** The objective of the study was to evaluate the impact of age, gender, and ethnicity quality of patients with Graves disease. **Materials and Methods:** The study evaluated the quality of life of 164 patients with Graves disease in a euthyroid state. The patients were divided according to their current age (patients under 60 years old and patients with 60 or more years), gender (male and female), and ethnicity (Caucasian and non-Caucasian). The patients were analyzed according to symptom scores in the Thy-PRO 39 questionnaire, epidemiological features, and thyroid function biomarkers. **Results:** Evaluating patients according to age; Group 1 (N=65), mean serum TSH = 2.47 ± 1.63 UI/mL, and mean serum FT4 = 1.23 ± 0.27 ng/dL, 3% of the patients were current smokers. In Group 2 (N=99), the mean serum TSH = 2.44 ± 3.07 UI/mL, and mean serum FT4 = 1.28 ± 0.34 ng/dL, 7% of the patients were current smokers. Regarding patient symptoms of hypothyroidism, Group 1 had more severe symptoms when compared to Group 2 ($p < 0.005$), regarding symptoms of goiter, hyperthyroidism, eye, tiredness, cognitive complaints, anxiety, depression, emotional susceptibility, impact on emotional and daily life both groups showed similar results. There were no differences in impact quality of life when comparing the patients based on gender or ethnicity. **Conclusion:** Although in euthyroidism, elderly patients with Graves' disease had more symptoms related to hypothyroidism. Further studies are needed to clarify this relationship

HYPERTHYROIDISM

1114289 - RADIOFREQUENCY ABLATION FOR AUTONOMOUS THYROID NODULES: SINGLE-CENTER CASE SERIES AND PROCEDURAL FACTORS

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Introduction: Autonomous thyroid nodules (ATN) are a common cause of subclinical or overt hyperthyroidism. While surgery and radioactive iodine remain standard treatments, radiofrequency ablation (RFA) has emerged as a minimally invasive alternative. **Objective:** To describe clinical outcomes and procedural parameters in a single-center case series of patients with ATN treated with RFA. **Methods:** This retrospective study included eight nodules in seven female patients (ages 24–73 years) treated with RFA for ATN. Key variables analyzed included initial nodule volume, volumetric reduction rate (VRR) at 3, 6, and 12 months, thyroid function tests (TSH, T4L), clinical symptom improvement, and procedural parameters (power, ablation time, electrode size). Correlations between these factors and VRR were assessed. **Results:** Initial nodule volumes ranged from 0.68 to 47.7 cc. Mean VRR was 72% at 3 months and 85% at 12 months. TSH normalized in all cases with follow-up data. All four symptomatic patients experienced clinical improvement. RFA was performed using 45–55 W power, 7–10 mm electrodes, and ablation times of 150–1020 s. The strongest positive correlation with VRR at 12 months was observed for energy per cubic centimeter ($r = +0.38$) and TSH suppression at baseline ($r = +0.31$). In contrast, larger initial volume ($r = -0.91$), older age ($r = -0.95$), and total energy administered without adjusting for volume ($r = -0.87$) correlated negatively with VRR. **Conclusion:** In this small series, RFA was effective in reducing nodule volume, normalizing thyroid function, and improving symptoms in patients with ATN. Energy administered per cc and lower baseline TSH were associated with better outcomes, while age and initial nodule size negatively influenced response. These findings suggest that procedural tailoring based on these parameters may enhance treatment success.

HYPERTHYROIDISM

1113884 - RADIOFREQUENCY ABLATION FOR BILATERAL AUTONOMOUS THYROID NODULES: SUCCESSFUL SINGLE-TREATMENT APPROACH

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Case Presentation: The traditional treatment for autonomous thyroid nodules disease includes radioactive iodine and surgery. However, less invasive, like radiofrequency ablation (RFA), alternatives have emerged due to the need for preserving thyroid function and reducing procedural risks. In this case we present the resolution of bilateral autonomous thyroid nodules with a single RFA session. A 35-year-old female with a history of multinodular goiter presented with progressive thyroid nodule growth and symptoms of palpitations, thermal dysregulation, and anxiety. Cardiovascular assessment revealed sinus tachycardia, and laboratory tests confirmed subclinical hyperthyroidism with declining TSH levels. Imaging studies showed a 29 mm mixed isoechoic nodule in the upper right thyroid lobe and a 15 mm similar nodule in the left lobe. Thyroid scintigraphy identified two hyperfunctioning areas corresponding to these nodules. Cytology classified them as Bethesda II, confirming benign follicular lesions. **Discussion:** In December 2023, the patient underwent RFA targeting both nodules in a single session. Using a 7 mm electrode at 45 W power, the total ablation time was 2.5 minutes. No immediate complications occurred. Three months post-procedure, the patient reported complete symptom resolution, and follow-up ultrasound demonstrated significant volumetric reduction rates of 80% and 87% for the right and left nodules, respectively. Thyroid function tests normalized (TSH: 0.9; free T4: 1.1). **Final Comments:** This case demonstrates the efficacy and safety of RFA in treating bilateral autonomous thyroid nodules within a single procedure. The successful outcome highlights RFA as a viable alternative to traditional therapies, offering effective nodule reduction and symptom relief with minimal risk and without altering thyroid function.

HYPERTHYROIDISM

1112361 - RAIDIODONE AND PRETIBIAL MYXEDEMA DEVELOPMENT: UNDERSTANDING THIS COMPLICATION

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Introduction: Radioiodine treatment (RAI) treatment is a well-established therapy for Graves' disease associated with an autoimmune exacerbation that, in some cases, results in pretibial myxedema (PM). This rare complication has been described in the literature, but the full spectrum of this complication is unknown. **Objective:** The study objective was to analyze the incidence of Graves dermopathy after RAI and the risk factors associated with its development. **Results:** A retrospective study included 213 patients treated with RAI in a single center. The RAI group (n=209) consisted of patients treated with RAI and did not develop PM, and the PM group (n=4) consisted of patients who developed PM after RAI treatment. The mean age in the RAI group was 40±12 years, 85% of the group was female, and 40% of the patients smoked. Regarding thyroid function prior to treatment, the mean TSH was 0.021±0.059 uUI/mL, and the mean FT4 was 4.26±2.18 ng/dL. 82% of the patients had positive TRAb, and 73% had positive TPO. The mean age in the PM group was 40 ±15 years, 50% of the group was female, and smoking was present in 50% of the patients. Regarding thyroid function prior to treatment, the mean TSH was 0.005±0.003 uUI/mL, and the mean FT4 was 3.39±1.41 ng/dL. All of the patients had positive TRAb and positive TPO. Regarding TED, the mean CAS in group RAI was 1 ± 1 and 2±1 in group PM. Follow-up time was 64±52 months. **Conclusions:** In conclusion, PM related to RAI treatment is a rare condition that correlates to a higher presence of autoimmune markers, the use of tobacco, and a more active TED. The full spectrum of mechanisms involved in pathogenesis is unclear, and further research is necessary.

HYPERTHYROIDISM

1114227 - TEPROTUMUMAB AS A PROMISING THERAPEUTIC OPTION FOR REFRACTORY THYROID EYE DISEASE: A CASE REPORT

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Case Presentation: A 51-year-old female with Graves' Disease was managed with methimazole, followed by radioiodine after three years. At onset, she had periorbital edema - Clinical Activity Score (CAS) 1, indicative of Thyroid Eye Disease (TED), progressing to CAS 5, moderate to severe form. Over nine-years, she underwent three cycles of methylprednisolone (total dose: 17 g) and multiple courses of oral corticosteroids, achieving partial and transient improvement with inflammatory relapses. Attempts to taper corticosteroids resulted in exacerbation and increased thyroid-stimulating hormone receptor antibody (TRAb) levels, with corticosteroid dependence, Cushing's syndrome manifestations, and diabetes. Despite decompression surgery and ocular radiotherapy, the disease progressed. Manifestations included severe proptosis, extraocular muscle thickening, inflammatory infiltration, constant diplopia, and restricted ocular motility. TRAb levels remained persistently elevated, reaching 29 times the assay's upper reference limit. Symptoms lead to significant impaired quality of life, and for that, Teprotumumab was initiated. Remarkable improvement was observed after infusions, with a reduction in the CAS from 5 to 0. To date, she has received seven infusions with a satisfactory therapeutic response. Hepatic enzyme elevations were noted, with transaminases exceeding three times and gamma-glutamyl transferase ten times the upper reference limit. These subsequently normalized. Hyperglycemia was successfully managed by adjusting metformin. **Discussion:** TED results from autoimmune inflammatory response by TRAb and insulin-like growth factor 1 receptor (IGF-1R) signaling in retro-orbital compartment, affecting extraocular muscles, adipose and soft tissues, leading to functional/structural impairments. Historically, available treatments included corticosteroids, ocular radiotherapy, and decompression surgery, providing symptomatic relief but not modifying the underlying mechanism. Teprotumumab, a monoclonal antibody recently approved in Brazil, targets IGF-1R, interrupting activation and downstream signaling pathways, addressing the TED's pathophysiology, an effective alternative for refractory cases. **Final Comments:** Teprotumumab represents a significant advancement in TED conventional therapies, with potential to transform management and improve patient outcomes even in chronic cases.

HYPERTHYROIDISM

1112493 - THE IMPACT OF GENDER, ETHNICITY, AND AGE ON THYROID EYE DISEASE EVOLUTION

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Introduction: Thyroid eye disease (TED) represents the main extrathyroidal manifestation of Graves disease (GD), with a wide variety of clinical courses. **Objective:** To identify factors contributing to TED evolution patterns. **Methods:** The study included 203 patients with GD who developed TED during the 60-month follow-up as determined by the clinical activity score (CAS). Group 1 (n=131) consisted of patients who followed the Rundles Curve pattern, and Group 2 (n=72) consisted of patients with GO evolution characterized by increased and decreased CAS. **Results:** In Group 1, mean age was 39±11 years, and 80% of patients were female, mean initial TSH was 0.017±0.026 uUI/mL, mean initial FT4 was 4.40±2.08 ng/dL, initial CAS was 1.27±1.27; 85% were TRAb-positive, 50% were treated with radioiodine, 48% smoked. In Group 2, the mean age was 41 ± 11 years, and 73% of patients were female, mean initial TSH was 0.014±0.031 uUI/mL, mean initial FT4 was 3.92±1.84 ng/dL, initial CAS was 2.19±1.49; 84% were TRAb positive, 44% were treated with radioiodine, 38% smoked. There were no statistical differences between the groups. Regarding CAS evolution, Group 1 was marked by a steady decrease in CAS during the 60-month observation period (p<0.005), and CAS evolution was marked by periods of increase and decrease of CAS (p<0.005). The evolution pattern between the groups was significantly different (p<0.005). There was no significant difference in thyroid function between the groups during follow-up. **Conclusion:** This study described a group of patients with TED evolution, with periods of worsening and improvement of TED that correlate to more inflammatory signs at the diagnosis.

HYPERTHYROIDISM

1114117 - THYROID ARTERY EMBOLIZATION AS PRE-THYROIDECTOMY BRIDGING THERAPY IN A PATIENT WITH THYROTOXICOSIS: CASE REPORT

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Thyroid artery embolization (TAE) is a minimally invasive technique that allows selective ischemic necrosis of the thyroid parenchyma, reducing thyroid hormone synthesis, with few associated complications. However, there are few reported cases of successful TAE as a bridge therapy associated with plasmapheresis prior to total thyroidectomy in patients with thyrotoxicosis with therapeutic refractoriness. A 36-year-old man with a history of Graves' disease, poorly adherent to treatment. He was admitted with symptoms of frontal headache, vomiting episodes, palpitations, subjective fever, fine distal tremor, diplopia, episodes of anxiety and irritability, insomnia onset, altered intestinal transit, and involuntary weight loss. Physical examination revealed sinus tachycardia, hypertension not in the crisis range, severe orbitopathy according to the EUGOGO classification, and grade III goiter. Paraclinical tests showed a clearly elevated free T4 (100.00 pmol/L) and suppressed thyroid-stimulating hormone (TSH). Uncontrolled hyperthyroidism was considered, Burch-Wartofsky score of 35, intermediate probability of thyroid storm, thyrostatics were started at maximum tolerated doses, and due to scanographic findings of severe orbitopathy (elevated Hertel index, involvement of the right optic nerve and rectus muscles) steroid pulses were started. However, due to persistent thyrotoxicosis, it was decided to perform thyroidectomy after therapeutic apheresis sessions, however due to intolerance to it, EAT was performed as a bridge therapy, achieving total occlusion of the left superior and inferior thyroid arteries, by infusion of microparticles, with adequate clinical response, making the performance of total retrosternal thyroidectomy feasible, without complications. The patient was discharged from hospital with resolution of symptoms and progressive normalization of thyroid hormone levels. EAT is a therapeutic option in patients with hyperthyroidism refractory to thyrostatic agents, which, together with plasmapheresis prior to total thyroidectomy, allows an effective and safe therapeutic approach, with few complications.

HYPERTHYROIDISM

1114114 - THYROID CARCINOMA IN SURGERY-TREATED HYPERTHYROID PATIENTS: EXPERIENCE OF A TERTIARY CARE PUBLIC HOSPITAL IN COLOMBIA, 2012-2023

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Introduction: Hyperthyroidism has been associated with no insignificant rates of thyroid cancer, frequently diagnosed incidentally, and with few studies available that analyze this relationship. **Objective:** The objective of this study was to determine the prevalence of thyroid carcinoma in surgically treated hyperthyroid patients. **Methods:** Observational, cross-sectional, retrospective study based on a review of data from the statistics department of a public tertiary hospital in Santander, Colombia. This study included patients over 18 years of age with Graves' disease (GD) and/or thyroid follicular nodular disease (TFND) who underwent total thyroidectomy for the control of hyperthyroidism between 2012 and 2023. All statistical analyses were performed using STATA version 16.1. **Results:** Were included 116 patients with a mean age of 43 years, 82.7% (n=96) were women. The main reason for choosing thyroidectomy as management was lack of symptom control in 74.1% (n=86), followed by compressive symptoms in 19.8% (n=23) and difficulty in clinical follow-up in 6.8% (n=8). 87.1% (n=101) of the patients had a histopathological diagnosis of TFND, 17.2% (n=20) of GD and 6.8% coexistence of GD with TFND. The prevalence of thyroid carcinoma was 11.2% (n=13), with the classic papillary histological variant predominating in 69.2% (n=9). **Conclusion:** Hyperthyroidism is associated with notable rates of thyroid cancer. It is necessary to carry out future studies to determine which risk factors make close clinical/ultrasound follow-up necessary in hyperthyroid patients.

HYPERTHYROIDISM

1112248 - THYROID STATUS OUTSIDE THE THERAPEUTIC GOAL FOLLOWING PROLONGED LOW-DOSE OF METHIMAZOLE TREATMENT VS LEVOTHYROXINE REPLACEMENT POST RADIOIODINE THERAPY IN PATIENTS WITH GRAVES' DISEASE

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Introduction: In most patients thionamides are the treatment of choice for Graves disease (GD) because they can induce remission, while radioiodine (RAI) and surgery lead to definitive hypothyroidism with the need to replace thyroid function with lifelong levothyroxine. Prolonged low doses of methimazole may be an alternative for GD patients who fail to achieve remission within the first 24 months. **Objective:** To assess the prevalence of patients with GD outside the therapeutic goal on prolonged methimazole treatment versus post-RAI hypothyroid patients on levothyroxine replacement. **Methods:** GD patients under follow-up who consulted from 5/2023 to 10/2024 were cross-sectionally analysed at their last visit. They were divided into 2 groups: MMI Group (patients on methimazole for at least 2 years on a dose ≤ 5 mg/d during the last 6 months) and LT4 Group (hypothyroid patients on LT4 replacement in whom RAI therapy was administered at least 12 months before the last visit). Therapeutic goal: MMI group = normal FT4 and in LT4 group = FT4 and TSH in reference range. We determine the percentage of patients outside the therapeutic goal in both groups. FT4 (RR: 0.93-1.70 ng/dL) and TSH (RR: 0.27-4.2 mIU/L) measured by chemiluminescence assay. Statistical analysis: Fishers exact test. **Results:** MMI Group: n = 42 (32 females); Age X(r) = 50(27-78) y/o LT4 Group: n = 22 (18 females); Age X(r) = 50.5(22-74) y/o. Patients outside the therapeutic goal: MMI group = 2/42 (4.8 %) vs LT4 group = 11/22 (50%) (p < 0,001). **Conclusion:** We observed a statistically significant lesser frequency of patients outside the therapeutic goal in MMI group vs LT4 group. We consider that MMI at a low dose for a prolonged period of time is a better therapeutic alternative than longlife LT4 replacement for 131I induced definite hypothyroidism.

HYPERTHYROIDISM

1112443 - THYROID STORM: A DIAGNOSIS TO REMEMBER IN THE CONTEXT OF ATRIAL FIBRILLATION

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A 71-year-old female presented to the emergency department with abdominal pain, diarrhea, disorientation, agitation, fever, tachycardia, and high-response atrial fibrillation recently treated with amiodarone. Her medical history revealed hypertension, chronic obstructive pulmonary disease (due to smoke and wood stove exposure), dementia syndrome, and a previous hospitalization four months ago for myocardial infarction, heart failure, atrial fibrillation, and hyperthyroidism. At that time, she received methimazole, which she did not continue after discharge. At the current admission, she was dehydrated. Her vital signals included temperature 36.8 °C, Glasgow Coma Scale 14/15, heart rate 140/min, blood pressure 110/80 mmHg, respiratory rate 24/min, and oxygen saturation of 97% with nasal cannula oxygen at 2 L/min. On physical examination, she did not have goiter or exophthalmos. Laboratory tests revealed TSH 0.005 mIU/L (reference values - RV: 0.4-4.0 mIU/L), free T4 2.92 ng/dL (RV: 0.93-1.7 ng/dL), TSH receptor antibody (TRAb) 15.8 U/L (RV < 1.75 U/L), and urine with uncountable leukocytes. Thyroid storm was recognized and, in addition to volume expansion and antibiotics for urinary tract infection, propylthiouracil 200 mg orally every four hours was started. She was transferred to the intensive care unit and received beta-adrenergic blocker and corticosteroid. Hyperthyroidism due to Graves disease was the etiology of thyrotoxicosis. Elderly people may not have classic symptoms of thyrotoxicosis and atrial fibrillation may be a common feature. Our patient scored 50 points on the Burch-Wartofsky scale for thyroid storm. The patient scored points for tachycardia (10 points), atrial fibrillation (10 points), diarrhea (10 points), central nervous system disturbance (10 points), infection and non-compliance to antithyroid medications were considered precipitating events (10 points). By the Japanese Thyroid Association diagnostic criteria, the patient was considered to have definite thyroid storm. It is important that the medical team promptly recognize thyroid storm, a rare and life-threatening condition, in order to initiate appropriate treatment.

HYPERTHYROIDISM

1112512 - THYROTOXIC PERIODIC PARALYSIS (TPP): A CASE REPORT

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Introduction: CASE REPORT: A Caucasian 36-year-old woman was admitted to a hospital after reporting that, following hysterectomy surgery, she experienced weakness in her lower limbs, episodes of tachycardia, and malaise. She experienced a loss of strength in her legs, becoming unable to walk but remaining able to move them, tachycardia and malaise. The symptoms disappeared after six hours, spontaneously. On physical examination, she was tachycardic and had mild bilateral exophthalmos. Her EKG showed sinus tachycardia. Investigations showed hypokalemia (K 3,0 mmol/L - 3,5-5,1), and oral and intravenous potassium replacement was performed. Arterial and venous angiography TC and neuraxial MRI were normal. Thyroid function tests revealed TSH 0,01 μ UI/mL (0,35, 5,50) and T4L 2,67 ng/dL (0,89, 1,76). Hyperthyroidism was confirmed with new test TSH 0,01 μ UI/mL, T4 16,40 μ g/dL (4,5-10,9) T3 1,96 ng/mL (0,6-1,81), T4L 2,70 ng/dL TRAB 16,40IU/L (<1,5), AATPO and AATg were negative. A thyroid ultrasound identified a hypervascularized goiter. A diagnosis of Graves' disease was made, and drug treatment was initiated (methimazole 10 mg daily), leading to symptom reversal. **Discussion:** TPP is a rare but potentially dangerous complication of thyrotoxicosis, with episodes of acute and reversible muscle weakness due to transient hypokalemia. It carries risks of falls, traumatic injuries, paralysis of the respiratory muscles, leading to acute respiratory failure. Factors that may precipitate these episodes include stress; medications (such as insulin, diuretics, and corticosteroids); intense physical activity; fasting; and carbohydrate-rich meals. TPP is most common in Asian populations (1:100.000) and occurs more frequently in men, with incidence from 17:1 to 70:1, with a higher incidence in the third and fourth decades of life. Genetic mutations in the Kir2.6 channel are involved in the pathogenesis of TPP. **Final Comments:** TPP may be the initial manifestation of Graves disease and is rare in women, but it is crucial to recognize and initiate treatment promptly.

HYPERTHYROIDISM

1112349 - THYROTOXIC PERIODIC PARALYSIS: A DIAGNOSTIC CHALLENGE

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Case Presentation: A 39-year-old male with an unremarkable medical history was admitted to the emergency department of a secondary hospital with complaints of persistent muscle weakness in all four limbs, which had begun one month prior and worsened the day before admission, following alcohol consumption. Upon hospital evaluation, a serum potassium level of 2.1 mEq/L (NR > 3,5mEq/L) was detected, along with a low urinary potassium/creatinine ratio. Potassium replacement therapy was initiated, leading to complete recovery of the deficit. Physical examination revealed enlargement of the cervical region, identified as a goiter, raising the hypothesis of thyroid disease. Laboratory findings suggested hyperthyroidism with elevated thyroxine (T4: 24.8 ng/dL, NR 0.91.7 ng/dL), suppressed thyrotropin (TSH: 0.01 mU/L) and positive thyroid autoantibodies (TPO: 391 U/mL, NR < 34 U/mL; TRAB 12.9 U/L, NR < 1,75). These findings, combined with clinical presentation, led to the diagnosis of thyrotoxic periodic paralysis (TPP). **Discussion:** TPP is a rare and often underdiagnosed condition, primarily affecting young males. It is characterized by episodes of sudden muscle weakness due to an abnormal shift of potassium into cells, associated with a genetic predisposition, and triggered by factors such as exercise, carbohydrate-rich diets, stress and alcohol. Diagnosis involves recognizing symptoms of hyperthyroidism and confirming hypokalemia during episodes. Thyroid function tests are crucial in patients presenting with periodic paralysis. The absence of overt hyperthyroid signs, such as classic clinical features, highlights the importance of comprehensive thyroid testing in cases of hypokalemia and transient muscle weakness, especially when episodes are triggered by specific factors. Treatment includes potassium replacement, control of thyroid function with antithyroid drugs, beta-blockers, and lifestyle changes. **Final Comments:** This case underscores the rare presentation of thyrotoxicosis in a Brazilian patient and emphasizes the critical need to consider thyroid dysfunction in the differential diagnosis of patients with muscle weakness.

HYPERTHYROIDISM

1112603 - RADIOFREQUENCY ABLATION OF TOXIC THYROID NODULES: ENHANCING TREATMENT EFFECTIVENESS WITH HYDRODISSECTION AND TARGETED VASCULAR ABLATION

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Radiofrequency ablation (RFA) has emerged as a valuable minimally invasive treatment option for toxic thyroid nodules, offering an alternative to surgery and radioactive iodine (RAI) therapy. A key advantage of RFA is its ability to preserve thyroid function, as the procedure selectively targets the nodule while sparing healthy thyroid tissue. This contrasts with surgery and RAI, which often lead to hypothyroidism and the need for lifelong thyroid hormone replacement. The treatment of toxic thyroid nodules with RFA is technically more demanding than the treatment of benign atoxic nodules. Beyond achieving volumetric reduction, it is critical to restore normal thyroid function, as residual viable tissue can result in persistent or recurrent hyperthyroidism. Recent advancements in RFA techniques, such as hydrodissection and targeted vascular ablation, have improved outcomes. Hydrodissection involves injecting fluid around the nodule to protect adjacent structures, enhancing procedural safety. Targeted ablation of vascular structures, including the feeding artery and marginal veins identified through Doppler ultrasound, is crucial for effectively reducing residual viable tissue and achieving long-term normalization of thyroid function. This presentation will highlight two cases: one with incomplete treatment, where residual viable tissue may lead to recurrent hyperthyroidism, and another with complete treatment, where successful ablation of the feeding artery and marginal veins resulted in no residual tissue and an excellent prognosis. These findings emphasize that RFA for toxic thyroid nodules, while technically more demanding, can achieve superior outcomes with refined techniques such as hydrodissection and vascular ablation. Compared to RAI and surgery, RFA offers a promising alternative with better preservation of thyroid function and represents an advancement in the management of toxic thyroid nodules.

HYPERTHYROIDISM

1113835 - TŌKU ARA ORANGA* (TAONGA): A MULTI-STAGE CODESIGN-INFORMED INDIGENOUS WĀNANGA (WORKSHOPS) PROJECT TO DEVELOP A NEW MODEL OF THYROTOXICOSIS CARE

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Introduction: Indigenous healthcare inequities in Aotearoa/New Zealand have long been recognised, and thyrotoxicosis is no different. Healthcare design and delivery is an integral determinant impacting these inequities. **Objective:** Grounded in Indigenous methodology, Tōku Ara OraNGA* (TAONGA) is an Indigenous-led four-stage mixed-methods project sharing what is known about thyrotoxicosis care with whānau (Māori patients and their families) and stakeholders to reimagine services. **Methods:** Three stages are completed, with the fourth underway soon (Stage 4 not being presented). Whakatakatū (Stage 1) established governance and responsibility relationships, then quantitative evidence of ethnic inequity in thyrotoxicosis in Aotearoa/New Zealand was reviewed. Kōrero mai, kōrero atu (Stage 2) added qualitative narrative of thyrotoxicosis care via focus groups with whānau, as well as stakeholders. Grounded in the principle of reciprocity, Stage 3 shared findings within facilitated wānanga (workshops) to identify areas of actions (define/engage) and allow “no-limit” solutions (test/finalise). **Results:** Indigenous governance and responsibility relationships informed all stages. A prototype “patient journey map” was created utilising a river metaphor to describe quantitative Māori health inequity points from epidemiology to outcomes. Thematic analysis of the qualitative stage identified seven themes represented in an Indigenous conceptualisation: a) recognisably Māori care, b) differential experiences, c) system access, d) autonomy, e) whānau, f) communication, and g) relationships. The co-design wānanga developed a model of care containing six design features: a) the right to high quality healthcare; b) safe environments; c) support services d) staff development; d) reciprocal relationships; and e) resources. This model will soon be tested in a pilot. **Conclusion:** Indigenous-led research can facilitate power-sharing with whānau, supported by stakeholders, to create innovative care design responsive to diverse Indigenous realities. It is anticipated this will translate to better healthcare experiences and outcomes. * “Tōku Ara Oranga” – translating to “My wellness path”.

HYPERTHYROIDISM

1112653 - TSH-SECRETING PITNETS: CHARACTERIZATION OF 11 CASES

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Introduction: TSH-secreting pituitary adenomas (PitNets) are a rare cause of hyperthyroidism (<1%). They typically present during the fourth decade of life, with no gender predilection. They are suspected in patients presenting with hyperthyroid symptoms without goiter, elevated or inappropriately normal TSH levels, increased T4 and T3, and imaging findings consistent with macroadenomas exhibiting mass effects. One-third of these adenomas are co-secreting, predominantly GH and PRL. Differentiation from thyroid hormone resistance (THR) is essential, as the latter is associated with family history, normal SHBG and alpha subunit levels, and a positive response to TRH stimulation testing. **Objective:** To characterize the clinical presentation of patients with TSH-secreting PitNets. **Methods:** A retrospective, descriptive study analyzing medical records of patients diagnosed with TSH-secreting PitNets between 2002 and 2024. The analysis included clinical, biochemical, and imaging characteristics. **Results:** Thirteen patients were identified: 7 females, with a mean age of 43.9 years. The median time from symptom onset to diagnosis was 25.7 months. The most common symptoms were tremor, palpitations, weight loss, increased bowel movements, and excessive sweating in 61% of patients. Visual disturbances were present in 46%. The average tumor size was 25.6 mm. Median TSH levels were 5.8 uIU/mL (range: 1.78-14.46), and median free T4 levels were 3.16 ng/dL (range: 0.91-4.87). Immunohistochemical co-secretion was observed in the biopsy: 2 patients presented with acromegaly symptoms, and 2 had prolactinomas. TRH testing was performed in 5 patients, showing no stimulation, with a median SHBG level of 142 nmol/L (range: 53-362). **Conclusion:** TSH-secreting PitNets are a rare cause of hyperthyroidism. Co-secretion was evident in one-third of the cases. High clinical suspicion and differential diagnosis with THR are required.

HYPERTHYROIDISM

1112356 - UNILATERAL THYROID INVOLVEMENT IN GRAVES DISEASE: CASE REPORT

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Case Presentation: A 50-year-old female presented with a history of a skin lesion on her leg for three months. Laboratory tests indicated thyroid abnormalities, serum TSH of 0.005 mIU/L (range: 0.27-5.5 mIU/L), with elevated free T4 at 1.81 ng/dL (range: 0.93-1.7 ng/dL) and negative thyroid autoimmunity biomarkers, leading to a referral to an endocrinology service. The patient exhibited no signs of hyperthyroidism and had no signs of TED in the initial evaluation. A dermatological assessment characterized the skin lesions as compatible with thyroid dermopathy. Thyroid scintigraphy showed a hyperfunctioning right lobe. Thyroid ultrasound reveals thyroid volume 9.3 cm³, with no nodules. Treatment with methimazole was initiated with 5 mg daily. After one year of treatment, the patient returned to the euthyroid state while maintaining thyroid scintigraphy, indicating hyperfunction of the right lobe, with negative serum TARb, suggesting an atypical form of Graves disease. Clinically, the patient exhibited spontaneous improvement of the dermatological lesions. Methimazole suspension was attempted after 18 months of use, with the subsequent relapse of Graves' Disease and methimazole reinitiation. After four years of treatment, the patient is in a euthyroid state with ongoing medication use. **Discussion:** Rarely Graves disease patients present unilateral involvement; the involvement of only one lobe of the thyroid gland may result from acquired conditions, such as unilateral bacterial or viral infections combined with potential differences in thyroid antigens in each lobe. The use of antithyroid drugs for patients with unilateral Graves disease is the first line of treatment, with up to 50% attaining remission after a course of drug therapy. **Final Comments:** Unilateral Graves disease is a rare occurrence where thyroid Scintigraphy and ultrasound are essential for confirming the diagnosis.

HYPOTHALAMIC-PITUITARY-THYROID AXIS

1112378 - AN UNUSUAL PRESENTATION OF A TSH-SECRETING PITUITARY ADENOMA: A CASE REPORT DIAGNOSED AFTER TRAUMATIC BRAIN INJURY

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Case Presentation: A 68-year-old previously healthy male was admitted for traumatic brain injury (TBI) following a ground-level fall. He reported unintentional weight loss and weakness. Imaging performed for the evaluation of TBI revealed an expansive lesion with sellar and suprasellar components measuring 3.3 x 3.4 x 5.5 cm, causing compression and displacement of the optic chiasm and extending into the left cavernous sinus. Laboratory evaluation showed TSH of 1.8 mIU/mL (RV: 0.45.8 mIU/mL) and free T4 of 2.93 ng/dL (RV: 0.61.12 ng/dL), with results confirmed upon repeat testing. Combined measurement of α -subunit 32,900 ng/L (RV: 120790 ng/L) and TSH 3.53 mIU/mL revealed a high serum α -subunit/TSH molar ratio of 9,320. Based on the diagnosis of a TSH-secreting pituitary adenoma (TSH-oma), the patient underwent surgical resection of the lesion. Due to persistent thyroid dysfunction postoperatively, lanreotide therapy was initiated, normalizing circulating T4 and TSH levels after four months of treatment. However, there was no reduction in the size of the lesion. **Discussion:** TSH-omas are characterized by autonomous TSH secretion, unaffected by negative feedback from thyroid hormones. They account for 2.8% of pituitary tumors and typically present with symptoms of thyrotoxicosis. In this case, the patient exhibited nonspecific symptoms of weight loss and fatigue without prior etiological investigation. Treatment involves surgical resection, with refractory cases requiring radiotherapy and/or somatostatin analogs. **Conclusion:** The diagnosis and management of TSH-omas remain challenging. In cases like this, where classical signs of thyrotoxicosis are absent, failure to recognize the condition can lead to inappropriate treatments, while delays in diagnosis may compromise quality of life and result in symptoms caused by compression of adjacent structures.

HYPOTHALAMIC-PITUITARY-THYROID AXIS

1112618 - OXCARBAZEPINE TREATMENT MIMICKING CENTRAL HYPOTHYROIDISM

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Introduction: Antiepileptic drugs such as carbamazepine, phenytoin, and oxcarbazepine can lead to low free T4 (FT4) and low normal-range T3 levels, without increasing TSH, mimicking central hypothyroidism. The mechanism behind remains unclear, potentially involving hypothalamic regulation interference. The clinical significance of reduced FT4 is uncertain, as many patients remain clinically euthyroid. Fatigue is common in these patients and may be misdiagnosed as a symptom of hypothyroidism. **Case Report:** A 76-year-old male patient presented with dizziness, dyspnea, and bradycardia (heart rate 51 bpm), reporting cold intolerance and hair loss. He had been treated for trigeminal neuralgia with oxcarbazepine since 2020 (1,500 mg/day), with gabapentin (1,200 mg/day) and amitriptyline (25 mg/day). He also had hypertension, pre-diabetes, dyslipidemia, and prostate cancer. Physical examination revealed slowed speech, normal body mass index (25.8 kg/m²), and a normal palpable thyroid. Thyroid function tests revealed low FT4 (0.77 ng/dL, NR 0.93-1.7) with inappropriately normal TSH (2.09 mIU/L). Total T4 and T3 were also low, while other pituitary hormones were in normal range. No lesions were found in the hypothalamic-pituitary region at magnetic resonance. Due to contraindications for suspending medications, the patient was started on a low dose of levothyroxine (LT4) (25 mcg/day). After six months, FT4 remained in low-normal values, with normal TSH and no clinical improvement. Following the suspension of LT4, FT4 was measured using equilibrium dialysis, revealing normal concentration (1.2 ng/dL, NR 0.9-2.2). The patient continued off-LT4. **Discussion and Conclusion:** Central hypothyroidism occurs in about 20% of patients on oxcarbazepine or carbamazepine, independent of dosage. Thus, monitoring thyroid function is essential. If symptoms of hypothyroidism are present, FT4 determination by equilibrium dialysis is mandatory to prevent misdiagnosis of central hypothyroidism and overtreatment with LT4.

HYPOTHALAMIC-PITUITARY-THYROID AXIS

1112442 - PRE-SURGICAL TREATMENT WITH SOMATOSTATIN ANALOG IN A PATIENT WITH TSH-SECRETING ADENOMA: CASE REPORT

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A male patient 32y. presented with fatigue and excessive sweating. Blood tests revealed elevated levels of TSH, T4, T3, SHBG and alpha subunit. TRH stimulation test and MRI confirmed a TSH-secreting pituitary macroadenoma (TSHom). Octreotide treatment was initiated, which led to improved thyroid function within 10 months. The patient underwent transsphenoidal surgery of the adenoma 16 months from diagnosis without complications. Pre-surgical MRI of the pituitary showed a reduction in tumor size. Post-surgery levothyroxine was added to normalize thyroid hormone levels. The patient reported improved wellbeing. TSHom is a rare cause of hyperthyroidism, accounting for less than 1% of cases. Clinical presentation may include a diffuse goiter, visual deficits, headache, and deficiencies in the other pituitary axes. The definitive treatment is transsphenoidal surgery, often preceded by somatostatin analogs to restore euthyroidism. Long-term antithyroid therapy is not recommended due to the risk of tumor growth. Post-surgery cure is assessed by symptoms resolution and normalized thyroid function. Somatostatin analogs are used before surgery to restore euthyroidism and may reduce tumor size. Side effects include nausea, abdominal discomfort, and glucose intolerance. Most patients with microadenomas (≤ 10 mm) are typically cured. However, about half of patients with macroadenomas will require additional treatment for residual disease. In this case, treatment with Octreotide was effective, leading to normalized thyroid hormones after 10 months, and the patient underwent surgery after 16 months. The pre-surgical MRI showed a reduction in tumor size, and the patient clinically improved. After the surgery, the patient developed central hypothyroidism but has a well-functioning pituitary gland otherwise. In Long-term octreotide therapy was free of side effects and successfully reduced tumor size before surgery. The question is therefore whether long-term pre-operative treatment with octreotide can improve prognosis and reduce the risk of residual disease.

HYPOTHALAMIC-PITUITARY-THYROID AXIS

1112350 - THYROTROPINOMA: A CHALLENGE IN THE DIFFERENTIAL DIAGNOSIS OF HYPERTHYROIDISM

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Case Presentation: A 26-year-old man consulted an endocrinologist due to recently diagnosed diabetes mellitus in the “honeymoon phase.” Complementary laboratory investigations revealed thyroid function abnormalities: free T4 of 2.86 ng/dL (reference range 0.91.7), TSH of 7.0 μ IU/mL (reference range 0.345.33), and total T4 of 13.1 ng/dL (reference range 612), all confirmed upon repetition. The patient denied clinical symptoms of thyrotoxicosis. Magnetic resonance imaging (MRI) of the pituitary gland showed a hypointense nodular lesion measuring 25 x 22 x 19 mm (width x height x depth) occupying the entire sella turcica, with compression of the optic chiasm and deviation of the pituitary stalk. An alpha-subunit level of 5.490 ng/L (reference range 120790) confirmed the diagnosis of thyrotropinoma. The others pituitary hormone levels were normal. Based on these findings, the patient underwent pituitary resection. **Discussion:** TSH-secreting pituitary adenomas are a rare cause of hyperthyroidism, accounting for 0.53% of all functional pituitary tumors. Most patients present with typical hyperthyroidism or symptoms due to tumor compression, but the presentation may be mild or even absent, as in our patient. The diagnosis should be suspected in patients with elevated thyroid hormone levels and non-suppressed TSH. The subsequent finding of a pituitary macroadenoma on MRI strongly suggests a TSH-secreting tumor, which can also be differentiated from thyroid hormone resistance by the elevated alpha-subunit levels seen in thyrotropinomas. Definitive treatment involves transsphenoidal resection. Approximately half of patients with macroadenomas will require additional pharmacological therapy with somatostatin analogs for residual disease. **Final Remarks:** In the presence of elevated thyroid hormones associated with non-suppressed TSH levels, the possibility of thyrotropinoma should be considered. The diagnosis is challenging, particularly in asymptomatic cases, and failure to diagnose can lead to severe consequences. Once the disease is confirmed, surgical treatment is the definitive therapy.

HYPOTHYROIDISM

1112245 - A CASE OF ANAPHYLAXIS TO LEVOTHYROXINE, DESENSITIZATION WITH OMALIZUMAB AND LONG TERM MONOTHERAPY WITH LIOTHYRONINE

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Case Presentation: 29 year old female with history of asthma and allergic rhinitis, developed Graves' disease in 2019. Due to a cutaneous allergic reaction to thionamides, a total thyroidectomy was performed 6 month later. After starting levothyroxine (LT4) she suffered intermittent but serious allergic reactions, despite the use of multiple formulations and excipients. Because of her irregular adherence to LT4 therapy, she developed severe hypothyroidism (amenorrhea, TSH > 300 mUI/L, Free T4 0,07 ng/dL, and LDL 364 mg/dL). A desensitization trial with minimal doses of LT4 was attempted, but she presented a life-threatening anaphylactic crisis. One month later, we performed a desensitization trial with liothyronine (LT3), but pretreated her with subcutaneous Omalizumab 300 mg (Anti IgE monoclonal antibody), titrating LT3 dose up to 20ug bid, without adverse effects. She resumed regular menses, but hypothyroidism symptoms persisted, needing progressive dose adjustment, with favorable clinical response. 10 months later, using 40 ug tid, she had palpitations, TSH 9,5 mUI/L, and T3 2,3 ng/mL (reference value < 1,8). ECG-Holter discarded arrhythmias and LT3 dose was reduced to 40-20-20 ug. After 20 months of treatment, she is asymptomatic, without allergic symptoms and lost 4,4 kg. Her labs show: TSH 2,01 mUI/L, T3 2,02 ng/mL, Free T4 0,25 ng/dL, sex hormone binding globulin 57 nmol/L (14-94), and LDL 103 mg/dL. A Dual X ray absorptiometry is within normal range. **Discussion:** This case shows the exceptional and complex scenario of LT4 anaphylaxis refractory to usual desensitization protocols, with favorable response to omalizumab and LT3 monotherapy. Long term LT3 treatment requires careful dose adjustment guided by clinical elements, hormone levels and indirect thyroid function parameters, and permanent assessment of LT3 under and overdose. **Final Comments:** Omalizumab and LT3 therapy is a safe and effective alternative in severe anaphylaxis to LT4. LT3 monotherapy can be safely used in long term when LT4 therapy is not an option.

HYPOTHYROIDISM

1112463 - A NATIONAL RANDOMIZED PLACEBO-CONTROLLED DOUBLE-BLIND MULTICENTER TRIAL OF LT4/LT3 COMBINATION THERAPY IN PATIENTS WITH AUTOIMMUNE HYPOTHYROIDISM: T3-4-HYPO TRIAL

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Despite normalized serum thyroid hormone levels, 10% of hypothyroid patients treated with levothyroxine (LT4) have persistent complaints, of which tiredness is the most commonly reported. This could be explained by the fact that the physiological T4/T3 ratio is not achieved with LT4 monotherapy. Studies have reported contradicting results as to whether the addition of liothyronine (LT3) is effective in relieving these persistent complaints. However, all of these studies suffer from one or more important limitations (e.g., patient selection, limited sample size, supraphysiological LT3 dose, limited follow-up time, non-validated questionnaires), hampering their interpretation. The T3-4-Hypo trial is a national, randomised, placebo-controlled, double-blind, multi-centre study in patients with auto-immune hypothyroidism and persistent complaints despite LT4 monotherapy. Patients are randomized to either LT4/LT3 combination therapy or LT4/placebo, and the primary endpoint is the ThyPRO tiredness subscale score at 52 weeks follow-up. In case of an effect, we will investigate whether effect sizes are higher in patients with genetic variations in a thyroid hormone converting enzyme (DIO2) and transporter (MCT10). Secondary analyses include effects on the most important thyroid hormone target organs including cardiovascular, metabolic, bone and neurocognitive outcomes. The first patient was enrolled in October 2022. The trial is still open for enrolment.

HYPOTHYROIDISM

1112505 - ASSESSMENT OF LEVOTHYROXINE REPLACEMENT DOSAGES IN PATIENTS WITH HYPOTHYROIDISM UNDERGOING BARIATRIC SURGERY

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Introduction: Insulin and leptin resistance, which occurs in obesity, mediate TRH hypothalamic regulation. Elevated levels of TSH can be observed in obesity. Bariatric surgery (BS) is effective in improving thyroid metabolism in patients with hypothyroidism; however, after surgery, the reduction in levothyroxine (LT4) dosages per kilogram of body weight remains unclear. **Objective:** To evaluate LT4 replacement dosages in patients with hypothyroidism before and after bariatric surgery. **Methods:** An observational, retrospective study was conducted with 46 hypothyroid patients who underwent BS at two Public Healthcare Brazilian centers. LT4 dosage per kilogram (LT4/kg) and total LT4 doses were analyzed before surgery and at 1-, 3-, 6-, and 12-months post-surgery. These dosages were adjusted according to TSH levels to achieve euthyroidism. **Results:** Forty-five out of 46 patients were female. The mean age was 47 ± 8.8 years. Forty patients underwent Roux-en-Y gastric bypass and six sleeve gastrectomies. The preoperative body mass index (BMI) was 45.23 kg/m^2 (IQR 42.12-49.19), and 30 kg/m^2 (IQR 26.62-35.29) one year after surgery. The median total LT4 dosage was 100 (IQR 68.5-150), 100 (IQR 68.5-150), 100 (IQR 68.5-131.3), 100 (IQR 68.5-125), and 81.5 (IQR 50-125) mcg at baseline, 1, 3, 6, and 12 months, respectively, with no statistical difference between baseline and post-surgery evaluations. The median LT4/kg was 0.79 (IQR 0.53-1.15), 0.89 (IQR 0.58-1.29), 1.03 (IQR 0.66-1.44), 1.09 (IQR 0.77-1.47), and 1.15 (IQR 0.79-1.50) mcg/kg at baseline, 1, 3, 6, and 12 months, respectively, with a statistically significant difference between all post-surgery evaluations compared to baseline ($p < 0.05$). **Conclusions:** LT4/kg doses progressively increased after BS, indicating higher dosages of LT4 relative to body weight, while total LT4 dosages did not change during the first year post-surgery. Our study suggests a possible role in impairing LT4 absorption after BS.

HYPOTHYROIDISM

1112334 - ASSESSMENT OF LIPOPROTEIN METABOLISM IN SUBCLINICAL HYPOTHYROIDISM

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Introduction: The association between subclinical hypothyroidism (SH) and cardiovascular risk factors remains controversial. Therefore, evaluating the status of novel biomarkers involved in lipoprotein metabolism, including those responsible for HDL antiatherogenic properties, is essential. Among these functions, HDL antioxidant activity is highly relevant. Moreover, the activities of lecithin:cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein (CETP), lipoprotein-associated phospholipase A2 (Lp-PLA2), and paraoxonase 1 (PON1) are crucial contributors. This study aims to evaluate these lipoprotein-associated enzymes and lipid transfer proteins in adult women with SH and 12 healthy controls were included. Anthropometric data were registered. Levels of thyroid-stimulating hormone (TSH) and free thyroxine (fT4), lipid profile, and high-sensitivity C reactive protein (hsCRP) were measured using standardized methods. LCAT and CETP activities were determined by employing developed radiometric methods. Lp-PLA2 and PON1 activities (PON and ARE) were assessed using colorimetric methods, and HDL antioxidant activity (AA) using an in-house fluorometric method. **Results:** Age and body mass index were similar in both groups. Patients with SH, in addition to higher TSH levels [6.81 ($6.097.98$) vs. 1.82 ($1.552.20$) $\mu\text{IU/mL}$; $p < 0.01$], presented higher triglyceride levels ($p < 0.05$), CETP activity ($p < 0.05$) and hsCRP ($p < 0.05$). Both groups had similar LCAT, Lp-PLA2, PON activities, and HDL AA. Positive associations of PON activity with HDL-C ($r = 0.40$; $p < 0.05$), apo A-I ($r = 0.56$; $p < 0.05$) and fT4 ($r = 0.46$; $p < 0.05$) were observed, as well as of HDL AA with ARE ($r = 0.54$; $p < 0.05$) and HDL-C ($r = 0.52$; $p < 0.05$). CETP activity correlated with LDL-C ($r = 0.51$; $p < 0.05$) and lipoprotein(a) ($r = 0.59$; $p < 0.01$). Triglycerides were associated with TSH ($r = 0.39$; $p < 0.05$). **Conclusions:** Patients with SH exhibited an altered lipid profile, consistent with increased CETP activity, a key factor in lipoprotein remodeling. Our findings emphasize the importance of close monitoring of SH patients to identify the need for early intervention.

HYPOTHYROIDISM

1114213 - ASSOCIATION OF HYPOTHYROIDISM WITH ADVERSE OUTCOMES IN PATIENTS UNDERGOING BARIATRIC SURGERY: A RETROSPECTIVE STUDY USING TRINETX

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Introduction: Hypothyroidism negatively affects cardiovascular and bone health. While bariatric surgery is an effective intervention for reducing obesity-related risks, its impact on patients with preexisting hypothyroidism remains uncertain. **Objective:** To evaluate the impact of overt hypothyroidism on adverse health outcomes following bariatric surgery. **Methods:** A real-time search and analysis of the Global Collaborative Network database (160,177,684 patients, 141 HCO) on TriNetX was conducted in February 2025. We included adults (≥ 18 years) with a BMI ≥ 35 kg/m² who underwent bariatric surgery, with and without overt hypothyroidism. Propensity score matching (1:1) was applied using age, sex, race, and diagnosis of type 2 diabetes, hypertension, dyslipidemia, and chronic kidney disease. The short-term outcomes comprised mortality, readmission, ICU admission, and surgical and systemic complications. The long-term outcomes included mortality, major adverse events, bone health, and metabolic, endocrine, renal, and neurological outcomes. Risk (RR) and hazard (HR) ratios were calculated using the built-in analytical tools in the TriNetX platform. **Results:** After matching, there were 5,700 patients in each cohort (47 ± 12 years, 88% female). In the short term, hypothyroidism was associated with higher risks of readmission (RR, 1.25; CI95%, 1.14-1.36), incisional hernia (RR, 1.56; CI95%, 1.12-2.18), and biliary diseases (RR, 1.39; CI95%, 1.05-1.86). In the long term, patients with hypothyroidism were associated with a higher risk of incident cerebrovascular events (HR, 1.25; 95%CI, 1.00-1.55), diabetes (HR, 1.39; 95%CI, 1.12-1.74), and dyslipidemia (HR, 1.20; 95%CI, 1.02-1.42). They also had a higher risk of falls (HR, 1.20; 95%CI, 1.02-1.40), osteoporosis (HR, 1.30; 95%CI, 1.07-1.58), polyneuropathy (HR, 1.34; 95%CI, 1.08-1.66), hypoglycemia (HR, 1.51; 95%CI, 1.23-1.87), as well as iron (HR, 1.17; 95%CI, 1.04-1.31) and vitamin B (HR, 1.34; 95%CI, 1.20-1.49) deficiencies. **Conclusion:** Preexisting hypothyroidism in bariatric patients increases the risks of readmission and short and long-term adverse outcomes. The findings highlight the importance of careful preoperative assessment and postoperative monitoring for bariatric patients with hypothyroidism.

HYPOTHYROIDISM

1114081 - BODY FLUID COMPOSITION AND MYXEDEMA IN BOTH HYPOTHYROIDISM AND HYPERTHYROIDISM: AN EXAMPLE OF HORMETIC REGULATION BY THYROID HORMONES

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Introduction: The occurrence of extracellular water retention and myxedema are well-recognized clinical features of overt hypothyroidism. Myxedema was also reported in hyperthyroidism as early as 1965. The exact pathogenic mechanism of myxedema occurring in thyroid disorders is not fully clear yet and the reason why it can be observed in both hypothyroidism and hyperthyroidism is not known either. **Objective:** Aim of our study was to analyze the characteristics of myxedema in both hyperthyroidism and hypothyroidism by means of a single-frequency bioelectrical impedance analysis (BIA). **Methods:** A total of 103 patients affected by various thyroid dysfunctions, including 57 euthyroid, 21 hyperthyroid (4 with overt hyperthyroidism and 17 with subclinical hyperthyroidism) and 25 hypothyroid (12 with subclinical hypothyroidism, 7 with overt hypothyroidism, and 6 with severe hypothyroidism) were enrolled. The results have been analyzed by means of the GraphPad Prism software. **Results:** Many of the BIA parameters related to fluid balance show a peculiar behavior, with medium values that appear to be similarly altered in the two opposite conditions of overt hyperthyroidism and severe hypothyroidism. In particular, reactance (Xc) and phase angle (PhA) were reduced, while hydration, measured as Total Body Water/Free Fat Mass (TBW/FFM), and the sodium/potassium exchangeable ratio (NAe:Ke) were increased when compared to euthyroid condition. The visualization of the bar graphs of the medium values of these parameters indicates the occurrence of a non-linear relationship between BIA parameters, especially those related to body fluid compartments, and the thyroid functional status. They appear to be better represented as U-shaped or inverted U-shaped (bell-shaped) curves. **Conclusion:** In conclusion, BIA represents a very low-cost and easy-to-apply method, useful to analyze and monitor body fluid composition and distribution in overt and severe thyroid dysfunctions. The occurrence of myxedema in both hyperthyroidism and hypothyroidism represents an example of hormetic response to thyroid hormone action.

HYPOTHYROIDISM

1112217 - ENTERAL LIOTHYRONINE AS A RESCUE THERAPY IN MYXEDEMA COMA

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Case Presentation: A 45-year-old male arrived at the emergency department of our hospital with symptoms of dyspnoea and altered consciousness. With no known history of hypothyroidism, myxedema coma was suspected due to bradycardia (48 bpm) and hypothermia (34.5 °C). Laboratory results revealed a TSH level greater than 49 µIU/mL, undetectable T4L, and ATPO > 999 U. Treatment with intravenous hydrocortisone 100 mg and LT4 400 µg daily for 48 hours was initiated. As there was no clinical improvement by the third day, it was decided to administer 10 µg LT3 every 8 hours via nasogastric tube, in combination with 200 µg intravenous LT4. After 24 hours of combined treatment, heart rate and body temperature normalized, and the patient regained consciousness after 72 hours. The LT3 dose was gradually reduced and discontinued upon discharge, three weeks after admission.

Discussion: Treatment recommendations for myxedema coma typically involve the administration of high doses of hydrocortisone and intravenous LT4, with the need for intravenous LT3 being debated. There are few reports on the use of LT3 via enteral route through nasogastric tube in these cases. Given the unavailability of intravenous LT3 formulation in our region and the lack of clinical improvement, we opted for its administration with a favorable response. **Final Comments:** Conducting randomized clinical trials for managing myxoedema coma is challenging due to the condition's rarity. Therefore, case reports and series are essential for determining effective strategies. Considering that intravenous LT3 may not be available in other countries, our experience using the enteral route may be valuable for clinicians treating patients unresponsive to standard intravenous LT4 therapy, both in terms of dosage and timing of combined therapy initiation.

HYPOTHYROIDISM

1112366 - HYPOTHYROIDISM AND LACTOSE INTOLERANCE: THE INFLUENCE OF LACTOSE ON THYROID DISEASE MANAGEMENT

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Introduction: Hypothyroidism is a common endocrine disorder and typically treated with levothyroxine (LT4), a synthetic form of the hormone. Effective absorption is crucial for treatment success and is influenced by gastrointestinal conditions. Lactose intolerant patients (LI) seems to require higher levothyroxine doses and the dose be influenced by lactose-restricted diet. There is limited data that assesses lactose in levothyroxine formulation, and it is unclear if lactose containing levothyroxine tablets are related to higher levothyroxine requirement. **Objective:** This study compares the levothyroxine dose and thyroid function in well treated patients with hypothyroidism depending on presence of lactose intolerance and the influence of lactose-restricted diet. **Methods:** This is a crossover study. Patients received levothyroxine formulations, both with and without lactose, for at least 6 weeks. Unrelated gastrointestinal disorders were excluded. Thyroid stimulant hormone (TSH) and free thyroxin (fT4) were measured in each intervention. Levothyroxine requirement was evaluated in mcg/kg of body weight, and lactose intolerance was detected by glucose curve test. **Results:** as a preliminary result, 74 patients with hypothyroidism were enrolled, of those, 93% were female with age range from 21 to 79 years. 32 of them were diagnosed with LI. Lt4 was adjusted after switching from lactose free tablet to lactose tablet in 17 patients; 10 of them had LI but this variation was not significant (p 0.819). No significant difference in both TSH and fT4 were observed in shifting LT4 to lactose containing tablets in patients with LI (TSH 2.21 vs 1.71, p 0.247 and fT4 1.15 vs 1.10, p 0.631). No difference was observed in Lt4 dose as well (mean 1.09 mcg/kg vs 1.15, p 0.819). Lactose-free diet did not change either thyroid function or Lt4 dose in patients with LI. **Conclusion:** presence of LI does not cause a clinically significant variation in thyroid function or levothyroxine demand.

HYPOTHYROIDISM

1112189 - HYPOTHYROIDISM OF COMMON ETIOLOGIES WITH UNCOMMON PRESENTATION

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Case Presentation: 30 years old female who delivered a baby 4 months ago was referred to Endocrine Clinic for painless anterior neck swelling for 1 month. There was no preceding respiratory tract infection. She denied hyper or hypothyroid symptoms and any change in her eyes to suggest thyroid eye disease. She was not on any long term medication or supplement. She didn't smoke or consume alcohol. There was no family history of any thyroid disease. On examination, she had BMI of 22.1 kg/m², blood pressure of 121/68 mmHg and pulse rate of 78 beats/minute. There was a non-tender and diffusely enlarged goiter. Signs of thyroid eye disease and other specific signs of hyper- or hypothyroidism were absent. Examinations of her lung, abdomen, cardiovascular system and neurological system were unremarkable. Biochemical investigations showed FT4 7.8 pmol/L (8-16) and TSH 15.64 mIU/L (0.45-4.50), consistent with hypothyroidism, and mildly elevated Anti-TPO Ab 103 IU/mL (0-50). Interestingly, ultrasound reported a diffusely enlarged thyroid gland with thyroid inferno on color Doppler suggestive of hyperthyroid Graves disease. However, her TRAb was normal 0.6 IU/L (0-1.0). Diagnosis of postpartum thyroiditis was made instead of hyperthyroid Graves disease in view of hypothyroidism and negative TRAb. At 2-months follow-up, her thyroid function normalized with FT4 13 pmol/L and TSH 2.29 mIU/L. At 6 months, her thyroid function test confirmed recurrent hypothyroidism with FT4 6.6 pmol/L and TSH 24.20 mIU/L. Anti-TPO Ab was elevated to 323 IU/mL, confirming the diagnosis of Hashimoto's thyroiditis. She was started on thyroxine. **Discussion:** Although patient in acute phase of postpartum thyroiditis, a form of subacute thyroiditis, has hypovascular gland on color Doppler ultrasound, increased vascularity has been reported in the recovery phase. **Final Comments:** Periodic thyroid function testing is recommended following recovery from postpartum thyroiditis due to high lifetime risk of developing permanent hypothyroidism.

HYPOTHYROIDISM

1114322 - HYPOTHYROIDISM TREATMENT WITH LEVOTHYROXINE INCREASES THE RISK OF DEMENTIA AND MORTALITY COMPARED WITH INCLUDING LIOTHYRONINE: A RETROSPECTIVE COHORT AND META-ANALYSIS

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Introduction: Hypothyroidism increases the risk of dementia and mortality. Yet, levothyroxine (LT4) monotherapy may not reduce those risks, even in adherent patients with normal thyroid-stimulating hormone (TSH) levels. Combination therapy including liothyronine (LT3) might show promising benefits. **Objective:** To assess the risk of dementia and mortality associated with hypothyroidism treated with LT4 alone compared with adding therapies containing LT3. **Methods:** A retrospective cohort study using electronic health records from TriNetX compared 1,247,508 hypothyroid patients on replacement therapy (LT4 monotherapy vs LT4 with LT3/desiccated thyroid extract) with 3,322,088 euthyroid controls. Outcomes included dementia (all causes, vascular etiology, and Alzheimer's) and mortality over 20 years. Endpoints were analyzed by propensity score matching and Cox proportional hazards models. Additionally, we performed a meta-analysis of observational studies to evaluate dementia risk associated with hypothyroidism treatment (LT4 alone vs LT4 with LT3). **Results:** Our cohort showed that patients with hypothyroidism were associated with an increased risk of dementia (HR 1.16; 95% CI 1.14-1.18) and mortality (HR 1.91; 95% CI 1.89-1.94) compared with euthyroid controls. Compared with LT4 + LT3/ desiccated thyroid extract, LT4 monotherapy was associated with a higher risk of dementia (HR 1.16; 95% CI 1.08-1.25) and mortality (HR 1.25; 95% CI 1.20-1.31). The meta-analysis, including 12 studies (seven cohorts and five case-controls), showed consistent results, with a significant association between hypothyroidism treatment and increased dementia risk (RR 1.41; 95% CI 1.35-1.47). **Conclusion:** LT4 monotherapy in patients with hypothyroidism is associated with an increase in the risk of dementia and mortality compared with therapies including LT3. This finding is supported by both retrospective cohort and meta-analysis. These results highlight the potential benefit in cognition and mortality of incorporating LT3 into hypothyroidism standard care.

HYPOTHYROIDISM

1114330 - LEVOTHYROXINE INCREASES THE RISK OF CARDIOVASCULAR, METABOLIC, AND RENAL POOR OUTCOMES COMPARED WITH INCLUDING LIOTHYRONINE: A RETROSPECTIVE COHORT STUDY

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Introduction: Patients with hypothyroidism on adherent levothyroxine (LT4) monotherapy with normal levels of thyroid-stimulating hormone (TSH) are associated with poor cardiovascular, metabolic, and renal outcomes compared with healthy controls. The impact of adding liothyronine (LT3) to therapy warrants investigation. **Objective:** To compare the long-term cardiovascular, metabolic, renal, and mortality outcomes in hypothyroid patients treated with LT4 alone versus combination therapy containing LT3. **Methods:** Electronic health records from TriNetX Global Network were analyzed in this retrospective cohort study, involving 1,022,193 patients on LT4 monotherapy and 61,171 patients receiving LT3-containing therapies (LT4 with LT3/desiccated thyroid extract). Propensity score matching was used to balance baseline characteristics. Outcomes assessed included type 2 diabetes, obesity, cardiovascular events, renal disease, major adverse kidney events (MAKE), intensive care admissions, and mortality using Cox proportional hazards models. **Results:** Compared with combination therapy with LT3, LT4 monotherapy showed an association with an elevated risk of type 2 diabetes (HR 1.41; 95% CI 1.34-1.48), obesity (HR 1.17; 95% CI 1.13-1.21), cardiovascular events (HR 1.14; 95% CI 1.09-1.19), acute kidney failure (HR 1.32; 95% CI 1.26-1.38), chronic kidney disease (HR 1.28; 95% CI 1.23-1.34), MAKE (HR 1.33; 95% CI 1.18-1.51), mortality (HR 1.30; 95% CI 1.24-1.37), and intensive care admissions (HR 1.29; 95% CI 1.22-1.35). **Conclusion:** Incorporating LT3 into hypothyroidism treatment might reduce the risk of cardiovascular, metabolic, and renal poor endpoints compared with LT4 monotherapy. Therefore, suggesting clinical advantages for patients receiving combination therapy.

HYPOTHYROIDISM

1114315 - MITOCHONDRIAL DYNAMICS AND MITOPHAGY MAY BE DISRUPTED IN THE TESTIS OF HYPOTHYROID RATS

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Introduction: Thyroid hormones play an essential role in testicular development and function, and reproductive dysfunction is commonly observed in hypothyroidism. Mitochondria are vital for male reproduction, as they play a key role for testosterone biosynthesis and spermatogenesis in the testis. Mitochondria continuously undergoes fusion and fission processes that can alter their morphology and function, a homeostatic mechanism known as mitochondrial dynamics. An imbalance in mitochondrial dynamics has been associated with multiple pathological conditions. However, the impact of hypothyroidism in mitochondrial dynamics in the testis remains unknown. **Objective:** Analyze mitochondrial dynamics and mitophagy in the testis of hypothyroid rats. **Methods:** Male Wistar rats (n=18) were divided into two groups: euthyroid and hypothyroid. Hypothyroidism was induced with methimazole (0.03%) diluted in drinking water, for 3 weeks. Testis were frozen at -80 °C for analysis. mRNA expression were analyzed by qPCR. All protocols were approved by CEUA/UFF #2488110221. **Results:** Analysis of mitochondrial fission genes revealed a significant decrease in Fis1 expression (p=0.0086), while Mff and Dnm1l showed no statistically significant differences. Regarding fusion-related genes, Mfn1 (p=0.0009) and Mfn2 (p=0.0055) exhibited reduced expression, whereas Opa1 showed no significant changes. In the mitophagy pathway, hypothyroidism led to decreased expression of Bnip3l (p<0.0001) and Bnip3 (p=0.0018), while Park2 and Fundc1 remained unchanged. For the autophagy pathway, all analyzed genes showed reduced expression, including Map1lc3b (p=0.0014), Becn1 (p=0.0224), Atg7 (p=0.0106), and Lamp2 (p=0.0398). Finally, concerning mitochondrial biogenesis, Ppargc1a expression was significantly reduced (p=0.0005), while Tfam levels remained unchanged (p=0.3100). **Conclusion:** The data suggest a decline in both mitochondrial fission and fusion processes. The downregulation of all investigated autophagy-related genes, along with reduced expression of Bnip3 and Bnip3l, may indicate impaired mitophagy.

HYPOTHYROIDISM

1112654 - PREDICTORS OF RADIATION-INDUCED HYPOTHYROIDISM IN NASOPHARYNGEAL CARCINOMA PATIENTS FOLLOWING INTENSITY-MODULATED RADIOTHERAPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Intensity-modulated radiotherapy (IMRT) is a widely used treatment for patients with nasopharyngeal carcinoma (NPC), valued for its precision in targeting tumors while protecting nearby healthy tissues. Despite its benefits, IMRT can sometimes cause unwanted side effects, such as hypothyroidism, which can deeply affect the patients well-being. **Objective:** Investigate predictors of hypothyroidism in NPC patients treated with IMRT, focusing on the correlation between thyroid dose parameters, such as V40, V50, and V60, and the risk of developing the condition. **Methods:** This study conducted a systematic review and meta-analysis to evaluate whether dose-volume parameters could reliably predict hypothyroidism in NPC patients treated with IMRT. Data were extracted from retrospective studies, as well as non-randomized and randomized controlled trials, identified through searches of the PubMed, Embase, and Cochrane databases. Statistical analyses were conducted using RevMan 5.4 software. **Results:** We analyzed 6 studies investigating the risk of radiation-induced hypothyroidism in NPC patients. The pooled hazard ratios for V40, V50, and V60 were similar, ranging from 1.02 to 1.04, suggesting no significant differences in risk across these dose levels. The results for V40 (95% CI: 1.021.06; $p < 0.00001$; figure 1A; $I^2=90\%$), V50 (95% CI: 1.011.03; $p < 0.00001$; figure 1B; $I^2=98\%$), and V60 (95% CI: 1.001.03; $p=0.01$; figure 1C; $I^2=26\%$) indicate that radiation exposure at these levels carries a comparable risk for developing hypothyroidism. **Conclusion:** Our findings indicate that V40, V50, and V60 are comparable predictors of radiation-induced hypothyroidism, showing an equivalent level of risk across these dose levels. However, the small differences in HRs and the significant variability among studies make the results inconclusive. To gain a clearer understanding, larger and more comprehensive studies are needed.

HYPOTHYROIDISM

1113927 - PREVALENCE OF HYPOTHYROIDISM IN PATIENTS WITH OBESITY TREATED BY HOSPITALIZATION

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Introduction: Thyroid dysfunction alters body metabolism and can lead to weight gain. **Objective:** This study aims to describe the prevalence of hypothyroidism and the anthropometric characteristics of patients with obesity treated by hospitalization. **Methods:** Retrospective, descriptive study with data collection from 1026 patients, admitted between 2016 and 2022, to a hospital unit for obesity treatment with hypocaloric diets (500-1000 Kcal/day) and multidisciplinary support. Anthropometric and laboratory data of thyroid profile were obtained at the time of admission. Continuous variables were compared using the t-test for independent samples and categorical variables were analyzed with Pearson's chi-square test. This study was approved by the Research Ethics Committee, opinion no.: 6,071,858. **Results:** The majority were female (68.4%) and the mean length of hospital stay was 118 ± 47 days. Women were significantly older than men (47.2 ± 16.6 years vs. 42.53 ± 16.81 years; $p < 0.001$). Men had a higher Body Mass Index (44.01 ± 6.18 kg/m² vs. 42.61 ± 5.19 kg/m²; $p < 0.001$) and waist circumference (126.08 ± 59.06 cm vs. 112.84 ± 10.76 cm, $p < 0.001$). Hypothyroidism was diagnosed in 160 patients (15.6%), being more present in women than in men [141 (88.1%) vs. 19 (11.9%); $p < 0.001$]. **Conclusion:** In this study, there was a significant prevalence of hypothyroidism. The literature demonstrates an association between thyroid disorders and obesity, both as a contributing factor to weight gain and/or through obesity-related thyroid dysfunction (chronic inflammation, leptin resistance, and metabolic dysfunction). The higher prevalence of female individuals corresponds to the proportion observed for the normal population. In this sample of patients hospitalized for obesity treatment, a significant prevalence of this comorbidity was observed, whose association may be related both as a contributing mechanism and as a consequence of the pathophysiological process secondary to obesity.

HYPOTHYROIDISM

1112613 - REFRACTORY HYPOTHYROIDISM: CHALLENGES IN MANAGEMENT AND THERAPEUTIC STRATEGIES

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Case Presentation: A 41-year-old female with a history of Graves Disease and total thyroidectomy 5 years ago, presented with refractory hypothyroidism. Despite escalating doses of levothyroxine (up to 1500 mcg/day), her condition remained unresponsive, leading to multiple hospital admissions in unsuccessful attempts to stabilize her thyroid hormone levels. She presented TSH levels between 50-100 UI/mL (RV = 0.45 - 4.5), with low free T4 (fT4) (no higher than 0.5 ng/dL, RV = 0.93-1.70 ng/dL). A levothyroxine absorption test demonstrated an absorption rate of 1.47%. She was evaluated by the Gastroenterology team, which performed a thorough assessment, ruling out malabsorptive syndrome. For the past 2 years, various alternative methods of levothyroxine administration suppository, oral solution, sublingual, transdermal, patch, and vaginal formulations have been tested, but none have proven successful. Since the past year, she has been hospitalized several times to receive levothyroxine enemas, starting at a dose of 500 mcg per enema and increasing to 1,500 mcg. Initially, she demonstrated good clinical and laboratory response. However, after each admission, higher doses were required to achieve minimal improvement in her serum fT4 and in symptoms. LT4 enemas at doses of 10,000 mcg twice weekly are currently being administered with no significant improvement (fT4 levels = 0.3-0.5 ng/dL). **Discussion:** Some hypothyroid patients resist standard thyroid therapy and require high levothyroxine doses, often due to malabsorption syndrome. Since this was ruled out, we propose that this refractory case may stem from a specific channel disturbance, possibly autoimmune or genetic. Reports of isolated thyroxine malabsorption are rare and typically resolved with parenteral levothyroxine, a method unavailable in Brazil. **Final Comments:** This case highlights the challenges in managing refractory hypothyroidism when conventional and alternative therapies fail, emphasizing the need for innovative approaches and broader access to parenteral treatments.

HYPOTHYROIDISM

1114183 - SEX-SPECIFIC IMPAIRMENTS IN THYROID HORMONE AVAILABILITY AND ACTION IN A MURINE MODEL OF ALZHEIMER'S DISEASE

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Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder marked by cognitive decline. Thyroid hormones (TH), which regulate key genes involved in AD pathology, have been linked to the disease, with altered T3 and T4 levels observed in AD patients. However, the evidence remains inconsistent, and the peripheral and central levels of TH, as well as sex differences and underlying mechanisms, is unclear. **Objective:** To assess the levels of T3 and T4 in plasma, cortex, and hippocampus, and their metabolism and action in male and female 5XFAD mice, a model of AD. **Methods:** Thirty-two 7-month-old mice (16 5XFAD and 16 wild-type; WT), both sexes, were studied. T3 and T4 concentrations in plasma, cortex, and hippocampus were measured by radioimmunoassay. Additionally, RT-qPCR was used to analyze gene expression related to TH metabolism (Dio2, Dio3) and T3 action on Hairless (Hr), a T3-regulated gene. **Results:** 5XFAD mice weighed less than WT mice, with females of both genotypes being lighter than males. No significant differences in brain weight were observed. Male 5XFAD mice had lower plasma T3 and T4 levels compared to WT, while female 5XFAD mice did not show significant differences. Females also had higher T4 levels than males of the same genotype. In the cortex and hippocampus, TH levels were normal in 5XFAD mice. Dio2 mRNA levels were unchanged, while Dio3 mRNA was lower in the hippocampus of male 5XFAD mice. Hr expression was higher in the hippocampus of 5XFAD mice compared to WT. **Conclusion:** Sex-dependent alterations in TH availability and action were observed. Male 5XFAD mice exhibited peripheral hypothyroidism, likely compensated by reduced Dio3 activity to maintain elevated intracellular TH levels, which may lead to mild hyperthyroidism, as reflected by higher Hr levels in the hippocampus. The mechanisms behind these sex- and genotype-dependent differences require further investigation.

HYPOTHYROIDISM

1112404 - THYROXINE FAILS TO PROMOTE MUSCLE RECOVERY AFTER BARIUM CHLORIDE-INDUCED DAMAGE IN AGED MICE

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Introduction: Aging is associated with decreased muscle function, sarcopenia, and reduced thyroid hormone serum levels. In young subjects, thyroid hormones stimulate muscle growth and regeneration; however, their effect on muscle repair in older individuals remains unclear. **Objective:** Therefore, this study explores the impact of low-dose thyroxine (T4) replacement therapy on muscle regeneration in aged mice. **Methods:** Herein, we administered a low dose of T4 (7.5 ng/g BW) to 22- to 27-month-old male mice and analyzed tibialis anterior regeneration seven days after 1.2% barium chloride (BaCl₂)-induced injury. All animal experiments were approved by the Ethics Committee on Animal Use at the Federal University of Rio de Janeiro (CEUA-UFRJ- n° A16/23-025-20) and complied with the ARRIVE 2.0 guidelines. **Results:** Our findings indicate that aged skeletal muscle exhibits localized resistance to thyroid hormone, with no change in the expression of thyroid hormone positively regulated gene (Hr) in T4-treated muscle under regeneration. We also did not observe myogenesis-related gene changes in the T4-treated muscle. However, T4 reduced the cross-sectional area of injured tibialis anterior muscles, leading to a higher proportion of small-diameter fibers and increased laminin expression. These changes suggest atrophic effects and extracellular matrix remodeling, but not improved muscle regeneration. **Conclusion:** This study highlights that despite the role of thyroid hormones in muscle regeneration in younger animals, T4 therapy does not benefit muscle recovery in aged mice after injury. These findings alert clinical practice regarding thyroid hormone treatment in elderly patients with sarcopenia and subclinical hypothyroidism, particularly cautioning against T4 therapy after injury, as it may impair muscle regeneration and promote atrophy.

HYPOTHYROIDISM

1112346 - USE OF LT4+LT3 IN HYPOTHYROID PATIENTS: RESULTS OF AN INTERNATIONAL SURVEY AMONG THYROID EXPERTS

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Introduction: Evidence indicates nonsuperiority of combination treatment with levothyroxine (LT4) + liothyronine (LT3) compared with LT4 alone for hypothyroidism. **Objectives:** Surveys documenting the frequency of thyroid specialists LT4+LT3 use in hypothyroid patients. **Methods:** Data collected 2019-2022 by THESIS (Treatment of Hypothyroidism in Europe by Specialists; An International Survey), a large-scale survey of European, Australian and Latin American thyroid experts focused on the use of thyroid hormones for hypothyroid and non-hypothyroid indications. Eight questions explored respondent characteristics, and 23 the use of thyroid hormones. Here we report on use of LT4+LT3 in three different scenarios of hypothyroid patients, euthyroid on LT4: 1) recovering from protracted hypothyroidism; 2) complaining of symptoms suggestive of hypothyroidism 3) complaints of unexplained weight gain. **Results:** Of 18,543 endocrinologists invited, 5,863 (31.6%) valid responses were obtained (938 from Western Europe, 1,679 from Eastern Europe, 2,053 from Southern Europe, 713 from Northern Europe, 312 from Western Asia, 87 from Australia, 81 from Latin America). Between 29%-55% stated that LT4+LT3 combination treatment should never be used due to the low quality of evidence; 5%-27% would consider it for recovery from protracted hypothyroidism; 32%-61% for persistent symptoms of hypothyroidism; <5% for unexplained weight gain despite biochemical euthyroidism. LT4+LT3 was more frequently proposed by endocrinologists (vs non-endocrinologists) with a high-volume practice, working in countries with high gross national income per capita, and less frequently by males working in Western Europe (uni-multivariate analyses). Suggesting LT4+LT3 was significantly associated with respondents view that LT4 alone cannot restore normal physiology and inversely associated with the view that the patients unrealistic expectations condition persisting symptoms. **Conclusion:** Our survey indicates that LT4+LT3 combination treatment is particularly used in patients with persistent symptoms compatible with hypothyroidism, despite being euthyroid on LT4. This concerning finding not based on current evidence of LT4+LT3 treatment efficacy and should be addressed.

HYPOTHYROIDISM

1112665 - USE OF THYROID HORMONES IN BIOCHEMICALLY EUTHYROID PATIENTS WITH TREATMENT-RESISTANT DEPRESSION: ANALYSES OF DATA FROM THE THESIS SURVEY OF EUROPEAN SPECIALISTS

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Introduction: Treatment-resistant depression (TRD) is most commonly defined as depression that has not responded to two different pharmacological agents. There is lack of international consensus on the use of thyroid hormones (TH) for TRD and there is limited evidence for its use. **Objective:** To explore the views of European specialists regarding the use of TH in euthyroid patients with TRD. **Methods:** The question Thyroid hormones may be indicated in biochemically euthyroid patients with treatment-resistant depression was posed to specialists whose professional organisations were invited to partake in Treatment of Hypothyroidism in Europe by Specialists: An International Survey (THESIS). **Results:** We received 5,695 valid responses following 17,232 invitations (33% valid response rate, 65% women, 90% endocrinologists, 28 countries). Of these, 348 (6.1%) stated that TH may be indicated in biochemically euthyroid patients with TRD. This view was more common in males (7.3% vs. 5.5%, $p < 0.01$), specialists who saw ≥ 100 patients with hypothyroidism per year (7% vs 4.7%, $p < 0.01$), specialists who worked in private practice (7.1% vs 5.7%, $p = 0.05$) and specialists who were not members of professional societies (8.1% vs 6.1%, $p = 0.05$). Geographical variation existed amongst respondents who indicated use of TH in TRD (Eastern Europe 8.6%, Southern Europe 5.5%, Western Asia 5.4%, Northern Europe 5%, Western Europe 4.2%), with respondents in Eastern Europe significantly more likely to use TH in TRD compared to Western Europe ($p < 0.01$). Linear regression showed a significantly lower use of TH for TRD with increasing gross national income (F statistic = 7.35, CI -0.15 - -0.02, $p = 0.01$). **Conclusion:** Over 6% of specialists stated that they would consider TH in biochemically euthyroid patients with TRD, which is at odds with international recommendations. Further education and guidance may be helpful to avoid use of TH in inappropriate clinical scenarios.

HYPOTHYROIDISM

1114132 - USE OF THYROID SCINTIGRAPHY AS PART OF THE DIAGNOSTIC PROCESS IN CONGENITAL HYPOTHYROID

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Introduction: Congenital Hypothyroidism (CH) results from thyroid dysgenesis or dyshormonogenesis, leading to thyroid hormone deficiency identified by elevated TSH levels on newborn screening. TSH control is especially critical the first three years of life in optimizing growth and neurodevelopmental outcomes. In the U.S., the underlying cause is typically not pursued, with treatment based on serial thyroid hormone levels. Although thyroid scintigraphy (TS) is considered the gold standard for identifying the etiology of CH, its clinical benefit remains uncertain, especially given the cost and radiation exposure. The role of TS in influencing long-term outcomes, particularly TSH control, has not been clearly established. **Objective:** This study aims to assess whether TS at diagnosis affects the management and clinical outcomes, particularly TSH control, during the first three years of life in CH patients. **Methods:** We conducted a retrospective cohort study at Children's Hospital Los Angeles (1998-2017), comparing 40 infants with CH who underwent TS to 40 matched controls who did not. Data was collected on demographics, TSH and Free T4/Total T4 levels, levothyroxine dosing, and anthropometrics. The primary outcome was time-weighted TSH levels, and secondary outcomes included TSH normalization time, growth measurements, and follow-up compliance. **Results:** There were no significant differences between the two groups in time-weighted TSH levels, time to normalization of TSH, levothyroxine dosing, or anthropometric outcomes over the first three years. Additionally, follow-up compliance and the number of dose adjustments were similar across groups. **Conclusion:** This study suggests that TS at diagnosis does not significantly affect TSH control or clinical outcomes in the first three years of life in CH patients. Given its costs and radiation exposure, larger prospective studies are needed to better define the role of TS and its impact on clinical management and patient outcomes.

IODINE DEFICIENCY

1112548 - ASSESSMENT OF URINARY IODINE CONCENTRATION IN WOMEN OF CHILDBEARING AGE IN SIX BRAZILIAN STATES OF THE LONGITUDINAL ADULT HEALTH STUDY (ELSA-BRASIL)

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Introduction: Adequate iodine intake in women of reproductive age is essential for fetal development. Iodine deficiency during pregnancy can cause irreversible brain damage to the fetus, such as cretinism and intellectual and behavioral deficits. Pregnancy increases iodine needs by 50%, and universal salt iodization, although effective, does not cover all regions. Therefore, iodine supplementation in deficient areas is necessary. Public health policies must promote iodine supplementation to prevent deficiencies and ensure healthy fetal and newborn development. **Objective:** To analyze urinary iodine concentration in Brazilian women of reproductive age in the ELSA-Brasil study and correlate it with sociodemographic factors and thyroid status. **Methods:** The analysis included 321 women aged 35 to 44 years from six Brazilian capitals. Urinary iodine concentration (UIC) was measured, and thyroid status was assessed by serum TSH and free T4 (T4L) levels. **Results:** Among the 321 women, urinary iodine levels were classified into three categories: deficiency (<150 µg/L), normal (150-249 µg/L), and excess (>250 µg/L). The majority (42.3%) had iodine deficiency, 30.8% had excess iodine, and 26.9% had normal iodine levels. No significant correlation was found between iodine levels and thyroid function. **Conclusion:** The prevalence of both iodine deficiency and excess in women of reproductive age presents potential health risks. Iodine deficiency can cause thyroid dysfunction, fetal growth delay, and cognitive difficulties in children. Excess iodine may lead to hyperthyroidism, autoimmune diseases, and increased risk of spontaneous abortion. Maintaining adequate iodine levels is critical for women's health and pregnancy outcomes. Nutritional monitoring and iodine supplementation should be prioritized in public health policies to mitigate these risks.

IODINE DEFICIENCY

1114304 - IODINE DEFICIENCY DIRECTLY REGULATES THYROID GENE EXPRESSION AND SIGNALING PATHWAYS IN PCCL3 CELLS

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Introduction: Iodine is an essential micronutrient for thyroid hormone production and thyroid function. However, iodine deficiency (ID) continues to be a major public health concern, affecting millions of people worldwide. The molecular effects of ID involve alterations in the hypothalamic-pituitary-thyroid axis, leading to increased TSH levels and its stimulatory effect on the thyroid. However, the direct effects of iodine deficiency on gene expression and signaling pathways in the thyroid remain unexplored. **Objective:** To evaluate the molecular effects of severe iodine deficiency on thyroid cells using an in vitro model. **Methods:** Normal rat thyroid cells (PCCL3 cells) were cultured for seven days in a medium with either a physiological iodine concentration (10^{-8} M) or severe iodine deficiency (no iodine in the medium). The concentration of other nutrients and hormones remained the same across all experimental groups. Gene expression was analyzed by qPCR, and protein expression by Western Blotting. Signaling pathways were evaluated using specific antibodies for pERK and pAMPK. **Results:** Iodine deficiency increased the expression of thyroid differentiation markers, including Slc5a5, Tpo, Tg and Tshr. Interestingly, it also altered the gene expression of enzymes involved in epigenetic processes, such as DNA methylation (Dnmts), histone acetylation/deacetylation (Hat1, Hdac3), and histone methylation/demethylation (Kdm5c, Kdm6a, Ezh2). Finally, cells exposed to iodine-deficient conditions showed a reduction in pERK and pAMPK protein levels, which are involved in thyroid cell dedifferentiation processes. **Conclusion:** Our study provides, for the first time, evidence that iodine deficiency itself regulates gene and protein expression in thyroid cells, even in the absence of TSH level alterations. The data further suggests that epigenetic mechanisms may play a role in increasing the expression of differentiation-related genes. However, further studies are needed to explore the correlation between epigenetic enzyme alterations and thyroid differentiation gene expression changes.

IODINE DEFICIENCY

1114266 - IODINE DEFICIENCY DISORDERS IN THE STATE OF ESPÍRITO SANTO BETWEEN JANUARY 2014 AND DECEMBER 2024: AGE AND SEX DISTRIBUTION

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Introduction: Iodine is an essential micronutrient for thyroid hormones in view of growth and cellular metabolism. In the general population, especially in pregnant women and children, iodine deficiency can lead to serious physical (goiter and hypothyroidism) and cognitive consequences, therefore, prevention in vulnerable populations is essential to avoid irreversible damage. However, inadequate policies persist, directly affecting the health of vulnerable populations nationwide. **Objective:** To analyze hospitalizations due to iodine deficiency in the state of Espírito Santo (ES), from January 2014 to December 2024. **Methods:** Cross-sectional, descriptive, ecological and exploratory study, based on the database of the Department of Hospital Information of the Unified Health System (SIH/DATASUS) between January 2014 and December 2024. Hospitalizations registered with the ICD-10 corresponding to Iodine deficiency disorders were considered, covering Race, Character of Care, Age Group and Annual Distribution. **Results:** A total of 33,142.69 cases of iodine deficiency disorders were registered in ES between 2014 and 2024. The incidence increased in 2015 (+291.93%) and 2022 (+870.14%), possibly due to screening campaigns or changes in notification. Most cases occurred in the age groups of 40 to 49 years (33.29%) and 50 to 59 years (33.28%), with lower prevalence in children, adolescents and the elderly. Regarding the distribution by gender, there was a significant predominance of females, who accounted for 73.99% of the cases (24,520.90), while males accounted for 26.02%. **Conclusion:** Iodine deficiency has varied significantly in the last 10 years, with greater exposure in the age groups of 40 to 59 years, especially among women and blacks, indicating possible inequalities in access to health or late diagnosis. Iodine supplementation, population screening and health education are essential measures to reduce the impact of this deficiency.

IODINE DEFICIENCY

1114275 - IODINE DEFICIENCY-RELATED THYROID DISORDERS: AN EPIDEMIOLOGICAL ANALYSIS OF HOSPITAL ADMISSIONS IN BRAZIL, 2024

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Introduction: Thyroid disorders related to iodine deficiency remain a significant public health concern, especially in areas with inadequate iodine intake. Iodine is essential for the synthesis of thyroid hormones, and its deficiency can lead to goiter, hypothyroidism, and impaired physical and mental development, particularly in children. In Brazil, the National Iodine Supplementation Policy has contributed to reducing these disorders, although hospitalizations are still observed among vulnerable populations. **Objective:** To describe the epidemiological profile of hospital admissions due to iodine deficiency-related thyroid disorders (ICD-10: E01) in Brazil in 2024, according to sex, age group, and race/ethnicity. **Methods:** This was a descriptive study using data from the Brazilian Hospital Information System (SIH-SUS). All hospitalizations with ICD-10 code E01 in 2024 were included, across all age groups. Variables analyzed included sex, age group, and race/ethnicity. Pearson's chi-square test was used to assess the association between sex and hospitalizations, with a significance level of 5%. **Results:** A total of 53 hospital admissions were recorded for iodine deficiency-related thyroid disorders in 2024. There was a predominance of females (88.7%; n=47), with a statistically significant association ($\chi^2=31.5$; $p<0.001$). Regarding age, the highest frequencies occurred in the 40-49 age group (n=11), followed by 50-59 years (n=10) and infants under 1 year (n=10). As for race/ethnicity, most patients were identified as mixed-race (47.2%), followed by white (41.5%) and Black (9.4%). **Conclusion:** Iodine deficiency-related thyroid disorders primarily affect adult women and mixed-race individuals, with a notable number of cases already present in infancy. These findings highlight the importance of nutritional monitoring and early-life prevention strategies.

IODINE DEFICIENCY

1113673 - IODINE NUTRITIONAL STATUS IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Introduction: Polycystic Ovarian Syndrome (PCOS) and thyroid disease are highly prevalent endocrine disorders among women of reproductive age. Both conditions show overlapping features including oligomenorrhea, infertility, insulin resistance and dyslipidemia. Recent systematic reviews have demonstrated a higher incidence of both hypothyroidism in women with PCOS and PCOS in women with hypothyroidism. However, the precise interplay between PCOS and thyroid function remains unclear. **Objective:** Define the correlation between inadequate iodine nutritional status with altered thyroid metabolism in women with PCOS compared to control women of childbearing age. **Methods:** This study involved a prospective cohort of 34 women with PCOS (according to Rotterdam criteria) and 83 control women (age 18-44 y) of the Instituto de Medicina Reproductiva, Mendoza, Argentina. Urine iodine (UI) levels were measured using the Sandell-Kolthoff method. Thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels were measured by chemiluminescence immunoassay. **Results:** Compared to controls, women with PCOS exhibited significantly lower UI (mean $\pm$ SEM: 101.3 ± 5.65 vs. 130 ± 2.87 $\mu\text{g/L}$, $p < 0.0001$) and higher TSH levels (2.24 ± 0.16 vs. 1.79 ± 0.08 mIU/L, $p = 0.024$), while FT4 levels were comparable between groups (0.9694 ± 0.018 vs. 0.9477 ± 0.013 ng/dL, $p = 0.55$). A significant inverse correlation was observed between TSH and UI levels ($r = -0.18$, 95% CI: -0.3517 to -0.0003 , $p = 0.0498$). Iodine deficiency (UI levels below $100 \mu\text{g/L}$) was significantly higher in PCOS patients compared to controls (61.76% vs. 12.05% [RR, 5.13; 95% CI 2.752 to 9.691], $p < 0.0001$). **Conclusion:** Our findings demonstrate that women of childbearing age with PCOS are at increased risk of iodine deficiency, suggesting a link between PCOS and altered thyroid metabolism. This is particularly important in areas with iodine deficiency. Further studies are needed to elucidate the underlying mechanisms linking iodine deficiency to the pathophysiology of PCOS.

IODINE DEFICIENCY

1112559 - LONG-TERM EFFECTS OF IODINE DEFICIENCY OR EXCESS ON THE RISK OF DYSLIPIDEMIA AND GLUCOSE METABOLISM DISORDERS: AN ANALYSIS OF RECENT DATA FROM A 20-YEAR PROSPECTIVE COHORT

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Introduction: This study evaluates the impact of long-term iodine status abnormalities on dyslipidemia and glucose metabolism disorders over a 20-year follow-up. **Methods:** From 1999 to 2019, we followed residents from three regions in northern China with different iodine statuses (Panshan, Zhangwu, Huanghua). Participants ($n=3,761$) were stratified based on urinary iodine (UIC) at baseline and 20 years later into groups of iodine deficiency ($\text{UIC} < 100 \mu\text{g/L}$), adequate/more than adequate ($100 \leq \text{UIC} < 300 \mu\text{g/L}$), and iodine excess ($\text{UIC} > 300 \mu\text{g/L}$). After excluding participants with missing information, 630 participants were included in the UIC and dyslipidemia analysis dataset. Following the exclusion of participants with missing glucose metabolism data ($n=203$), 397 participants were included in the UIC and glucose metabolism disorders dataset. The chi-square test was used to compare disease prevalence, and logistic regression was performed to assess the effect of urinary iodine on disease risk. **Results:** Long-term iodine deficiency did not affect the prevalence or risk of dyslipidemia or glucose metabolism disorders. In participants with long-term iodine excess, the prevalence of hypertriglyceridemia, hypercholesterolemia, low HDL-C, and high LDL-C was 34.72%, 31.48%, 31.94%, and 30.09%. After adjusting for confounders, $\text{UIC} > 300 \mu\text{g/L}$ was associated with a reduced risk of hypertriglyceridemia (OR [95% CI] = 0.64 [$0.43-0.95$], $p = 0.027$) and low HDL-C (OR [95% CI] = 0.61 [$0.41-0.90$], $p = 0.014$) compared to UIC $100-300 \mu\text{g/L}$. The prevalence of impaired glucose tolerance was lower in those with iodine excess (6.63% vs. 11.36%, $p = 0.049$), and $\text{UIC} > 300 \mu\text{g/L}$ significantly reduced the risk of impaired glucose tolerance (OR [95% CI] = 0.38 [$0.15-0.87$], $p = 0.031$). **Conclusions:** Long-term iodine deficiency does not impact lipid or glucose metabolism. Iodine excess significantly reduces the risk of hypertriglyceridemia and impaired glucose tolerance, suggesting potential metabolic benefits from appropriate iodine intake.

IODINE DEFICIENCY

1112411 - MOTHERBABYIODINE PROJECT: AN AWARENESS CAMPAIGN WWW.MOTHERBABYIODINE.COM

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1 - Thyroid Federation International

Iodine is an element that plays an important role in the function of a healthy thyroid gland. It is used for the production of thyroid hormones needed to meet the metabolic requirements of the body. It is especially important before and during pregnancy and lactation to ensure the development of the baby's brain from conception until the first one thousand days of its life. Without iodine the growth of the child is slowed down and brain development cannot take place in the right way. Even mild iodine deficiency can lead to a lower IQ of 5-15 points. The MotherBabyIodine project is based on awareness to populations with IDD and is already present in various countries e.g. The Philippines, Indonesia, Bangladesh. One way of communicating awareness to those women in reproductive age is through simple and whimsical infographics, but with very clear messages. A Multi Stakeholder approach is essential to tackle iodine deficiency. Thyroid Federation International (TFI) leads the project and visualizes a coalition of cross-sectored, like-minded stakeholders who are involved in raising awareness to minimize iodine deficiency in women of reproductive age. It is envisioned to involve International Organizations, Industry (salt and food and feed), Medical Professionals (especially Endocrine, Obstetrical & Pediatric Societies, Patients Organizations), and Ministries of Health. The objective is to set a path via prominent project leaders to opinion leaders in order for them to spread the message not only through traditional instructional methods but more so by using social media and other means of communication. TFI joins in a coalition for the EU to find a harmonized policy for iodine fortification. The MBI project is an example of how TFI leads in a significant Awareness Campaign. Brochures/infographics have been created and distributed in several languages to promote the project in countries where IDD is ongoing.

IODINE DEFICIENCY

1112521 - THE EFFECT AND MECHANISM OF PRUNELLA VULGARIS L. ON AMELIORATING GOITER IN WISTAR RATS

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Introduction: Goiter, characterized by thyroid enlargement, is prevalent in regions with insufficient iodine intake. *Prunella vulgaris* L. (PV), a traditional Chinese herb with anti-inflammatory, antioxidant, antiproliferative, and antitumor properties, is frequently used to treat thyroid disorders in China. **Objective:** This study aims to assess the therapeutic efficacy of PV in treating goiter and to identify the specific pathways and target proteins regulated by PV using TMT-based quantitative proteomics. **Methods:** Seventy-two four-week-old SPF-grade Wistar rats (90-110 g) were fed with an iodine-deficient diet for 3 months to induce goiter. The rats were then randomly divided into five groups: model group, Levothyroxine Sodium group, low-dose PV group (PV-L), medium-dose PV group (PV-M), and high-dose PV group (PV-H). All rats resumed a normal diet and received daily gavage of their respective treatments, while the control group was given deionized water. Thyroid volume was measured every 4 weeks using the Visual Sonic Vevo3100 system. Key outcomes included thyroid volume, weight, function, histomorphology, transmission electron microscopy (TEM), and TMT-based proteomics. **Results:** After 16 weeks, the thyroid weight decreased significantly in all PV-treated groups, and the thyroid shrinkage rates in PV-M and PV-H groups were significantly higher compared to the model group at 12 and 16 weeks. Hematoxylin and eosin staining showed reduced inflammation in thyroid tissues of PV-treated rats. To further investigate the underlying mechanisms of PV in goiter recovery, TMT-based quantitative proteomics were conducted. KEGG pathway analysis indicated that differentially expressed proteins (DEPs) were enriched in pathways related to cell proliferation, angiogenesis, sodium-iodine transporter, and the Golgi apparatus. Western blotting confirmed the altered expression of these proteins. **Conclusion:** A certain amount of PV can ameliorate goiter to some extent in Wistar rats, and the mechanism may involve the down-regulation of related proliferative signaling through the inhibition of the PI3K-AKT pathway.

IODINE DEFICIENCY

1112545 - URINARY IODINE CONCENTRATION AND THYROID STATUS IN 2,195 PARTICIPANTS OF THE LONGITUDINAL STUDY OF ADULT HEALTH (ELSA-BRASIL)

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Introduction: Iodine is essential for thyroid function, playing a key role in the production of the hormones thyroxine and triiodothyronine. Adequate iodine levels are crucial for the regulation of metabolism, growth, and human development. Iodine deficiency, which was once a public health problem, has been mitigated by salt iodization programs. Urinary iodine concentration (UIC) is the ideal method for assessing iodine status in populations, as it reflects dietary intake of this micronutrient. **Objective:** To assess urinary iodine concentration in Brazilian adults from the Longitudinal Study of Adult Health (ELSA-Brasil), correlating it with sociodemographic factors and thyroid status. **Methods:** The analysis included 2,195 participants aged 35 to 74 years from six Brazilian capitals. UIC was measured, and thyroid status was assessed based on serum TSH and T4L levels. The association between sociodemographic factors and UIC was also investigated. **Results:** Among the participants, 61.4% had adequate iodine levels (UIC between 100 and 299 mcg/L), 16% had excessive levels, and 22% had iodine deficiency (<100 mcg/L). Daily fruit consumption was associated with a lower prevalence of excessive iodine levels ($p = 0.002$). No significant differences in UIC were observed based on thyroid status. State-level distribution showed variations, with São Paulo exhibiting a higher prevalence of iodine insufficiency (26%). Lack of daily fruit consumption was linked to a higher prevalence of excessive iodine levels. **Conclusion:** The study confirms that Brazil has met the target for population iodine supplementation. In contrast to a previous study with 880 participants, a larger portion of the population exhibited insufficient iodine levels, highlighting the need for further studies across different regions to better understand the true iodine status. No direct relationship was found between iodine concentration and thyroid dysfunction, and the consumption of ultraprocessed foods may influence iodine levels.

NONTHYROIDAL ILLNESS SYNDROME (NTIS)

1112220 - ANALYSIS OF THYROID FUNCTION TESTS AS RISK FACTORS FOR MORTALITY AFTER CARDIAC SURGERY IN A PROSPECTIVE COHORT OF OLDER ADULTS

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Introduction: Thyroid disorders, and in particular, low T3 syndrome, are linked to cardiovascular risk, but their predictive value for mortality post-cardiac surgery in older adults remains unclear. **Objective:** This study evaluated the association between thyroid function tests and postoperative mortality in older adults undergoing coronary artery bypass grafting myocardial (CABG) revascularization surgery and valve intervention (VI). **Methods:** Patients ≥ 60 ys admitted to the hospital for CABG/VI between June 2022 and June 2024 were consecutively included. Preoperative TSH, total T4, FT4 and FT3 serum levels were assessed together with Rockwood Clinical Frailty Scale (CFS), instrumental activities of daily living (IADLs), EuroSCORE (ESII) and comorbidities with Charlson index (CCI). Mortality during hospitalization was the primary outcome. The t test, Chi2 test and logistic regression were assessed. The receiver operating characteristic (ROC) curve was used to determine the optimal prediction threshold for postoperative mortality. **Results:** Out of 143 patients, 82% were male sex and had ($\bar{x} \pm DS$) 71.5 $\pm$ 5 years, CFS: 2.67 $\pm$ 0.99, IADLs: 37.19 $\pm$ 1.70, ESII: 1.75 $\pm$ 1.1 and CCI: 4.39 $\pm$ 1.63. The mortality rate was 14% (n:20). Serum values of ($\bar{x} \pm DS$) TSH: 3.25 $\pm$ 9.3 mU/L, FT4: 1.15 $\pm$ 0.23 ng/dL, total T4: 8.14 $\pm$ 2.17 ug/dL and FT3: 3.01 $\pm$ 0.55 pg/mL. Deceased patients had significantly lower FT3 levels (2.66 $\pm$ 0.5 vs 3.07 $\pm$ 0.53 pg/mL, $p=0.002$) than survivors, with no differences for the rest of the thyroid profile. After adjustment for confounding factors (age, CFS, IADLs, ESII, and CCI), FT3 was independently associated with increased mortality (OR, 0.153, 95% CI 0.050-0.470, $p=0.001$). The ROC curve analysis showed that 2.8 pg/mL was the optimal prediction threshold. Mortality was higher in patients below this FT3 cutoff (OR, 3.625, 95% CI 1.367-9.613, $p=0.01$). **Conclusion:** Preoperative FT3 is a robust and independent predictor of mortality in older adults undergoing CABG/VI. FT3 levels <2.8 pg/mL could guide risk stratification and perioperative management to improve outcomes.

NONTHYROIDAL ILLNESS SYNDROME (NTIS)

1112326 - EXPRESSION MITOCHONDRIAL COMPLEXES IS DECREASED BY ADMINISTRATION LOW DOSES OF THYROID HORMONES TO LIMB-MUSCLES DURING SEPSIS

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Introduction: Sepsis is a leading cause of hospitalization worldwide, with Brazil reporting higher mortality rates than the global mean. Septic patients often develop non-thyroidal illness syndrome and muscle failure, which is not well understood or treated. Our group demonstrated that administering septic mice with thyroid hormone (TH) reduced diaphragm mitochondrial dysfunction. However, the effects of sepsis and TH on limb muscles remain unclear. **Aim:** Investigate TH impact on mitochondrial dynamics in septic gastrocnemius. **Methods:** Sepsis was induced in adult male C57BL6 mice by cecal ligation and puncture (CLP). Control animals underwent sham surgery (Sham). Septic mice received low-dose TH (T4: 7.5 ng/g BW and T3: 250 ng/g BW; CLP+TH) or saline 8 and 23h after surgery. Sepsis severity was assessed using a symptom scale. **Results:** 8h post-surgery, CLP groups already showed moderate sepsis symptoms. After 23h, TH treatment reduced the severity of sepsis from moderate (CLP) to mild (CLP+TH). Analysis of mitochondrial complexes revealed that CLP only tended to decrease, while CLP+TH reduced proteins I and IV expression (complex I: SHAM: $1.02 \pm 0.39a$ /CLP: $0.70 \pm 0.24a$ /CLP+TH: $0.54 \pm 0.22b^*$; complex IV: SHAM: $1.12 \pm 0.35a$ /CLP: $0.79 \pm 0.24a$ /CLP+TH: $0.52 \pm 0.27b^*$; $*p < 0.05$). This suggests that TH treatment did not mitigate mitochondrial activity loss caused by sepsis in limb muscle and may have worsened it. We also investigated protein expression related to ROS balance, Sod2, and mitochondrial fusion, Opa1. However, no difference was observed in the limb mixed fiber muscle, while we had previously observed a difference in the CLP diaphragm. **Conclusion:** Low-dose TH treatment affects limb muscles differently than the diaphragm. It seems to worsen mitochondrial function in gastrocnemius, despite alleviating sepsis symptoms. Therefore, TH treatment may not be safe for septic patients.

NONTHYROIDAL ILLNESS SYNDROME (NTIS)

1112437 - PERCUTANEOUS ETHANOL INJECTION (PEI) WITH AND WITHOUT CINACALCET IN MANAGING SECONDARY HYPERPARATHYROIDISM IN END-STAGE RENAL DISEASE

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This study investigates the efficacy of percutaneous ethanol injection (PEI), with and without Cinacalcet, in managing secondary hyperparathyroidism (sHPT) among patients with end-stage renal disease (ESRD) on dialysis. A total of 63 patients (33 women and 30 men, aged 17-69 years) with persistently elevated intact parathyroid hormone (iPTH) levels, despite standard therapies, were analyzed. Two groups were formed: Group A received PEI alone, while Group B received PEI combined with daily Cinacalcet. The procedure involved ultrasound-guided ethanol injections directly into hyperplastic parathyroid glands, with the ethanol volume adjusted to 2050% of the gland's size. In Group B, patients also took 30 mg of Cinacalcet daily. The study measured iPTH levels before and after treatment, along with the number of sessions and treatment duration. Results showed that Group B achieved greater and faster iPTH reduction than Group A, with fewer treatment sessions required (median of 3 in Group B vs. 7 in Group A). The average final iPTH in Group B was significantly lower (164.0 ± 52.8 pg/mL) than in Group A (288.6 ± 129.0 pg/mL). Treatment in both groups was well-tolerated, with minimal side effects such as mild discomfort and transient dysphonia, which resolved within days. This combined approach of PEI and Cinacalcet offers a promising, minimally invasive alternative to surgical parathyroidectomy, particularly for patients who are not suitable surgical candidates due to comorbidities. By enhancing the efficacy of PEI, Cinacalcet improves calcium and phosphate homeostasis while reducing iPTH levels more effectively. These findings support the use of this dual therapy to optimize outcomes and improve the quality of life for patients with ESRD and sHPT. The procedure's safety profile and efficiency make it a valuable tool in endocrine and renal care.

NONTHYROIDAL ILLNESS SYNDROME (NTIS)

1112383 - PROGNOSTIC ROLE OF NTIS AND FRAILITY IN EXTREMELY ELDERLY PATIENTS IN INTENSIVE CARE UNITS - A PROSPECTIVE COHORT STUDY

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Age is one factor contributing to frailty, a complex syndrome that primarily affects the elderly. It is crucial to understand the various factors that contribute to frailty to determine how extremely elderly patients benefit from intensive care (ICU) treatment. The aim of this study is to assess the prevalence and prognosis of frailty, and its correlation with non-thyroidal illness syndrome (NTIS) in elderly patients admitted to the ICU. This cohort study included patients aged 80 and older admitted to the ICU in one year. At admission, frailty was assessed using a validated scale, the thickness of the quadriceps muscle was measured, and blood was collected. In-hospital mortality was evaluated at discharge. A total of 92 patients were included, with a mean age of 84.5 years, and 53% were male. 57.6% of the cohort was classified as frail. This group had a mean age of 85 years and scored 10 points higher on the SAPS. Length of stay in the ICU did not differ between the groups, in-hospital mortality was 52% for the frail compared to 30% for the non-frail ($P=0.02$). A correlation of 60% was found between the clinical frailty score and ultrasound measurements. Regarding thyroid hormone levels, 51% of frail had undetectable T3 levels. Low T3 was associated with a 1.44 increased risk of in-hospital death. Low levels of FT4 were an independent predictor of mortality ($P=0.01$, Specificity of 0.7). Therapeutic limitations were established for 47% of frail patients and for 20% of the non-frail ($P=0.007$). These results emphasize the importance of a better understanding of the pathophysiological mechanisms of NTIS in the extremely elderly and highlight the need to consider frailty in risk-benefit assessments for elderly patients in the ICU.

NONTHYROIDAL ILLNESS SYNDROME (NTIS)

1112420 - THYROID HORMONE METABOLISM IN CRITICAL ILLNESS: INSIGHTS INTO NONTHYROIDAL ILLNESS SYNDROME (NTIS)

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Introduction: Nonthyroidal Illness Syndrome (NTIS), also referred to as euthyroid sick syndrome, occurs when thyroid hormone levels are altered during critical illnesses despite an intact thyroid gland. The condition is characterized by low T3, variable T4, and normal or suppressed TSH levels. Although common in ICU patients, its clinical significance and management remain subjects of debate. This study aims to evaluate the relationship between NTIS, disease severity, and outcomes in critically ill patients. **Objective:** To investigate the alterations in thyroid hormone metabolism in ICU patients and their association with disease severity and clinical outcomes. **Methods:** This prospective cohort study included 150 critically ill patients admitted to a tertiary ICU. Thyroid Function Assessment: Blood samples were taken within 48 hours of ICU admission to measure TSH, free T3, free T4, reverse T3 (rT3), and thyroid-binding globulin (TBG) levels. Disease Severity and Outcomes: APACHE II scores were calculated to assess severity. Data on length of stay, mortality, and recovery time were collected. Analysis: Statistical correlations between thyroid hormone levels, disease severity, and outcomes were assessed using multivariate regression models. **Results:** NTIS was observed in 54% of patients, characterized by significantly lower free T3 and elevated rT3 compared to non-NTIS patients ($p < 0.01$). Higher APACHE II scores were noted in NTIS patients (mean: 27 vs. 18, $p < 0.05$), along with prolonged ICU stays (mean: 12 vs. 7 days, $p < 0.05$). Mortality rates were 2.5 times higher in NTIS patients ($p < 0.01$), with reverse T3 showing a strong correlation with disease severity ($r = 0.62$, $p < 0.01$). **Conclusion:** NTIS is prevalent in critically ill patients and is associated with greater disease severity and worse outcomes. Regular monitoring of thyroid hormone levels, particularly reverse T3, may provide valuable prognostic information and help guide patient management in critical care settings.

NONTHYROIDAL ILLNESS SYNDROME (NTIS)

1112358 - THYROID PROFILES IN CRITICAL ILLNESS: EXPANDING THE DIAGNOSTIC THRESHOLDS

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Introduction: Differential diagnosis of Non-thyroidal illness (NTI) can be complex. It is classically defined with low serum T3 profile, and normal or low T4 and TSH. Variations of this profile have been reported. The aim of this work is to analyze the thyroid profile of patients admitted to the Medical Clinic of our hospital. **Objective:** To analyze the thyroid profiles of hospitalized patients referred for endocrinological consultations at J.M. Ramos Mejía Hospital, focusing on NTI-related alterations. **Methods:** A retrospective analysis was conducted on 579 patients with complete thyroid profiles, extracted from a population of 4225 hospitalized patients between 2013 and 2024. Thyroid function was assessed using TSH, free T4, and T3 levels, with reference ranges set as TSH: 0.54 uUI/mL, T4L: 0.81.4 ng/dL, and T3: 85175 ng/dL. Patient diagnoses included sepsis, cardiovascular, neurological, and oncological conditions. Data were expressed as percentages. Statistical analysis: chi-square, significance was established at $p < 0.05$. **Results:** Among the patients analyzed: 73.08% exhibited low T3 with normal TSH levels. Patients with $TSH \leq 0.1$ or ≥ 30 showed thyroid profiles consistent with clinical hyperthyroidism or hypothyroidism, respectively. All with an etiologic diagnosis of thyroid dysfunction. The majority (84.2%) with TSH between 0.130 displayed homogenous thyroid hormone levels, with high, low, or normal T3 and FT4. Elevated FT4 was noted in TSH ranges of 0.110, while low FT4 occurred predominantly but not exclusively in patients with high TSH levels. **Conclusions:** The study highlights the need to expand TSH reference ranges for NTI differential diagnosis (0.130 uUI/mL) and recognizes FT4 elevation as a potential NTI characteristic. Differentiating NTI from intrinsic thyroid dysfunction requires patient follow-up and careful interpretation of thyroid profiles. These findings underscore the complexity of NTI management in hospitalized patients.

NONTHYROIDAL ILLNESS SYNDROME (NTIS)

1112268 - TYPES 2 AND 3 DEIODINASES ARE ALTERED IN THE BLOOD CELLS OF CRITICALLY ILL PATIENTS AND CORRELATED WITH PROGNOSIS

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Altered types 2 and 3 deiodinases (D2 and D3) disrupt the metabolism of thyroid hormones and contribute to non-thyroidal illness syndrome (NTIS). The effects of D2 and D3 colocalization and their expression in immune cells from critically ill patients still need to be more adequately understood. The aim of our study was to evaluate D2 and D3 dysfunction in neutrophils and monocytes from patients admitted to the intensive care unit (ICU) for any reason. We collected blood samples from ninety-six ICU patients at the time of admission and on day seven. We assessed redox parameters, including carbonyls, sulfhydryls, and glutathione (GSH). The expression and colocalization of D2 and D3 were analyzed using RNAscope, real-time PCR, and immunohistochemistry in sorted neutrophils and monocytes. T3 levels were measured in these cells. We observed elevated carbonyl levels alongside reduced sulfhydryls and GSH, confirming an altered redox status. The expression and protein concentration of D2 and D3 differed between surviving and deceased patients in both cell types. Notably, type 3 deiodinase intensity and distribution in neutrophils was associated with lower serum and intracellular T3 levels and sepsis at admission. Our results suggest that the localization of D3 on immune cells and variations in its distribution in the neutrophil might be directly related to patient outcomes.

THYROID AND COVID-19

1114230 - ENDOCRINE DYSFUNCTION AMONG PATIENTS WITH COVID-19: A SINGLE-CENTER EXPERIENCE FROM A TERTIARY HOSPITAL IN NORTH INDIA

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Introduction: Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) has emerged as a multi-system disease with the potential for endocrine dysfunction. The presence of endocrine disorders like diabetes appears to be a risk factor for COVID-19 disease, the relationship between COVID-19 disease and the endocrine system remains unexplored. **Objective:** This paper was designed to study the pituitary, thyroid, and adrenal function in COVID-19 patients admitted at the tertiary care NITRD Hospital in Delhi, India. **Methods:** A hospital-based clinical study of the endocrine profile of COVID-19 patients was conducted from 15th January to 30th June 2021 after ethical approval. Fasting blood samples for free thyroxine (T4), free tri-iodothyronine (T3), thyroid stimulating Hormone (TSH), serum prolactin; basal and 1 h post-intramuscular adrenocorticotrophic hormone (ACTH) stimulated cortisol, interleukin-6 (IL-6), and high sensitivity C-reactive protein (hsCRP) were collected within 24 h of admission after written informed consent. All hormones and IL-6 were analyzed by chemiluminescent immunoassay. hsCRP was measured by immune-turbidimetric assay. **Results:** Of 435 patients studied, 14% had severe disease, and 5.5% died. Adrenal insufficiency was present in 14%, most of whom had mild disease. A robust adrenal response was observed in those with severe disease. Basal and post-ACTH serum cortisol were significantly increased in severe disease or those who died compared to those who were mild or asymptomatic. Basal and post-ACTH serum cortisol showed a significant positive correlation with hsCRP but not with IL-6. Low T3 and low T4 syndrome were documented in 25% and 5%, respectively. Serum TSH and FT3 levels declined significantly from the asymptomatic to the severe category. Hyperprolactinemia was found in 21 patients. hs-CRP showed a rising trend with disease severity, while IL-6 did not. **Conclusion:** Endocrine dysfunction in the form of adrenal insufficiency, low T3, and low TSH syndrome and hyperprolactinemia were common COVID-19 hospitalized patients.

THYROID AND COVID-19

1112330 - IMPACT OF COVID-19 ON THE EPIDEMIOLOGICAL PROFILE OF HOSPITALIZATIONS FOR THYROTOXICOSIS IN BRAZIL

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Thyrotoxicosis, marked by an excess of thyroid hormones, causes severe symptoms requiring urgent medical intervention. The SARS-CoV-2 virus, associated with COVID-19, has been linked to increased thyroid dysfunction, as it utilizes the ACE2 receptor in the thyroid, potentially triggering inflammatory responses. This study examines the impact of COVID-19 on the epidemiological profile of hospitalizations for thyrotoxicosis in Brazil. A retrospective, exploratory analysis was conducted using data from Brazil's Hospital Information System (SIH/SUS) - DATASUS. Hospitalizations for thyrotoxicosis (ICD-10 E05) were compared between the pre-pandemic period (November 2017 to February 2020) and the post-pandemic period (May 2022 to August 2024), with variables including gender, age, type of care, mortality rate, length of stay, and costs. The study found a 17.9% rise in hospitalizations for thyrotoxicosis post-pandemic, totaling 1,906 cases. Female prevalence dropped from 80.1% to 76.2%, while male hospitalizations increased proportionally. The age group most affected remained 30-59 years in both periods. Hospitalizations rose by 27.9% among mixed-race individuals, from 264 to 338, and declined by 64.3% Indigenous individuals. Regionally, cases fell by 33.3% in the South but increased in the Southeast, from 1,011 to 1,137 cases. The average length of hospital stay decreased from 6.8 to 6.2 days, and the mortality rate slightly declined from 2.10% to 1.78%, with total deaths stable at 34. Hospitalization costs rose by 55.7%, from R\$ 986,557.76 to R\$ 1,535,978.62 (adjusted for inflation). These findings underscore the importance of ongoing monitoring to understand COVID-19's long-term impact on endocrine health, as demographic shifts, hospitalization rates, and healthcare costs highlight evolving trends in thyrotoxicosis management in Brazil.

THYROID AND COVID-19

1114163 - PROLONGED SUBACUTE THYROIDITIS POST-COVID-19 IN A PATIENT WITH LONG-STANDING HASHIMOTO'S THYROIDITIS: CASE REPORT

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Case Presentation: Female, 45 years, diagnosed with Hashimoto's thyroiditis (HT) in 2003, presented for the first time in 2005 with neck pain, taking Levothyroxine (LTX) 25 mcg/day, and: TSH: 4.3 (0.55-4.78 uIU/mL); Free T4 (T4L): 0.91 (0.7-1.7 ng/dL) and positive Anti-TPO and Anti-TG. In April/2020, she returned with severe neck pain, thyroid enlargement, tremor, palpitations and insomnia, starting 15 days after COVID-19, taking LTX 100 mcg/day. Tests showed suppressed TSH, increased T3, T4L, thyroid antibodies, Thyroglobulin (TG), C-reactive protein, erythrocyte sedimentation rate and COVID IgM negative and IgG positive. Thyroid USG/Doppler showed hypoechogenic, heterogeneous parenchyma, increased volume and vascularization. LTX was reduced to 50 mcg/day and Prednisone was prescribed for pain. Fifteen days later, T3 and T4L normalized, other tests increased and LTX was adjusted to 75 mcg/day. In July/2020, TSH and T4L were normal, TG and AntiTG decreased and AntiTPO increased, but the pain continued and enlarged thyroid was leading to compressive symptoms. By the end of 2020, LTX was 100 mcg/day. In February/2021, thyroid tests, glandular volume and vascularization were normal and only Anti-TPO was high. In 2023, she had a short episode of thyroid enlargement and pain. The patient is currently asymptomatic, euthyroid and with a slight goiter. **Discussion:** Despite low thyroid reserve due to HT, the patient presented subacute thyroiditis (ST) with severe thyrotoxicosis. ST is associated with viral infections and have been reported after COVID-19 infection but thyrotoxicosis has been reported only in patients hospitalized for COVID-19. There are no reports of prolonged thyroid pain related to ST post-COVID-19. **Final Comments:** ST is a rare complication of COVID-19 and there is no data in the literature of ST by COV SARs in patients with previous HT.

THYROID AND COVID-19

1114219 - SPECTRUM OF ENDOCRINE DYSFUNCTION AND ASSOCIATION WITH DISEASE SEVERITY IN PATIENTS WITH COVID-19

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Introduction: The pandemic of COVID-19, caused by SARS-CoV-2, has established itself as one of the greatest challenges to healthcare globally. Despite the lower case fatality rate as compared to other coronaviruses, COVID-19 has underscored the vulnerability of certain subsets of populations to emerging diseases, particularly with respect to gender, age, and co-morbidities (diabetes, hypertension, and obesity). **Objective:** This was a single-centre, cross-sectional study to evaluate endocrine function in patients with COVID-19 and to investigate whether the hormonal function is similar or different between patients with mild (symptomatic or asymptomatic) and moderate-to-severe disease. **Methods:** Consecutive patients enrolled at NITRD Delhi were stratified on the basis of disease severity as group I (moderate-to-severe disease including oxygen saturation <94% on room air or those with comorbidities) (n=55) and group II (mild disease, with oxygen saturation >94% and without comorbidities) (n=69). Hypothalamopituitary-adrenal, thyroid, gonadal axes, and lactotroph function were evaluated. Inflammatory and cell-injury markers were also analysed. **Results:** Patients in group I had higher prevalence of hypocortisolism (38.5 vs 6.8%, p=0.012), lower ACTH (16.3 vs 32.1 pg/mL, p=0.234) and DHEAS (86.29 vs 117.8 µg/dL, p=0.086) as compared to group II. Low T3 syndrome was a universal finding, irrespective of disease severity. Sick euthyroid syndrome (apart from low T3 syndrome) (80.9 vs 73.1%, p=0.046) and atypical thyroiditis (low T3, high T4, low or normal TSH) (14.3 vs 2.4%, p=0.046) were more frequent in group I than group II. Male hypogonadism was also more prevalent in group I (75.6% vs 20.6%, p=0.006) than group II, with higher prevalence of both secondary (56.8 vs 15.3%, p=0.006) and primary (18.8 vs 5.3%, p=0.006) hypogonadism. Hyperprolactinemia was observed in 42.4% of patients without significant difference between both groups. **Conclusion:** COVID-19 can involve multiple endocrine organs and axes, with a greater prevalence and degree of endocrine dysfunction in those with more severe disease.

THYROID AND COVID-19

1114221 - SUBACUTE THYROIDITIS AFTER RECOVERY FROM COVID-19: EMERGING CLINICAL FINDINGS FROM A NORTH INDIAN HOSPITAL

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Introduction: The SARS-CoV-2 virus has been shown to affect multiple endocrine organs, including the thyroid. Diverse alterations of thyroid functions have been observed during and following COVID-19 infection. Subacute thyroiditis (SAT) is a form of granulomatous thyroiditis which can occur during or after a viral illness. Recent reports have suggested a link between COVID-19 infection and SAT.

Objective: Thus, this study aimed to examine the variations in clinical and biochemical parameters in patients developing post-COVID SAT. **Methods:** A retrospective-prospective study on patients presenting with SAT within 3 months of recovery from COVID-19 infection, who were subsequently followed up for a further 6 months since diagnosis of SAT at the NITRD Delhi was considered.

Results: Out of 670 patients with COVID-19, 11 patients presented with post-COVID-19 SAT (6.8%). Those with painless SAT (PLSAT, n = 5) presented earlier, had more severe thyrotoxic manifestations and exhibited higher C-reactive protein, interleukin 6 (IL-6), neutrophil-lymphocyte ratio and lower absolute lymphocyte count than those with painful SAT (PFSAT, n = 6). There were significant correlations of total and free T4 and total and free T3 levels with serum IL-6 levels (pall <0.04). No differences were observed between patients with post-COVID SAT presenting during the first and second waves. Oral glucocorticoids were needed for symptomatic relief in 66.67% of patients with PFSAT. At 6 months of follow-up, majority (n = 9, 82%) achieved euthyroidism, while subclinical and overt hypothyroidism were found in one patient each. **Conclusion:** The findings of this study demonstrated two distinct clinical presentations – without and with neck pain – depending on the time elapsed since COVID-19 diagnosis. Persistent lymphopaenia during the immediate post-COVID recovery period could be a key driver of early, painless SAT. Close monitoring of thyroid functions for at least 6 months is warranted in all cases.

THYROID AND COVID-19

1114329 - SUBACUTE THYROIDITIS SECONDARY TO COVID-19: CASE REPORT

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Case Presentation: Subacute thyroiditis is an inflammation of the thyroid gland that can be precipitated by viral infections. With the emergence of COVID-19, reports of endocrine manifestations associated with the disease have increased, including cases of subacute thyroiditis. The present the case of a previously healthy 47-year-old woman who developed fever, anterior neck pain and mild flu-like symptoms. She was diagnosed with COVID-19 after a positive RT-PCR test for SARS-CoV-2. After two weeks, the patient reported intense pain in the anterior cervical region, fatigue, palpitations and significant weight loss. Physical examination revealed a painful thyroid on palpation. Laboratory tests revealed an increase in free T4 levels and suppression of TSH. A thyroid ultrasound showed a diffusely enlarged gland, with no obvious nodules. The patient was diagnosed with subacute thyroiditis secondary to COVID-19 infection. **Discussion:** Initial treatment included non-steroidal anti-inflammatory drugs (NSAIDs) to control pain and inflammation. Due to the persistence of symptoms and the significant increase in inflammatory markers, prednisone was started, with rapid clinical and laboratory improvement. This case highlights the importance of considering subacute thyroiditis as a possible post-COVID-19 complication. Early recognition is crucial for proper management and to avoid further complications. Further studies are needed to elucidate the pathogenesis and frequency of this association. **Final Comments:** Subacute thyroiditis may be a relevant post-viral endocrine manifestation of COVID-19. Early diagnosis and treatment are essential for a good prognosis and full recovery of patients.

THYROID AND COVID-19

1114228 - THYROID FUNCTION ABNORMALITIES AND OUTCOMES IN HOSPITALIZED PATIENTS WITH COVID-19 INFECTION

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Introduction: The thyroid gland can be affected by the COVID-19 infection. The pattern of thyroid function abnormality reported in COVID-19 is variable; in addition, some drugs used in COVID-19 patients, like glucocorticoids and heparin, can affect the thyroid function tests (TFT). **Objective:** Thus, this study looked at the abnormalities in TFT and thyroid autoantibodies before the initiation of interfering drugs like glucocorticoids and heparin in subjects with COVID-19 infection. **Methods:** An observational, cross-sectional study of thyroid function abnormalities with thyroid autoimmune profile in COVID-19 patients with varying severity from November 2020 to December 2021 was conducted at NITRD Delhi, India. Serum FT4, FT3, TSH, anti-TPO, and anti-Tg antibodies were measured before the initiation of treatment with steroids and anti-coagulants. **Results:** A total of 271 COVID-19 patients were included in the study, of which 27 were asymptomatic and remaining 158, 39, and 47 were classified to mild, moderate and severe categories, respectively, according to MoHFW, India criteria. Their mean age was 49 ± 17 years and 64.9 % were males. Abnormal TFT was present in 37.2 % (101/271) patients. Low FT3, low FT4, and low TSH were present in 21.03 %, 15.9 % and 4.5 % of patients, respectively. Pattern corresponding to sick euthyroid syndrome was the most common. Both mean FT3 and FT3/FT4 ratio decreased with increasing severity of COVID-19 illness ($p = 0.001$). In multivariate analysis, low FT3 was associated with increased risk of mortality (OR 12.36, 95 % CI: 1.23-124.19; $p = 0.033$). Thyroid autoantibodies were positive in 58 (27.14 %) patients; but it was not associated with any thyroid dysfunction. **Conclusion:** Thyroid function abnormality is common among COVID-19 patients. Both low FT3 and FT3/FT4 ratios are indicators of disease severity, while low FT3 is a prognostic marker of COVID-19-associated mortality.

THYROID AND COVID-19

1114226 - THYROID FUNCTION TEST IN COVID-19 PATIENTS: INSIGHTS FROM A CROSS-SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL IN NORTH INDIA

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Introduction: Alteration of the thyroid gland function in COVID-19 has been described. Whether the abnormalities of thyroid function associated with COVID-19 can be explained with that due to Sick Euthyroid Syndrome has also remained elusive. **Objective:** The objective of this study aimed to assess thyroid function in patients with COVID-19 admitted with varying degrees of severity in the NITRD hospital, India. **Methods:** Seventy-five patients with COVID-19 detected by RT-PCR admitted in the General Medicine isolation ward and COVID block of a tertiary care hospital were selected by semi-purposive sampling. These patients were assessed for thyroid function tests, including total T3, free T3, total T4, free T4, TSH and anti-TPO antibody, along with other baseline investigations. Patients with pre-existing thyroid-related ailments, those on levothyroxine or anti-thyroid drugs or other drugs known to interfere with the results were excluded. **Results:** There were 43.3% of patients in the mild, 26.7% in moderate, and 30% in the severe category, according to local COVID-19 severity classification protocol. 35% of patients had one or more abnormalities in thyroid function, low TSH being the most common (18.33%). 9.1% of patients had characteristic patterns of thyroiditis. In most of the others, thyroid function did not match any typical pattern. There was no significant difference in any of the parameters of the thyroid function test between mild, moderate, and severe groups. **Conclusion:** Thyroid function may be abnormal in all categories of patients during COVID-19 infection, even in the absence of pre-existing thyroid ailments. Although low TSH is the commonest abnormality and a typical pattern of thyroiditis can be seen in a subsection of patients, in the majority of the patients, thyroid function abnormality does not follow any characteristic pattern and likely represents a combination of thyroiditis and sick euthyroid syndrome in different points of its spectrum.

THYROID AND PEDIATRIC DISEASE

1112452 - DECREASED GROWTH RATE DUE TO HYPOTHYROIDISM

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13-year-old male who comes due to decreased growth rate. For the past year, he has not shown any growth. Previously, normal growth at p 50, for years he has changed growth rate, currently at p 3. On physical examination, height 142 cm (z 1.96). BMI: 18.6. P 50 Palpable thyroid, grade 2 goiter. Dry skin. CV: regular rhythm of 80 cm. Genitals: Tanner II. Testicles: 6 cc. Pubic hair: Tanner II. Prepubertal penis. Perinatally, normal TSH. Family history: maternal height 175 cm, menarche at 12 years. Paternal height 177 cm. Normal pubertal growth spurt. Studies were requested due to decreased growth rate presenting: TSH 554 uIU/mL (0.23-5.20), T4L: 0.16 ng/dL (0.70-1.89). Negative celiac profile, Glycemia: 0.79 g/L. Creatininemia 1.17 mg/dL (0.25-1.00). Complete blood count: Hemoglobin: 10.6 g/dL (13-17). IGF1: 44.7 ng/mL (133-471). Bone age of 8 years. Confirmation of hypothyroidism with TSH: 630 uIU/mL, T4L 0.16 ng/dL, T3L 1.31 pg/mL (2.00-4.20). Anti-thyroid peroxidase antibodies > 13,000 IU/mL (positive > 60 IU/mL). Anti-thyroglobulin antibodies 53.5 IU/mL (positive > 4.5 IU/mL). Thyroid ultrasound with Doppler: volume of 6.5 cc. The contours are lobulated, the echogenicity is heterogeneous, less than usual, it has multiple scattered fibrous bands, the vascularization is increased, it presents some subthyroid nodes. The most common manifestation of hypothyroidism in children is decreased height velocity. Growth retardation tends to be insidious at the beginning, severe hypothyroidism is rare in children so this presentation is not frequently observed. The other alterations can also be explained by hypothyroidism. It is important to take this presentation into account to make an early diagnosis and prevent short stature.

THYROID AND PEDIATRIC DISEASE

1112288 - EPIDEMIOLOGICAL PROFILE OF IODINE DEFICIENCY-RELATED THYROID DISORDERS IN BRAZILIAN CHILDREN (2024)

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Introduction: Iodine deficiency remains a significant public health issue in various parts of the world, particularly affecting thyroid function. Iodine is essential for the synthesis of thyroid hormones, and its absence can result in a range of disorders, including goiter, hypothyroidism, and developmental delays, especially in children. The impact of these conditions during childhood can be profound, affecting growth, neurodevelopment, and overall quality of life. Despite national iodization programs, vulnerable populations may still be affected. This study aims to evaluate the epidemiological distribution of thyroid disorders related to iodine deficiency in Brazilian children under 15 years of age in 2024. **Objective:** To describe the epidemiological profile of hospitalizations for thyroid disorders related to iodine deficiency (ICD-10: E01) in children aged 0-14 years in Brazil in 2024, according to sex, race/skin color, and age group. **Methods:** This is a descriptive study based on data from the SUS Hospital Information System (SIH-SUS). All hospitalizations recorded in 2024 with ICD-10 code E01 in individuals under 15 years of age were included. Variables analyzed included sex, race/skin color, and age group. Data were presented in absolute and relative frequencies. **Results:** In 2024, there were 12 pediatric hospitalizations due to thyroid disorders related to iodine deficiency. All occurred in females, indicating a strong gender disparity. Regarding age, 83.3% (n=10) of cases occurred in children under 1 year old, while 16.7% (n=2) were in the 10-14 age group. In terms of race/skin color, 75% (n=9) of the cases were among children identified as "parda", 16.7% (n=2) as white, and 8.3% (n=1) as Black. **Conclusion:** The data highlight a strong female predominance and early age of onset for iodine deficiency-related thyroid disorders in Brazil. Public health initiatives should ensure adequate iodine intake during pregnancy and early childhood, particularly in socially vulnerable populations.

THYROID AND PEDIATRIC DISEASE

1112626 - EPIDEMIOLOGY OF MORTALITY DUE TO CONGENITAL HYPOTHYROIDISM IN MATO GROSSO DO SUL FROM 2019 TO 2023 IN INDIVIDUALS UNDER 5 YEARS OF AGE

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In the state of Mato Grosso do Sul (MS), between 2019 and 2023, 203 deaths of children under 5 years of age were recorded due to preventable and reducible causes through appropriate diagnostic and treatment actions, such as meningitis, severe acute respiratory infections (SARIs), pneumonia, diabetes mellitus, and congenital hypothyroidism. Congenital hypothyroidism (CH) is characterized by insufficient activity of the thyroid gland from birth. This condition may be caused by iodine deficiency, anomalies in thyroid gland development, or errors in thyroid metabolism. CH can lead to various functional and developmental abnormalities, manifesting in different forms, including delayed physical and mental development, goiter, impaired cognitive function, stunted growth, and increased perinatal mortality and morbidity. In Brazil, neonatal screening can identify all forms of CH and is one of the mandatory tests conducted between the 3rd and 5th day of a newborn's life. The "Heel Prick Test", free exam offered by Brazil's healthcare system, is performed by collecting drops of blood from the baby's heel and analyzing the concentration of TSH hormone in the baby's blood. From this perspective, between 2019 and 2023, only 2 deaths were attributed to CH in the state, representing 0.98% of the total deaths during this period. These data highlight the effectiveness of neonatal screening programs carried out in the country.

THYROID AND PEDIATRIC DISEASE

1112405 - PEDIATRIC GRAVES ORBITOPATHY: RUNDLES CURVE DOES NOT FIT ALL?

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Introduction: Thyroid eye disease (TED) is rare in children and adolescents and possibly evolves differently in the pediatric age group. Our study aimed to analyze the clinical features and classify patients on the EUGOGO and CAS scales in this group. **Methods:** Patients were studied retrospectively, and a series of patients was organized between the years 2019 and 2023. **Results:** Our patient group has eight (8) patients with TED, including 7 girls (87,5%) and 1 boy (12,5%). The mean age at diagnosis was 11,5 years (range 4 to 14). All patients were diagnosed with hyperthyroidism and presented with important difficulty in achieving control under regular use of antithyroid drugs. The mean age at diagnosis of ophthalmopathy was 11,8 years (range 8 to 14). All patients were taking antithyroid drugs, and some required definitive therapy with total thyroidectomy (37%) due to the large thyroid volume and poor response without achieving euthyroidism. Clinical findings included proptosis (100%) and eyelid retraction (75%). No patient had diplopia or compressive optic neuropathy. Half of the patients were classified as mild disease and the other half as moderate to severe orbitopathy. No patient had active disease, with CAS ranging from 0 to 2. Therefore, none received systemic corticosteroids or orbital radiotherapy. All patients had a predominant lipogenic pattern on tomography. **Conclusion:** Although TED has similar clinical manifestations in pediatric and adult populations, our study showed that orbitopathy was less severe in childhood than adults and does not seem to follow the classic two-phase pattern of the Rundle curve.

THYROID AND PEDIATRIC DISEASE

1112219 - RADIOIODINE-REFRACTORY DIFFERENTIATED THYROID CANCER IN CHILDREN AND ADOLESCENTS: A RETROSPECTIVE SINGLE-CENTER STUDY

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Introduction: Differentiated thyroid cancer (DTC) in pediatric patients is rare but often aggressive, with a high prevalence of regional and distant metastases. Tailored management strategies are particularly critical for radioiodine-refractory (RAIR) cases, which represent 1030% of all DTCs. Current RAIR classification systems lack pediatric-specific criteria, necessitating new frameworks to address the unique clinical course and therapeutic needs of this population. **Objective:** To evaluate outcomes in pediatric DTC patients treated with surgery and radioiodine (RAI) therapy, with a focus on RAIR cases and those presenting with advanced disease. Additionally, to propose a new RAIR classification based on iodine avidity and therapeutic outcomes. **Methods:** A retrospective review of medical records for 278 pediatric DTC patients treated between 2008 and 2022 was conducted. Patients underwent surgery followed by RAI therapy, with follow-ups every 3 to 6 months. Advanced cases were identified by high-risk presentation and resistance to RAI therapy. Kaplan-Meier analysis was used to assess progression-free survival (PFS). Cox regression adjusted for age, sex, and interaction terms was performed to evaluate predictors of outcomes. **Results:** Among 278 patients, 39 (14%) had advanced disease. In this subgroup, 4 achieved remission, 29 had disease stabilization, and 6 experienced biochemical or structural progression, with one patient requiring lenvatinib therapy. The PFS rate among RAIR patients was 84.62%, with an overall 5-year survival rate of 100%. Patients with RAI-non-avid metastases exhibited poorer outcomes in terms of PFS and remission probability. **Conclusion:** This study highlights the need for personalized therapeutic approaches for pediatric DTC patients. A new classification system categorizing RAIR cases based on iodine avidity and therapeutic outcomes should be proposed. This framework aims to guide treatment and follow-up strategies, potentially informed by the molecular and genetic distinctions between iodine-avid and non-avid subgroups. Patients with non-avid metastases demonstrated worse prognoses, underscoring the importance of tailored interventions

THYROID AND PEDIATRIC DISEASE

1112541 - SURGICAL TREATMENT OF GRAVES DISEASE IN CHILDREN

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Introduction: Graves' disease is a rare disorder in the pediatric population. It is the most common cause of hyperthyroidism in children. Treatment strategy includes antithyroid drugs, radioactive iodine, and thyroidectomy. The optimal treatment of Graves' disease is still controversial. **Objective:** Our aim is to evaluate the indications and results of thyroidectomy for Graves' disease in children. **Methods:** We report the clinical, therapeutic aspects, and long-term results of 10 children (< 18 years old) operated for Graves disease, from 2000 to 2024. **Results:** The mean age at diagnosis was 14 years [9 years 17 years]. Our study included 3 boys and 7 girls. One patient had coeliac disease. No patient had Graves orbitopathy. All our patients were treated with anti-thyroid drugs and beta-blockers. Indications for surgery were: failed medical therapy after 2 years of treatment (6 cases) and the presence of a compressive goiter (4 cases). Total thyroidectomy was performed in all cases. The postoperative course was complicated by transient hypocalcemia in 2 cases. After an average follow-up of 5 years, all patients had control of the diseases manifestations with biological euthyroidism. No recurrence was noted. **Conclusion:** Total thyroidectomy for Graves' disease offers rapid and durable control of hyperthyroidism. Surgery performed by high-volume surgeons could be a definitive treatment of choice.

THYROID AND PEDIATRIC DISEASE

1112428 - THE SODIUM-IODIDE SYMPORTER (NIS) IS ESSENTIAL FOR THE ADJUVANT TREATMENT OF DIFFERENTIATED THYROID CARCINOMA (DTC). HOWEVER, THERE IS LIMITED INFORMATION REGARDING NIS EXPRESSION IN PEDIATRIC DTC, WHICH OFTEN PRESENTS MORE AGGRESSIVELY

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Objective: This study aimed to evaluate the detection and expression of NIS in pediatric DTC and associate these findings with normal adjacent thyroid tissue, the tumor's molecular landscape, radioactive iodine (¹³¹I) therapy and treatment response at the end of the follow-up. **Methods:** We evaluated tissue samples from 72 patients under 19 years of age who were diagnosed with DTC. We used immunohistochemistry (IHC) to detect NIS protein, quantitative polymerase chain reaction (qPCR) to analyze the expression of the NIS-related gene (SLC5A5), and next-generation sequencing (NGS) to assess the tumor's genetic profile. **Results:** Our findings indicated that NIS detection was significantly lower in pediatric DTC compared to normal thyroid tissue ($p < 0.001$), with NIS present in only 25% of the samples, while 54% showed SLC5A5 expression. We found a positive correlation between NIS protein levels and SLC5A5 gene expression ($p = 0.02$). Additionally, there was no association between NIS detection or expression and the tumor's molecular landscape, including RET-PTC, NTRK, ALK (excluding STRN::ALK), AGK::BRAF fusions, or BRAF_V600E mutations. Furthermore, there were no significant differences in treatment responses at the end of the follow-up period, regardless of NIS expression or the molecular landscape. **Conclusion:** In conclusion, NIS expression is diminished in pediatric differentiated thyroid cancer however, this expression was similarly lower regardless the molecular alterations found in each case. Thus, other factors may explain the lower detection of NIS compared to both normal adjacent tissue and SLC5A5 expression in pediatric DTC.

THYROID AND PEDIATRIC DISEASE

1112482 - THYROID CANCER IN A PATIENT POST HEMATOPOIETIC STEM CELL TRANSPLANT FOR PHILADELPHIA POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA IN PEDIATRIC AGE

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Case Presentation: A 15-year-old female patient, allergic to asparaginase and latex, was diagnosed with Philadelphia-positive B-cell acute lymphoblastic leukemia at the age of 7, for which she received a conditioning treatment based on radiotherapy and chemotherapy. Months after achieving complete remission, a hematopoietic stem cell transplant (HSCT) was performed in Miami, United States. She was monitored for 6 years by the Hematology service and 1 year later she was evaluated by Head, Neck and Maxillofacial Surgery for presenting an anterior cervical tumor dependent on the thyroid gland. A cervical CT scan with contrast was performed with the finding of an irregular hypodense nodular lesion in the left thyroid lobe and multiple suspicious lymph nodes. In addition, an ultrasound-guided fine needle aspiration biopsy resulted in Bethesda V. Therefore, it was decided to perform total thyroidectomy plus left lateral and central neck dissection, which was reported as classic variant papillary carcinoma. After 4 months she received iodine therapy showing abnormal uptake in the surgical bed. Recently, she was evaluated and the examination showed no signs of recurrence. **Discussion:** Children with acute leukemia, 85% are B-cell lymphoid type and the presence of the Philadelphia chromosome 2%-3% is a rare alteration with a poor prognosis. These patients receive a conditioning regimen based on chemotherapy or radiotherapy to undergo HSCT, increasing up to 3 times the risk of developing a second malignancy, such as thyroid carcinomas, prevailing in women than men. For this reason, continuous and safe follow-up after HSCT in children must be guaranteed. **Final comments:** The supervision and follow-up of each patient undergoing conditioning therapy for HSCT for acute lymphoblastic leukemia is essential. This allows for the early detection of the appearance of second malignancies, treating the patient immediately.

THYROID AND PEDIATRIC DISEASE

1112580 - THYROID CANCER IN ADOLESCENTS

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Introduction: 16-year-old male with a history of severe Hemophilia A treated with Emicizumab, and obesity presented for follow-up of differentiated thyroid carcinoma (DTC). **Clinical Presentation:** The patient had a long-standing cervical mass causing neck deformity, hard in consistency, and fixed to deep planes. **Ultrasound:** Large solid nodule occupying the left thyroid lobe and clustered lymphadenopathy in jugulocarotid, perithyroidal, and supraclavicular regions. **CT:** Asymmetry of thyroid lobes, intense, inhomogeneous contrast uptake, and a 20 cm lateral neck lymph node mass. **Fine-needle aspiration biopsy:** Papillary thyroid carcinoma; lymph nodes consistent with malignancy. **Management:** The patient underwent a total thyroidectomy with central and right lateral neck dissection, followed by left lateral neck dissection one month later. Postoperative complications included transient hypoparathyroidism and left recurrent laryngeal nerve paralysis. Levothyroxine (150 µg/day) was initiated. **Histopathology:** Thyroid: Classic papillary thyroid carcinoma with vascular, lymphatic, and perineural invasion, extrathyroidal extension. Right lymph nodes: 2/27 positive; recurrent nerve nodes: 4/4 positive. Left lymph nodes: 7/49 positive. **Staging and Treatment:** TNM: T3b N1b M1. Therapeutic target: TSH < 0.1 uUI/mL. Radioiodine therapy (150 mCi). Post-therapy SPECT/CT: Evidence of pulmonary and lymph node metastases. Bilateral thyroid remnants identified. TSH: > 100 uUI/mL. Thyroglobulin: 1843 ng/mL. Anti-thyroglobulin antibodies: 19.96 U/mL. **Follow-Up (6 Months Post-Radioiodine):** No residual glandular tissue was identified on ultrasound. SPECT-CT after levothyroxine withdrawal (4 weeks): Persistent bilateral thyroid remnants. Ongoing evidence of pulmonary and lymph node metastases in previously identified locations. TSH: > 100 uUI/mL; Thyroglobulin: 625.7 ng/mL. Anti-thyroglobulin antibodies: 19.4 U/mL. **Discussion:** This case is rare in adolescents, however the clinical presentation is not striking since it presents more frequently in an aggressive manner with a higher incidence of lung metastases as was evident in this patient. Although iodine-avid lesions often stabilize after treatment with I-131, complete remission is rare. Disease-specific mortality remains low (<2%) due to effective management strategies.

THYROID AND PEDIATRIC DISEASE

1112299 - THYROID EYE DISEASE IN PEDIATRIC PATIENTS

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Introduction: Pediatric thyroid eye disease (TED) is rare and often considered mild, typically presents with proptosis and eyelid signs. This study reports the clinical features and treatment outcomes of Japanese children with TED from a single centre. **Subjects:** We retrospectively analyzed 295 pediatric patients diagnosed with TED at Olympia Eye Hospital between January 2009 and December 2020. The cohort included 48 boys and 247 girls, aged 3 to 15 years (mean age: 12.7 years). Data on thyroid function, family history, ocular findings, and orbital MRI features were reviewed. **Results:** Hyperthyroidism was observed in 284 cases (96.3%), while euthyroid Graves disease accounted for 11 cases (3.7%). A family history of thyroid disease was identified in 45.8% of patients. Mean proptosis was 18.0 mm (range: 1,325 mm). Upper eyelid retraction was present in 43.4%, eyelid swelling in 61.3%, and diplopia in 2.4%. Visual impairment was reported in 2.0%, though this was psychogenic rather than due to compressive optic neuropathy. Among 276 patients who underwent orbital MRI, extraocular muscle enlargement was observed in 89 cases (32.2%). The inferior rectus was most commonly involved (54 cases, 60.7%), followed by the superior rectus (45 cases, 50.6%), medial rectus (42 cases, 47.2%), and lateral rectus (12 cases, 13.5%), with 45.2% showing involvement of more than one muscle. Enlargement of the levator palpebrae superioris was noted in 116 cases (42.0%). 57 patients (19.3%) received anti-inflammatory treatments, including steroid pulse therapy (3 cases), triamcinolone injections in the eyelids (55 cases), and extraocular muscles (3 cases). **Conclusion:** Pediatric TED often manifests with prominent eyelid abnormalities, including retraction and swelling. Although extraocular muscle enlargement was observed in some cases, diplopia was uncommon. Anti-inflammatory treatments with steroids were administered in 19.3% of cases, while the majority of patients were managed with topical medications and careful observation.

THYROID AND PEDIATRIC DISEASE

1112431 - THYROID-STIMULATING HORMONE IN MOTHERS AND NEWBORNS: INVESTIGATING THE LINK WITH RESPIRATORY DISTRESS SYNDROME RISK IN NEWBORN

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Introduction: Thyroid hormones are crucial for organogenesis and surfactant production. This study aims to evaluate the impact of maternal and newborn TSH levels on the risk of Respiratory Distress Syndrome (RDS). **Methods:** Approved by the ethical committee (CAAE: 44326821.8.3001.0086 and CAAE: 44326821.8.3002.5452), this study analyzed a cohort of 1,414 newborns admitted to a Newborn Semi-intensive or Intensive Care Unit (SICU). Maternal TSH levels were measured during pregnancy using the Advia Centaur XP platform, and newborn TSH levels were quantified from filter-paper blood spots using the Abbott Architect i2000 immunoassay. Newborn screening was recommended at 4872 hours after birth. Statistical analyses included Mann-Whitney, Kruskal-Wallis, chi-squared, Fishers Exact Test, Spearmans rank correlation, logistic regression, and unsupervised two-step cluster analysis, incorporating maternal thyroid history, TSH, and newborn characteristics: first Apgar score, weight, and TSH levels. **Results:** From 11,008 deliveries, 1,414 newborns were initially analyzed, with 1,031 cases included after exclusions. Of these, 17 newborns (1.6%) were born at < 28 weeks and 102 (9.9%) at < 32 weeks. Apgar scores were < 8 in 306 newborns (29.7%) at one minute and 55 (5.3%) at five minutes. Thyroid disease was reported in 22 mothers (2.1%), diabetes in 54 (5.2%), and hypertension in 145 (14.1%). Maternal ($p = 0.914$) and newborn ($p = 0.603$) TSH levels were not significant risk factors for RDS. However, maternal TSH levels between 4.0 and 9.99 mUI/L were associated with an RDS risk of 1.718 ($p = 0.037$, 95% CI: 1.0322.860). Four out of six cluster groups had higher RDS risk, with odds ratios ranging from 2.278 to 5.815 ($p < 0.001$). **Conclusion:** Despite the limitations of retrospective studies, maternal TSH levels and four distinct clusters were identified as predictors of RDS risk in newborns.

THYROID AND PEDIATRIC DISEASE

1114091 - THYROIDITIS IN THE PEDIATRIC POPULATION: A DESCRIPTIVE EPIDEMIOLOGICAL STUDY IN BRAZIL (2024)

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Introduction: Thyroiditis refers to an inflammatory process affecting the thyroid gland, which plays a key role in the regulation of various physiological systems through hormone production. This inflammation may result from viral, autoimmune, or bacterial causes, as well as from postpartum changes in women. Although thyroid disorders are more frequently reported in adults, children and adolescents are also susceptible, with cases ranging from congenital hypothyroidism to autoimmune thyroid disease. Both hormone deficiency and excess can severely impact pediatric bone development and growth. **Objective:** To describe the epidemiological profile of hospitalizations due to thyroiditis (ICD-10: E06) in children and adolescents aged 0 to 14 years in Brazil during 2024, based on sex, race/ethnicity, and age group. **Methods:** This is a descriptive study based on data extracted from the SIH-SUS database (Hospital Information System of the Brazilian Unified Health System). All hospital admissions with the ICD-10 code E06 in patients under 15 years were included. Age was categorized into: <1 year, 1-4 years, 5-9 years, and 10-14 years. Variables analyzed included sex, race/ethnicity, and age group. A chi-square test was applied to assess associations between categorical variables, with significance set at $p < 0.05$. **Results:** A total of 36 pediatric hospitalizations due to thyroiditis were reported in 2024. Most cases (80.6%) occurred in females ($n=29$), and only 19.4% in males ($n=7$), with a statistically significant difference ($\chi^2=12.44$; $p < 0.001$). Infants under 1 year represented 91.7% of hospitalizations. Racial distribution included 47.2% white, 41.7% brown (parda), and 11.1% black children. **Conclusion:** Thyroiditis hospitalizations in 2024 primarily affected females and infants under one year of age. These findings highlight the importance of early recognition and management, especially among newborns and girls, to mitigate long-term health impacts.

THYROID AND PREGNANCY

1112600 - A LADY WITH TSHOMA COMPLICATED PREGNANCY

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A newly immigrated 35-year-old lady first presented for irregular menses and had hyperprolactinaemia $<2 \times \text{ULN}$. MRI pituitary (2019) showed pituitary adenoma $18 \times 16 \times 15$ mm. She had sinus tachycardia with TSH 2.2 ($0.27-4.2$) mIU/L, fT4 32.2 ($12-22$) pmol/L, fT3 8.1 ($3.1-6.8$) pmol/L (11/2022). Family history, thyroid eye sign and anti-TSHR were all negative. After treating with carbimazole 5 mg daily, TFT became TSH 32 , fT4 9 in 2/2023. Carbimazole was stopped in 3/2023. TSH then became 5 , fT4 30.5 and fT3 9.1 in 4/2023. She was pregnant by natural conception in 7/2023 and referred to the Endocrine Clinic. The differential diagnosis were TSH resistance, familial dysalbuminaemic hyperthyroxinaemia or TSHoma. Genetics test for THR gene and FDH were negative. TSHoma was highly suspected. At 25th week, the TSH was 1.86 ($0.15-2.7$) mIU/L, fT4 20 ($9.7-15.3$) pmol/L, fT3 7.6 ($3.2-5.1$) pmol/L. USS at 24th week showed normal fetal growth. As the fT4 was 30% above the ULN, she was treated with low dose of carbimazole. Her fT4 was around $1.12 \times$ till time of delivery. Her visual field was normal. She gained 10 kg at week 37. A healthy baby was born at full term in 5/2024. Alpha subunit, TRH stimulation test and anterior pituitary hormone test were arranged after delivery. Discussion: 1. The prolactin was raised at the beginning and macroprolactinoma was first suspected. Retrospectively, it can be due to the stalk effect. 2. She had discordant TFT before pregnancy which showed high fT4 and normal TSH. 3. The patient was pregnant. Alpha-subunit is raised in normal pregnancy and TRH stimulation test cannot be done. The genetics test can only detect 85% of thyroid hormone resistance caused by THR mutation. 4. TSHoma complicated pregnancy is a rare condition with only case reports available. For the fetal well-being, maintaining euthyroid state by anti-thyroid medication is beneficial though there is risk of enlargement of the TSHoma. In this case, there was incomplete information and mis-documentation during handover which further added the diagnostic difficulty.

THYROID AND PREGNANCY

1112175 - ASSOCIATIONS OF THYROGLOBULIN ANTIBODY WITH PREGNANCY OUTCOMES IN EUTHYROID WOMEN

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Introduction: Whether euthyroid women with thyroglobulin antibody (TgAb) positivity is associated with adverse pregnancy outcomes is still unclear. **Objective:** To investigate the association between TgAb and pregnancy outcomes in euthyroid women. **Methods:** Serum concentrations of thyroid-stimulating hormone (TSH), free thyroxine (fT4), thyroid peroxidase antibody (TPOAb), and TgAb were assessed in the first and third trimesters of pregnancy. Participants were categorized into four groups (TgAb-/TPOAb-, TgAb+/TPOAb-, TgAb+/TPOAb+ and TgAb-/TPOAb+ group). Thirteen pregnancy outcomes and two composite outcomes were investigated. Logistic regression models were employed to explore associations between TgAb and pregnancy outcomes. Stratified analysis was conducted based on TSH levels in early pregnancy ($0.1 \text{ mIU/L} \leq \text{TSH} \leq 2.5 \text{ mIU/L}$ and $2.5 \text{ mIU/L} < \text{TSH} \leq 4.0 \text{ mIU/L}$). The dose-response associations were evaluated by employing restricted cubic spline (RCS) regression. **Results:** A total of $58,247$ euthyroid pregnant women were included in this study. The prevalence of TgAb and TPOAb positivity was 18.9% and 11.5% respectively in euthyroid women during early pregnancy. Adjusting for confounders, the TgAb+/TPOAb- group exhibited a higher risk of preterm birth (aOR: 1.13 , $95\% \text{CI}$: $1.01-1.28$, $P=0.04$), and a lower risk of gestational diabetes mellitus (GDM) and gestational hypertension (aOR: 0.91 , $95\% \text{CI}$: $0.84-0.99$, $P=0.03$; aOR: 0.80 , $95\% \text{CI}$: $0.67-0.96$, $P=0.02$) in comparison to the TgAb-/TPOAb- group. Stratified analysis revealed these associations were significant only among women with TSH levels between $0.1-2.5 \text{ mIU/L}$ in the first trimester, not in those with TSH levels between $2.5-4.0 \text{ mIU/L}$. **Conclusions:** In euthyroid women, TgAb positivity is associated with a higher risk of preterm delivery and a lower risk of GDM and gestational hypertension. These associations existed only in women with a TSH level of $0.1-2.5 \text{ mIU/L}$ at early pregnancy. Attention should also be paid to the effect of TgAb on preterm birth in addition to TPOAb in euthyroid women.

THYROID AND PREGNANCY

1114265 - BISPHENOL A ALTERS THE EXPRESSION OF IODIDE AND THYROID HORMONE TRANSPORTERS IN THE PLACENTA OF PREGNANT RATS

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Introduction: Endocrine disruptors impair placental function by altering gene expression, hormone transport, and nutrient exchange, potentially affecting fetal development and pregnancy outcomes. Bisphenol A (BPA), a common plasticizer, has been linked to placenta-related complications such as preeclampsia, fetal growth restriction, miscarriage, and preterm birth. **Objective:** To evaluate the impact of BPA exposure during pregnancy on the gene/protein expression of thyroid hormone and iodide transporters in the placenta. **Methods:** Pregnant Wistar rats were treated with BPA (0.1 or 1 ppm) in drinking water throughout pregnancy. On gestational day 20, the placenta was collected for gene and protein expression evaluation through RT-PCR and Western Blot. Offspring and placental weights were measured to assess potential impairments in fetal development. **Results:** BPA exposure reduced the number of offspring at 0.1 ppm but did not significantly affect maternal weight. However, it lowered offspring birth weight, with the lowest dose causing significant body weight reduction despite increased placental weight. At 1 ppm, placental weight remained unchanged, yet offspring birth weight was still reduced, suggesting placental dysfunction. BPA also significantly decreased the mRNA expression of NIS and thyroid hormone transporters (Oatp4a1, Mct8, Mct10, Lat1, Lat2). NIS and MCT8 protein content were also reduced in BPA-exposed dams. **Conclusion:** BPA exposure disrupted placental gene expression/function by altering thyroid hormone and iodide transporter expression, potentially impairing fetal development.

THYROID AND PREGNANCY

1112257 - CENTRAL HYPOTHYROIDISM IN NEWBORNS OF MOTHERS WITH GRAVES' DISEASE. DIRECTING FOCUS WHERE NEONATAL HYPOTHYROIDISM SCREENING PROGRAMS ARE BLIND

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Introduction: Central Hypothyroidism (CH) may develop in newborns of uncontrolled hyperthyroid mothers. Unknowledge, absence of clinical expression and non-detection by TSH neonatal screening programs lead to underdiagnosis. **Objective:** 1) Describe our long-time experience with CH in the offspring of hyperthyroid mothers with Graves' disease. 2) Draw attention to a lesser-known entity. **Methods:** Retrospective study (from 1997 to 2022). Newborns with serum T4 < 8 ug/dL, FT4 < 0,9 ng/dL and normal/suppressed TSH and their respective mothers with hyperthyroidism due to Graves' disease, were evaluated. **Results:** Neonates: 15 newborns met CH diagnostic criteria; 13/15 full-term with 5/13 LWGA. An initial transient phase of hyperthyroidism was observed in 4/15. Levothyroxine was started in 13/15 at X(r) = 19 (2-124) days of life to at least 2 y/o. Long-term reassessment of thyroid function was made in 11/15 infants. Only 1 presented non-autoimmune primary hypothyroidism with decreased ultra-sonographic thyroid volume. Mothers: 14 (one twin) pregnant women with uncontrolled hyperthyroidism. No mother consulted during the first trimester. Antenatal diagnosis was made in 10 and post-delivery in 4 mothers. Only 50% of women achieved FT4 target levels on methimazole treatment at X(r) = 31.3(25.2-37.2) wksGA. **Conclusion:** To our knowledge, this is the largest series of CH diagnosed due to an exhaustive case finding, as in our country, neonatal screening program of hypothyroidism does not include T4/FT4. Prolonged follow-up of these newborns will allow diagnosing CH because it can even occur after a transient phase of hyperthyroidism, observed in 27% of them. In this series, most children did not present evident long-term functional or morphological thyroid damage, though we cannot rule out that subtle changes in the regulation of thyroid function might persist over time.

THYROID AND PREGNANCY

1114278 - EVALUATION OF THE SELENIUM CONTENT IN MAIN MULTIVITAMINS AND ITS SUPPLEMENTATION IN PREGNANT BRAZILIAN WOMEN

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Introduction: Selenium (Se) plays an essential role in protecting thyroid cells against oxidative stress, as well as in the activation and inactivation of thyroid hormones and placental health. Nutritional guidelines recommend a daily intake of 55-65 µg for pregnant women (PW) and the tolerable upper intake level of Se is a maximum of 255 µg per day. In Brazil, an important dietary source of Se is Brazil nuts, with an average portion providing between 50 and 100 µg. The average daily dietary intake of selenium in the Brazilian population varies widely, ranging from 24 µg to 155 µg, depending on the geographic region. Deficient levels of Se may lead to adverse maternal-fetal outcomes such as miscarriage, preterm birth, and low birth weight, while excessive levels may result in selenosis, causing nerve damage and increased mortality. **Objective:** This study aimed to evaluate the presence of Se in multivitamin supplements and quantify its concentration in supplements available in the Brazilian market. **Methods:** This study was conducted between June 15 and June 23, 2024, through an online search of multivitamin supplements recommended for PW in the Brazilian market. **Results:** A total of 38 types of multivitamin supplements for PW were identified, of which 32 contained Se, while 6 did not. The average selenium concentration was 42.65 µg, ranging from 20 µg to 100 µg. Among the Se-containing supplements, only five had amounts exceeding 65 µg, and none exceeded 255 µg. **Conclusion:** The analysis of multivitamin supplements for PW available in the Brazilian market revealed that most supplements contain Se. The average Se content in these supplements is below the recommended daily intake for PW. These findings highlight the need for a better evaluation of the pregnant population in Brazil, considering the country's significant dietary selenium intake. Routine supplementation may not always be necessary.

THYROID AND PREGNANCY

1113766 - GESTATIONAL HYPOTHYROIDISM PROMOTES DIET-INDUCED OBESITY IN THE ADULT OFFSPRING

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Introduction: Obesity, characterized by excessive adipose tissue and chronic low-grade inflammation, is a multifactorial condition influenced by overnutrition and prenatal factors. Emerging evidence suggests that adverse conditions during pregnancy, such as gestational hypothyroidism (HTX) – reduced maternal thyroxine levels – may increase offspring's obesity risk in adulthood. Maternal thyroid hormones are essential for fetal development, and HTX has been linked to adverse outcomes, including small-for-gestational-age (SGA) and large-for-gestational-age (LGA) neonates. Both SGA and LGA neonates are at higher risk for obesity later in life, but the effects of gestational HTX on adipose tissue biology and obesity susceptibility remain unclear. **Objective:** This study used a murine model to evaluate the impact of gestational HTX on birth weight distribution, adipose tissue characteristics, and obesity susceptibility. **Methods:** Birth weights were assessed, adipose tissue morphology analyzed, and expression of signature adipose tissue genes measured via RT-qPCR. Male offspring were exposed to a Western-like diet for 10 weeks to test obesity susceptibility. **Results:** HTX offspring exhibited an increased incidence of SGA and LGA neonates. They displayed obesity-associated traits, including hypertrophic adipocytes, adipose tissue inflammation, and metabolic dysregulation. When challenged with a Western-like diet, HTX offspring showed exacerbated weight gain, impaired glucose tolerance, and elevated blood triglycerides. **Conclusion:** These findings highlight the significant role of maternal thyroid hormones in shaping offspring metabolic health and underscore the heightened risk of obesity linked to gestational HTX. Understanding this relationship may inform interventions to mitigate obesity risk in affected offspring.

THYROID AND PREGNANCY

1112575 - HIGH TSH LEVELS IN PREGNANCY LOSS ARE UNDETECTED BY THE CURRENT STANDARD PRACTICE A CALL FOR REVISED SCREENING STRATEGIES

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Introduction: Pregnancy loss is the most common reproductive adverse event and affects > 30 million women each year. Current guidelines recommend TSH screening of infertile women and in pregnant women at risk of thyroid disorders. No guidelines address TSH screening in women experiencing pregnancy loss. **Objective:** We aimed to investigate the prevalence of high TSH in women experiencing pregnancy loss and if high TSH had been detected using the current guidelines. **Methods:** A prospective cohort study of women experiencing pregnancy loss at three Danish hospitals (November 2020 May 2024). Blood was collected at the time of pregnancy loss. Among women without known thyroid disease, we assessed the prevalence of TSH > 4 mIU/L (current guideline cut-off) and TSH > 6 mIU/L (proposed in ATA 2025 guidelines). Regional laboratory data from general practitioners and hospitals provided information on prior TSH measurements during the pregnancy, and whether a blood test had been drawn as part of the national first-trimester program (> 95% attendance). **Results:** Among 2,010 included women, 60 (3.0%) had a TSH > 4 mIU/L and 15 (0.7%) a TSH > 6 mIU/L. Of these, TSH had been measured in 8 of 60 (13.3%) and 3 of 15 (20.0%) during pregnancy. Only 16 of 60 (26.7%) with TSH > 4 and 3 of the 15 (20.0%) women with TSH > 6 mIU/L made it to the national first trimester blood test screening before their pregnancy loss. Two women had a TSH > 100 mIU/L. **Conclusion:** Women with pregnancy loss constitutes a black box in current screening programs. Using current practice, a minority of women with a high TSH had been tested during their pregnancy. Few would have been detected if TSH measurements were to be added to the national first trimester screening program. We suggest TSH screening of all women experiencing a pregnancy loss to avoid delayed diagnosis and improve future pregnancy outcomes.

THYROID AND PREGNANCY

1112226 - HYPOTHYROIDISM IN PREGNANCY: WHAT IS THE TSH TARGET DURING TREATMENT? A CASE-CONTROL STUDY

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Introduction: Hypothyroidism is a common dysfunction, especially in women of reproductive age. During pregnancy, it is associated with an increased risk of adverse outcomes. Although treatment is indicated, doubts persist about the best target level of thyroid-stimulating hormone (TSH). **Objective:** This study aims to compare maternal and fetal outcomes in pregnant women with primary hypothyroidism, treated with levothyroxine (LT4), maintained with mean TSH levels less than or equal to ($\leq$) 2.5 mIU/L or between 2.5 and 4.0 mIU/L. **Methods:** This was a retrospective case-control study of pregnant women with primary hypothyroidism treated with LT4. Simple arithmetic means were calculated with 4 dosages of TSH and free thyroxine after the 12th week of gestation. The “case” group included patients maintained with mean TSH between 2.5 and 4.0 mIU/L, and the “control” group consisted of pregnant women with mean TSH $\leq$ 2.5 mIU/L. Maternal and fetal outcomes were compared between the two groups. **Results:** 372 medical records were analyzed and 129 patients (34.7%) were selected, classified as control group [n=73 (56.5%)] or “case” group [n=56 (43.4%)]. Eighty-one (62.8%) patients presented some negative outcome in their pregnancy and an unfavorable fetal outcome occurred in 41 (31.8%) cases. When comparing the groups, the case group started follow-up at the specialized service later ($p < 0.001$), had higher TSH ($p < 0.001$) and had a lower percentage of cases in which thyroidectomy was the cause of the dysfunction ($p = 0.0427$). In fetal outcomes, the case group had higher birth weight ($p = 0.0311$) and higher Apgar score at the 10th minute ($p = 0.0143$), in addition to not presenting any cases of acute fetal distress ($p = 0.0458$). **Conclusions:** High percentages of unfavorable maternal and fetal outcomes were observed. TSH between 2.5 and 4.0 mIU/L was associated with better fetal outcomes, while no association was observed between TSH level and maternal repercussions.

THYROID AND PREGNANCY

1114291 - MATERNAL NITRATE EXPOSURE DISRUPTS PLACENTAL IODIDE TRANSPORT AND IMPAIRS FETAL DEVELOPMENT

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Introduction: The placenta plays a crucial role in transferring iodide and thyroid hormones from the mother to the fetus, supporting fetal growth and central nervous system development. Nitrate, a well-known endocrine disruptor, disrupts iodide transport in the thyroid. Since the placenta also expresses the sodium/iodide symporter, nitrate exposure may interfere with iodide transfer to the fetus, potentially leading to thyroid hormone imbalances during a critical developmental period. **Objective:** To evaluate the effects of nitrate exposure during pregnancy on placental expression of iodide and thyroid hormone transporters and its impact on offspring development. **Methods:** Pregnant Wistar rats were treated with sodium nitrate (20 or 50 ppm) in drinking water throughout pregnancy. On gestational day 20, placentas were collected for gene and protein expression analysis using RT-PCR and Western Blot. Offspring and placental weights were measured to assess potential impairments in fetal development. **Results:** Maternal nitrate exposure at both doses during pregnancy led to reduced maternal weight throughout gestation and decreased offspring birth weight, while litter size and placental weight remained unchanged. Pregnant rats exposed to nitrate showed increased gene and protein expression of NIS at both doses. Additionally, exposure to 50 ppm reduced MCT8 gene/protein expression. Lastly, Lat2 mRNA expression was elevated in placental tissue, but only at the highest treatment dose. It is worth noting that Mct10, Lat1, and Oatp4a1 were not altered in the placenta of nitrate-exposed animals. **Conclusion:** Maternal nitrate exposure reduced maternal and offspring weight and altered placental transporter expression, suggesting disrupted iodide and thyroid hormone transfer. These findings underscore nitrate's potential to impair thyroid hormone production and action during fetal development.

THYROID AND PREGNANCY

1112377 - MATERNAL TRIIODOTHYRONINE AS A PREDICTOR OF GESTATIONAL DIABETES. A PROSPECTIVE STUDY IN CUBA

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Introduction: Insulin resistance and alterations in glucose homeostasis characterize gestational diabetes mellitus. Thyroid hormones are involved in carbohydrate metabolism by several mechanisms. **Objective:** To identify the association between thyroid function variables and gestational diabetes. **Methods:** A prospective analytical study was carried out with 354 healthy pregnant women from the Plaza municipality in Havana, Cuba, who were divided into two groups: women with normal glucose tolerance and women with gestational diabetes mellitus. The factors associated with the presence of gestational diabetes were inquired about and the predictive variables of this disease were determined by means of a logistic regression analysis. **Results:** Of all the women studied, 36 had gestational diabetes mellitus (10.2%). Higher means of maternal age ($p=0.05$), pregestational body mass index ($p=0.02$), total T3 ($p=0.02$), free T3 ($p=0.00$), total T3 /total T4 ratio ($p=0.03$) and free T3/free T4 ratio ($p=0.01$) were significantly associated with gestational diabetes. In logistic regression, free T3 was identified as an independent predictor of gestational diabetes [Exp. (β)=1.925; $p=0.03$]. **Conclusion:** High free T3 is an independent predictor of gestational diabetes in healthy pregnant women with iodine sufficiency.

THYROID AND PREGNANCY

1112662 - MOLECULAR MECHANISMS UNDERLYING THE IMPACT OF GESTATIONAL HYPOTHYROXINEMIA ON THE T REGULATORY LYMPHOCYTE FUNCTION IN OFFSPRING INDUCED WITH EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS

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Introduction: Maternal hypothyroxinemia (HTX), characterized by low thyroxine (T4) levels with normal levels of triiodothyronine (T3) and thyroid-stimulating hormone (TSH), negatively affects the offspring (HTX-offspring) when exposed to an immune challenge through experimental autoimmune encephalomyelitis (EAE). These offspring exhibit early onset of symptoms and reduced immunosuppressive function of regulatory T lymphocytes (Treg). The immunosuppressive function of Tregs is closely related to the expression of Treg-specific biomarkers and mitochondrial metabolism. This study evaluates the molecular mechanisms responsible for the reduced suppressive capacity of Tregs of HTX-offspring. **Methods:** HTX was induced in pregnant C57BL/6 mice by methimazole (MMI) administration. Adult HTX-offspring were challenged with EAE and euthanized 10 days post-EAE. Treg lymphocytes were isolated from the spleens to evaluate Tregs-biomarkers, such as CD25 and CTLA-4 expression, by flow cytometry. Serum levels of IL-17A were quantified by ELISA. Mitochondrial membrane potential (MMP), mitochondrial biomass, and morphology were analyzed by flow cytometry and confocal microscopy, respectively. Oxygen consumption rate (OCR) and ExtraCellular Acidification Rate (ECAR) were assessed by SeahorseXFPro Analyzer. Mitochondrial dynamics and glycolytic profile were analyzed by RT-qPCR. This study was approved by the bioethics committee of Universidad Andrés Bello. **Results:** HTX-offspring challenged with EAE showed elevated serum IL-17A levels, suggesting increased inflammatory response. Treg lymphocytes from HTX-offspring challenged with EAE showed reduced surface expression of CTLA-4 and CD25 and increased intracellular expression of these markers. MMP, OCR, and ECAR were similar compared to controls. Glycolytic and mitochondrial mRNA expression levels were comparable between groups. Mitochondrial biomass and morphology were similar between all experimental groups, rod- and puncta-like structures in all Treg lymphocytes. **Conclusions:** HTX promotes an increase in systemic inflammation and affects the function of regulatory T lymphocytes of offspring, altering the expression of key suppressor phenotype markers, despite similar mitochondrial activity. Funding: FONDECYT #1231905 and #1191300; FONDEQUIP EQM220115; IMII ICN2021_045

THYROID AND PREGNANCY

1113743 - MOLECULAR MECHANISMS UNDERLYING THE IMPACT OF GESTATIONAL HYPOTHYROXINEMIA ON THE T REGULATORY LYMPHOCYTES FUNCTION IN OFFSPRING INDUCED WITH EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS

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Introduction: Maternal hypothyroxinemia (HTX), characterized by low thyroxine (T4) levels with normal levels of triiodothyronine (T3) and thyroid-stimulating hormone (TSH), negatively affects the offspring (HTX-offspring) when exposed to an immune challenge through experimental autoimmune encephalomyelitis (EAE). These offspring exhibit early onset of symptoms and reduced immunosuppressive function of regulatory T lymphocytes (Treg). The immunosuppressive function of Tregs is closely related to the expression of Treg-specific biomarkers and mitochondrial metabolism. This study evaluates the molecular mechanisms that could be responsible for reduced suppressive capacity of Tregs of HTX-offspring. **Objective:** To evaluate molecular mechanisms underlying the impact of gestational hypothyroxinemia on the Treg lymphocytes function in offspring induced with EAE. **Methods:** HTX was induced in pregnant C57BL/6 mice by methimazole (MMI) administration. Adult HTX-offspring were challenged with EAE and euthanized 10 days post-EAE, Treg lymphocytes were isolated from the spleens to evaluate Tregs-biomarkers such as CD25 and CTLA-4 expression, by flow cytometry. Serum levels of IL-17A, were quantified by ELISA. Mitochondrial membrane potential (MMP), mitochondrial biomass and morphology were analyzed by flow cytometry and confocal microscopy respectively. Oxygen consumption rate (OCR) and ExtraCellular Acidification Rate (ECAR) were assessed by SeahorseXFPro Analyzer. Mitochondrial dynamics and glycolytic profile were analyzed by RT-qPCR. This study was approved by the bioethics committee of Universidad Andrés Bello. **Results:** HTX-offspring challenged with EAE showed elevated serum IL-17A levels suggesting an increased inflammatory response. Treg lymphocytes from HTX-offspring challenged with EAE showed reduced surface expression of CTLA-4 and CD25 and increased intracellular expression of these markers. MMP, OCR, and ECAR were similar compared to controls. Glycolytic and mitochondrial mRNA expression levels were comparable between groups. Mitochondrial biomass and morphology were similar between all experimental groups, rod- and puncta-like structures in all Treg lymphocytes. **Conclusion:** HTX promotes an increase in systemic inflammation and affects the function of Tregs altering expression key suppressor-phenotype markers

THYROID AND PREGNANCY

1112507 - MORPHOLOGICAL AND FUNCTIONAL CHANGES OF THE THYROID DURING PREGNANCY: CASE OF PREGNANT WOMEN IN THE TOWN OF GBADOLITE/RD CONGO

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Introduction: The occurrence of goiter at pregnant women limits the clinicians field of intervention, both for diagnosis and therapeutic management. The current study aimed to describe the clinical and ultrasound aspects of the Thyroid and repercussions of goiter on pregnancy. **Methods:** This was a cross-sectional study of 60 pregnant women with goiter who were examined between June 2022 and June 2023 in the District hospital of Gbadolite/DR Congo. Parameters of interest included age, marital status, parity, family history of goiter, thyroid hormones and TSH measurements, ioduria rate, thyroid ultrasound. **Results:** The mean age was 32.2+/-4.9 years. More than 60% of participants consulted in the first trimester of pregnancy. Thyroid function revealed the disturbance in 35% in the first trimester ($p=0.02$). Ultrasound showed nodular or multinodular goiters in 85%. The prevalence of clinical hypothyroidism (high TSH & low T4) was 1%; subclinical hypothyroidism (TSH & normal T4) was 4%. Hyperthyroidism was found in 5% and was accompanied by uncontrollable vomiting in 72% of cases. The majority of multiparous women had ioduria < 100 ug/day. 81% of goiters were regressive in post-partum and 16% of goiters were persistent and progressive in post-partum. **Conclusion:** The current study reveals that goiter occurs more frequently during the first trimester of pregnancy. Most of goiters are regressive in post-partum; however, some cases persistent and involve to different stages of goiter.

THYROID AND PREGNANCY

1112413 - PREDICTIVE FACTORS FOR THYROTROPIN AND THYROID HORMONES IN CUBAN PREGNANT WOMEN

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Introduction: Thyrotropin and thyroid hormone values change during pregnancy, due to the physiological changes that occur in the function of the gland and clinical, biochemical and analytical factors that vary from one region to another. **Objective:** To identify predictive factors for thyrotropin and thyroid hormones in Cuban pregnant women. **Methodology:** a cross-sectional study was carried out with 362 healthy pregnant women. The following variables were examined: maternal age, gestational age, skin color, current smoking status, parity, use of iodinated supplements, body mass index, thyrotropin, total and free thyroid hormones, thyroglobulin, antithyroid antibodies, chorionic gonadotropin, cholesterol and triglycerides. **Results:** Chorionic gonadotropin (corrected $R^2=0.13$; $p=0.000$) was found as a predictive factor for thyrotropin; for total thyroxine (tT4), total triiodothyronine (tT3) and free thyroxine (fT4) (corrected $R^2=0.13$; $p=0.000$); for fT4, gestational age, tT4 and tT3 (corrected $R^2=0.24$; $p=0.03$); for tT3, tT4, body mass index and fT4 (corrected $R^2=0.12$; $p=0.00$); and for fT3 gestational age (corrected $R^2=0.05$; $p=0.00$). **Conclusions:** Thyroid function parameters were associated with some clinical and biochemical factors, particularly with gestational age and hormones.

THYROID AND PREGNANCY

1112256 - PRELIMINARY EXPERIENCE WITH ORALLY LUGOL[®] SOLUTION IN PATIENTS WITH HYPERTHYROIDISM DUE TO GRAVES' DISEASE IN FIRST TRIMESTER OF PREGNANCY. REPORT OF 10 CASES

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Introduction: Rapid control of hyperthyroidism during the early pregnancy reduces miscarriage rate. Avoiding the use of thionamides during the first trimester also prevents the increased risk of associated malformations. Replacement of thionamides by potassium iodide was reported in Japan, without any deleterious effects for mothers and neonates. To date, its efficacy in regions with lower iodine intake is unknown. **Objective:** To evaluate efficacy of Lugol's solution (LS) to control moderate hyperthyroidism due to Graves' disease in early pregnancy. **Methods:** Ten pregnant women with hyperthyroidism due to Graves disease were treated with orally 3% LS (Iodine 24-48 mg/day). LS as the only therapy was initiated before 7 weeks of gestation (wksGA) in 6 patients and between 9-10wksGA in 3. The remainder patient started LS + methimazole at 13wksGA. FT4 (1st trimester RV: 0.82-1.00; by QL) and TSH (1st trimester RV: 0.39-3.48; by QL) were weekly measured. Statistical analysis: Student T test. **Results:** Age X(r) = 31 y/o (27-42). Baseline thyroid status: FT4 ($\bar{x} \pm DS$) = 4.08 ± 1.7 ng/dL vs post LS FT4 levels ($\bar{x} \pm DS$) = 1.54 ± 0.4 ng/dL ($p < 0.0002$). A decrease in FT4 levels between 31,2 and 85% was observed after 2 weeks of LS treatment. One patient escaped from the Wolff-Chaikoff effect when LS dose was reduced on 11 wksGA, concomitantly with a remarkable increase in TRAb levels. TSH remained suppressed throughout the follow up in all patients. **Conclusion:** With a limited number of cases, LS therapy was effective in pregnant women with moderate hyperthyroidism due to Graves' disease during early pregnancy. LS promptly reduced FT4 levels and achieved a successful control of hyperthyroidism during the organogenesis period, avoiding exposure to potential teratogenic effects of thionamides.

THYROID AND PREGNANCY

1114118 - PSYCHOTIC HUNGRY STORM

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Case Presentation: A 29-year-old woman with Graves' disease discontinued antithyroid drugs during pregnancy without complications. However, postpartum presented with weight loss, irritability, coprolalia, verbosity, megalomania, increased libido to the point of hypersexuality, anxiety, insomnia, delusional thoughts, hallucinations, and heteroaggressive thoughts, even attempting to suffocate her baby. She was taken to a psychiatric hospital where she was diagnosed with psychomotor agitation, possible organic psychosis, and hyperthyroidism. She was prescribed antipsychotics and antithyroid drugs. Due to her poor outcome, she was transferred to a general hospital and classified as "thyroid storm with psychotic symptoms," with a Burch-Wartofsky score of 60, due to central nervous system involvement, unexplained jaundice, tachycardia, and pharyngotonsillar infection as the precipitating event. Given the poor response to management, with a slight decrease in circulating thyroid hormones and partial remission of psychotic symptoms, total thyroidectomy was decided upon as definitive treatment. Postoperatively, the psychotic symptoms resolved, but the patient presented with "hungry bone syndrome," which resolved with calcium supplements and levothyroxine, leading to a prolonged hospital stay. **Discussion:** The unusual presentation of thyroid storm and psychotic symptoms in a post-pregnancy relapse of Graves' disease, with no prior history of psychiatric problems, illicit substance use, or aggressive personality, with reversal of symptoms after surgical management, confirms the involvement of thyrotoxicosis and related autoimmunity. The hungry bone syndrome presented as a postoperative complication could be related to the severity of the thyrotoxicosis given the lack of regulation of osteoclasts and osteoblasts, also considering that the patient did not receive prophylactic medication to prevent the condition. **Final Comments:** This case demonstrates the importance of monitoring autoimmune thyroid diseases during pregnancy and postpartum, as well as preventing potential complications after emergency thyroidectomy due to unregulated calcium metabolism.

THYROID AND PREGNANCY

1114177 - REVISITING FREE T4 MEASUREMENT IN PREGNANCY: NOVEL EQUILIBRIUM DIALYSIS-LC-MS/MS CONFIRMS TRIMESTER-SPECIFIC DECLINES INDEPENDENT OF IMMUNOASSAY INTERFERENCE

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Introduction: Accurate measurement of free thyroxine (FT4) levels during pregnancy is essential due to pregnancy-induced physiological and biochemical changes that significantly affect thyroid function, including elevations in human chorionic gonadotropin (hCG) and thyroxine-binding globulin (TBG). During the first trimester, the structural similarity between hCG and thyroid-stimulating hormone (TSH) can cause variations in FT4 and TSH concentrations, complicating clinical assessment. Indirect immunoassays (IMA), widely used in routine clinical practice, encounter limitations during pregnancy, mainly due to altered concentrations and binding capacities of serum proteins. These assays may yield inaccurate FT4 measurements, emphasizing the need for reliable and precise analytical techniques unaffected by protein-binding variations. **Objective:** This study aims to validate and compare a new equilibrium dialysis (ED) combined with liquid chromatography-tandem mass spectrometry (LC-MS/MS) free T4 method with a commercial Immunoassay (IMA) in pregnant women. **Methods:** FT4 was measured by a novel ED-LC-MS/MS and by a commercial IMA with samples of 291 euthyroid (TSH in the range for trimester, negative antibodies, without medications) pregnant women, categorized by trimesters. **Results:** The developed ED LC-MS/MS method displayed robust analytical performance, with high sensitivity and precision. Notably, the value comparison between assays unexpectedly differed ($p < 0.001$); FT4 concentrations measured by ED LC-MS/MS were consistently higher. They demonstrated significant discrepancies over the IMA across all trimesters, underlining IMA limitations. Considering the correlation obtained through the linear regression correlation coefficient, the expectation was that $r = 0.79$ and $R^2 = 0.62$, $p < 0.001$. However, Bland-Altman analysis showed concordance between the two assays. Besides, there is a decline in FT4 levels for both assays by gestational weeks with Smoothed Curves. **Conclusion:** Results showed a trimester-dependent decline in FT4 for both methods. Despite IMA's TBG sensitivity, patterns were similar, suggesting pregnancy-related changes. These findings highlight the need for trimester-specific FT4 reference ranges across all measurement methods.

THYROID AND PREGNANCY

1112173 - THE EFFECT OF THYROID HORMONES ON COAGULATION SYSTEM DURING LATE PREGNANCY IN A CHINESE POPULATION

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Introduction: The exact mechanism of hemostasis in thyroid dysfunction has not been fully elucidated. Thyroid function may have a direct or indirect effect on platelet maturation and function, synthesis and activity of coagulation factors as well as altered blood viscosity. **Objective:** Whether maternal free thyroxine (FT4) and thyrotropin (TSH) levels in late pregnancy are associated with coagulation parameters. **Methods:** A total of 12,909 women with singleton pregnancies in our hospital were enrolled in this study. Each patient provided serum samples for analyses of thyroid function in late pregnancy. Available patient data for analysis included: maternal age, parity, educational levels, maternal anthropometrics, FT4, TSH, thyroperoxidase antibody (TPOAb), activated partial thromboplastin time (APTT), prothrombin time (PT), D- dimer and thrombin time (TT). **Results:** After adjusting for maternal age, BMI, parity, education levels, sex of the fetus and TPOAb titers, FT4 levels were found to be positively correlated with PT ($\beta = 0.028$, $p < 0.0001$), and inversely correlated with D- dimer ($\beta = -0.026$, $p = 0.003$). Additionally, TSH levels were inversely correlated with APTT ($\beta = -0.11$, $p = 0.006$) and positively correlated with D- dimer levels ($\beta = 0.032$, $p = 0.015$). There was no significant association between FT4 and TT as well as TSH and TT. **Conclusion:** Maternal thyroid function is closely related with APTT, PT and D-dimer measurements in late pregnancy. High thyroid hormone levels may contribute to bleeding.

THYROID AND PREGNANCY

1114127 - THE EFFECTS OF LEVOTHYROXINE DURING PREGNANCY ON FETAL VITALITY IN CASES OF SUBCLINICAL HYPOTHYROIDISM: A META-ANALYSIS

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Introduction: During pregnancy, physiological changes in thyroid function may lead to hypothyroidism, with subclinical hypothyroidism (SCH) being the most common form. SCH is characterized by elevated TSH levels with normal free T4 and has been associated with adverse obstetric outcomes such as pregnancy loss, preterm birth, and fetal growth restriction. Levothyroxine (LT4) treatment is recommended by some guidelines, but its efficacy and safety remain under debate. **Objective:** To evaluate the efficacy of levothyroxine in pregnancies complicated by SCH, focusing on outcomes such as live birth rate and pregnancy loss. **Methods:** A systematic review with meta-analysis of randomized controlled trials (RCTs) was conducted using the PubMed database. The search included the descriptors "subclinical hypothyroidism," "pregnancy," "levothyroxine," and "randomized controlled trial." Two RCTs were included, totaling 1,780 pregnant women, comparing LT4 with placebo or no treatment. Statistical analyses were performed using RevMan 5.4 software, calculating odds ratios (OR), 95% confidence intervals (95% CI), and heterogeneity using the I² statistic. **Results:** LT4 use was associated with a significantly higher live birth rate (OR: 1.61; 95% CI: 1.30-2.01; p < 0.0001), with low heterogeneity (I² = 0%), reinforcing the consistency of this finding. Regarding pregnancy loss, a favorable trend toward LT4 treatment was observed (OR: 0.02; 95% CI: 0.00-7.72), though without statistical significance (p = 0.21), and with high heterogeneity (I² = 93%), limiting interpretation. The limited number of included studies and events may explain the wide confidence interval. **Conclusion:** Levothyroxine treatment in pregnant women with SCH is associated with increased live birth rates. Although the reduction in pregnancy loss was not statistically significant, the trend suggests potential benefit. Additional high-quality studies are needed to confirm these findings and support evidence-based recommendations in clinical practice.

THYROID AND PREGNANCY

1113885 - THYROID STORM IN A PARTIAL HYDATIDIFORM MOLE: A CASE REPORT

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Case Presentation: This case report presents a 23-year-old, female, primigravid, diagnosed with hydatidiform mole presenting with vomiting and increase bowel movement, associated with body malaise, palpitations, excessive sweating, and heat intolerance. The patient was examined febrile at 38.8 °C and heart rate of 133 beats per minute. She was managed as thyrotoxicosis secondary to hydatidiform mole, in storm, with a Burch-Wartofsky score of 55. Thyroid panel showed evidence of thyrotoxicosis with suppressed TSH at 0.0105 uIU/mL (0.35-4.94 uIU/mL) and elevated fT3 and fT4 at >20 pg/mL (1.88-3.18 pg/mL) and >5 ng/dL (0.7-1.48 ng/dL), respectively. Beta HCG was substantially elevated at 225,000 mIU/mL (5-25 mIU/mL). Patient was given propylthiouracil, propranolol and hydrocortisone, and eventually, underwent suction curettage. Surgical pathology report revealed vesicular tissue compatible with partial hydatidiform mole. **Discussion:** In molar pregnancies, there is marked elevation of beta-human chorionic gonadotropin (b-hCG) due to increased production by the hyperplastic trophoblastic tissue. And because beta-hCG and thyroid-stimulating hormone (TSH) are structurally homologous in their alpha subunits, elevated beta-hCG leads to increased stimulation of the thyroid gland to produce T4 and T3 leading to hyperthyroidism. Despite having elevated thyroid hormone levels, most molar pregnancies do not present with clinical hyperthyroidism. And this could be attributed to varied increased sensitivity of the TSH-receptors and hCG isoforms or variants which are more potent receptor activators. **Final Comments:** Thyroid storm is a life threatening condition where prompt recognition and management is essential. Although, surgical evacuation is the cornerstone for management of hydatidiform mole, medical management of hyperthyroidism is equally important in preventing adverse maternal outcomes and further exacerbation of ongoing thyroid storm.

THYROID AND PREGNANCY

1113826 - TRANSIENT GESTATIONAL HYPOTHYROIDISM DISRUPTS HYPOTHALAMIC-PITUITARY-ADRENAL AXIS RESPONSES AT BASELINE AND AFTER ULCERATIVE COLITIS IN ADULT OFFSPRING

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Introduction: Maternal thyroid hormones (THs) are essential for fetal development, as early growth depends entirely on maternal THs. Hypothyroidism (HTX), common in pregnancy, increases offspring susceptibility to inflammation. HTX-offspring show exacerbated autoimmune encephalomyelitis and ulcerative colitis. Glucocorticoids (GCs), key immunosuppressors, are regulated by the hypothalamic-pituitary-adrenal (HPA) axis, which THs influence. Studies evidence that TH deficiency in mice reduces CRH, ACTH, and adrenal steroidogenesis, while thyroidectomized fetal sheep show adrenal atrophy. In humans, congenital hypothyroidism links to altered cortisol precursors. We propose that gestational HTX impairs HPA axis function, worsening UC. Our findings reveal, for the first time, deficient corticosterone, adrenal changes, and impaired feedback, highlighting gestational HTX influence on offspring stress regulation. **Objectives:** Specific aims: 1 - To assess HPA axis hormones and steroidogenic enzyme gene expression in HTX-exposed offspring with ulcerative colitis; 2 - To assess adrenal gland structural changes in HTX-exposed offspring with ulcerative colitis. **Methods:** Pregnant C57BL/6 mice received methimazole (0.025% w/v) from embryonic days 10-14 to induce HTX. Offspring were compared to controls gestated under normal T4 levels. Stress-related behavior was assessed using the marble-burying test. At postnatal day 55, offspring received 2% DSS for seven days to induce ulcerative colitis. To achieve the specific aims, serum ACTH and corticosterone were measured by ELISA, hypothalamic CRH mRNA by RT-qPCR, and adrenal steroidogenic enzyme mRNA by RT-qPCR. Colon and adrenal histopathology were analyzed using hematoxylin/eosin staining. **Results:** HTX-offspring buried fewer marbles, had lower basal ACTH levels, and showed reduced corticosterone (CORT) levels after UC. Adrenal glands were heavier, but histological and gene expression analyses revealed no significant changes in steroidogenic enzyme expression. **Conclusion:** Our findings reveal for the first time that gestational HTX disrupts HPA axis function and adrenal adaptation in offspring, leading to impaired ACTH and corticosterone responses. These results highlight the essential role of maternal thyroid hormones in programming the offspring's stress axis.

THYROID AND PREGNANCY

1114084 - UNIVERSAL MATERNAL HYPOTHYROIDISM SCREENING USING FILTER PAPER SPECIMENS IN 16.740 BRAZILIAN WOMEN

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Introduction: The use of Dried blood specimens (DBS) specimens is a cost-effective method of screening for hypothyroidism. **Objective:** We report our experience of screening PW for thyroid dysfunction in 88 municipalities from south of Bahia, Brazil. **Methods:** DBS samples were collected onto filter paper cards using the standard lancet finger prick method. The TSH and Total T4 (tT4) levels were analyzed with a time-resolved fluoroimmunoassay method. PW were categorized in 6 groups: (i) Normal, (ii) Overt hypothyroidism (OH): TSH >5.0 mIU/L and tT4 < 3 nmol/L, (iii) Subclinical hypothyroidism (SCH): TSH >5.0 mIU/L and tT4 >3 nmol/L, (iv) Isolated maternal hypothyroxinemia (IMH), (v) Overt hyperthyroidism (Ohyper), (vi) Subclinical hyperthyroidism (SCHyper). For DBS-tT4: 65-165 nmol/L. PW with abnormal results had confirmatory serum tests. **Results:** 16.740 women were analyzed. Trimester distribution: (i) first (67.1%), second (13.2%), third (19.5%). Age ranged from 11 to 50 years old, with a mean of 26.2±6.8 years. The median TSH was 0.8 mIU/L and the mean was 1.15±1.46 mIU/L (interquartile range [IQR]: 0.4-1.5 mIU/L). The median tT4 was 8.6 nmol/L and the mean was 8.97 ± 3.33 nmol. PW were categorized as: (i) Normal Thyroid function (16.437 of 16.740, 98.2%), (ii) OH (7 of 16.735, 0.04%), (iii) SCH (164 of 16.740, 0.97%), (iv) IMH (99 of 16.735, 0.59%), (v) Ohyper (0 of 16.740) and (vi) SCHyper (33 of 16.740, 0.19%). Age <25 years-old was associated with both 39% less risk of a TSH greater than 5 mIU/L [OR 0.61 (95% CI 0.44-0.83, P=0.001)] and diagnosis of HSC [OR 0.61 (95% CI 0.45-0.84, P=0.002)]. **Conclusion:** Universal DBS filter paper screening showed a low rate of OH and SCH. Women under 25 years-old had less risk of hypothyroidism. This strategy could be implemented for routine testing early in pregnancy after proper validation studies.

1112604 - EVALUATION OF TSH LEVELS DURING IN VITRO FERTILIZATION WITH FREEZE-ALL CYCLES AND THE FIRST TRIMESTER OF PREGNANCY IN EUTHYROID WOMEN

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Introduction: Thyroid function disorders may occur during ovarian stimulation, even in euthyroid patients. **Objectives:** To analyze the dynamics of the pituitary-thyroid axis through variation of thyroid hormones during ovarian stimulation (COS) in euthyroid women. **Methods:** Observational, prospective study involving 308 euthyroid women (baseline TSH < 2.5 mUI/L) who underwent COS with dydrogesterone as a pituitary blockade. Only freeze-all cycles were evaluated. TSH levels were measured at 7 different time points: D0 (up to 30 days before stimulation), D1 (on the day of GnRH agonist analogue application for triggering), D2 (at endometrial preparation beginning); D3 (the day of embryo transfer); D4 (pregnancy confirmation), and at 30 (D5), 60 (D6) and 90 days (D7) post-embryo transfer if pregnancy was achieved. **Results:** The mean age was 37.8±3.85 years. 166 women (53.8%) became pregnant after in vitro fertilization (IVF). 10.1% of women had TSH > 2.5 mUI/L at D2, and 4.3% at D7. Only 1 patient had TSH > 4.0 mUI/L at D7. Additionally, 8.3% of patients had positive TPO-Ab, and 5.5% positive for TgAb. Mean TSH and respective standard deviations remained < 2.5 mUI/L at all time points. TSH levels were statistically different between negative and positive TPOAb women only on D7: 1.41±0.62 x 1.04 ±0.40 mUI/L, respectively (p=0.03). In relation to negative and positive TgAb women, TSH was statistically different on D3 (1.81±0.78 x 1.27±0.77 mUI/L); D4 (1.86±0.85 x 1.15±0.34 mUI/L) and D5 (1.42±0.68 x 0.88±0.52 mUI/L), respectively. **Conclusion:** Mean TSH levels did not alter during IVF with freeze-all cycles. Antithyroid antibodies did not influence TSH levels after COS and during the first trimester of pregnancy. Surprisingly, higher values of TSH at certain points of dosage in women who had negative TPOAb or TgAb. These findings suggest that routine thyroid function assessment may not be necessary during assisted reproduction treatments in freeze-all cycles.

THYROID AND REPRODUCTION

1113698 - THYROID DYSFUNCTION IN POSTMENOPAUSAL WOMEN AND ITS ASSOCIATION WITH GYNECOLOGIC HISTORY: A CROSS-SECTIONAL STUDY IN VIETNAM

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Introduction: Thyroid dysfunction is a critical health concern in postmenopausal women. However, the need for routine thyroid screening in this population remains debated. Given the complex interplay between the thyroid gland and the gonadal axis, evidence suggests substantial alterations in thyroid function across reproductive stages. **Objective:** To determine the prevalence of thyroid dysfunction and its associated factors in postmenopausal women, with a particular focus on gynecologic history. **Methods:** A cross-sectional study was conducted on 742 postmenopausal women in Vietnam aged 50-90 years from April 2024 to February 2025. Data on sociodemographic factors, gynecologic history, and thyroid function were collected. Logistic regression analyses identified factors associated with thyroid dysfunction. **Results:** The prevalence of thyroid dysfunction was 29.5% (95% CI: 26.4-32.9%), comprising hypothyroidism (16%, 95% CI: 13.4-18.7) and hyperthyroidism (13.6%, 95% CI: 11.4-16.3). The prevalence of hypothyroidism increased with age; however, no age-related distribution was observed for hyperthyroidism. Diabetes mellitus was associated with an increased odds of both hypothyroidism (OR = 1.88, p = 0.018) and hyperthyroidism (OR = 2.56, p = 0.021). The odds of hypothyroidism were 1.67 times higher in individuals with hypertension (=0.045). Secondary menopause, and multiparity (≥6 births) were significantly associated with a higher likelihood of hypothyroidism (OR = 2.20, p = 0.047; OR = 2.43, p = 0.023, respectively). **Conclusion:** Thyroid dysfunction is common among postmenopausal women and is associated with diabetes, hypertension, and reproductive history. Routine thyroid screening is recommended for high-risk postmenopausal women to facilitate early diagnosis and optimal management.

THYROID AUTOIMMUNITY

1112315 - ABLATIVE VS CONSERVATIVE APPROACH FOR HYPERTHYROIDISM TREATMENT IN PATIENTS WITH GRAVES' ORBITOPATHY

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Introduction: Optimal treatment for Graves hyperthyroidism (GH) in patients with Graves orbitopathy (GO) is a matter of debate. We investigated the outcome of GO following intravenous glucocorticoids (ivGCs) in patients treated with a conservative vs an ablative approach. **Methods:** Retrospective investigation in patients with GH and moderate-to-severe, active GO. Patients were offered an ablative [radioactive iodine (RAI) or thyroidectomy (Tx); ABL group] or conservative [methimazole (MMI); MMI group] treatment. Fifty-two consecutive patients were studied, 50 of whom (25 per group) included in the analysis. All patients were treated with ivGCs. Primary endpoint was overall outcome of GO (composite evaluation) at week-24. **Results:** The proportion of responders for week-24 overall GO outcome was greater in ABL (52% vs 16%; OR5.68; 95%CI from 1.5 to 21.4; P=0.0102). Responders increased in MMI at week-48 and -72, with no differences between groups. Anti-TSH receptor antibodies (TRAbs) decreased in MMI across the follow-up, whereas they increased in ABL at week-24, to then progressively decrease up to week-72. TRAbs were associated with GO response to treatment, being their levels lower in overall GO responders at week-72. There was a trend to a better response in ABL for individual eye features. Quality of life questionnaire responders at week-24 were trendily more in ABL, but similar in the two groups later. At week-24 one patient (4%) in ABL and three (12%) in MMI worsened. Ninety-five adverse events were recorded in 50 patients, with no difference between groups except for infections (more common in ABL). **Conclusion:** An ablative approach to GH treatment is followed by an earlier response of GO to ivGCs. In the long run, a conservative approach is effective to a similar extent. Thus, both approaches can be offered to patients. RAI can be given safely to GO patients. Randomized clinical trials are needed to confirm these conclusions.

THYROID AUTOIMMUNITY

1113943 - ASSOCIATION OF DIFFERENT INTRA-ORBITAL LYMPHOCYTE INFILTRATES WITH CLINICAL PHENOTYPES OF THYROID EYE DISEASE

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Introduction: Thyroid Eye Disease (TED) is characterized by an active inflammatory phase followed by an inactive fibrotic phase, treated with immunosuppressants (i.e. intravenous methylprednisolone, ivMP) and rehabilitative orbital surgery, respectively. Dysthyroid optic neuropathy (DON) is a severe TED form requiring both emergency ivMP and surgery. **Objective:** To analyze the correlation between different orbital-infiltrating lymphocyte phenotypes and TED clinical manifestations. **Methods:** Lymphocytes were isolated from retro-orbital fat and extra-ocular muscles obtained during orbital decompression in 20 DON and 35 inactive TED (TED-I) patients, of which 13 received ivMP 3.9±4.4 (mean±SD) years before for disease inactivation (TED-I-MP) and 22 never received steroids before (TED-I-Naïve). All DON patients had active disease and were treated with ivMP 0.4±0.8 years before surgery. Lymphocytes were immunophenotyped by flow cytometry and lymphocyte infiltrates expressed as cell-number/tissue-grams (cell/g). **Results:** Fat lymphocytic infiltration was higher in DON and TED-I-MP compared to TED-I-Naïve patients, both as total leucocytes (23'632 vs 17'206 vs 5'948 CD45+/g, p<0.01), B cells (9'142 vs 6'703 vs 838 CD19+/g, p<0.05), and T follicular helper cells (Tfh; 1'670 vs 525 vs 100 CD3+CXCR5+/g, p<0.01). Fat Tfh infiltration also correlated with clinical activity score (R 0.58, p<0.0001) and disease duration (R -0.38, p=0.05). Any lymphocytic subtype infiltration within muscles was markedly higher compared to fat in all patient groups, especially DON (503'097 CD45+/g-muscle vs 23'632 CD45+/g-fat, p<0.0005). **Conclusion:** Different TED phenotypes present distinct orbital lymphocyte infiltrates. Interestingly, inactive TED patients previously treated with ivMP (TED-I-MP) showed orbital-fat lymphocytic infiltration different from those never treated (TED-I-Naïve), but similar to patients with active DON. The degree of orbital lymphocyte infiltration correlated with TED activity and disease duration, supporting immunosuppressants therapy in the early active phases of disease. Extraocular muscle infiltration was markedly increased especially in DON patients, with acute inflammatory muscle enlargement causing optic nerve compression.

THYROID AUTOIMMUNITY

1112635 - ASSOCIATION OF SERUM VITAMIN D LEVELS WITH ANTITHYROID DRUG THERAPEUTIC FAILURE AND GRAVES' OPHTHALMOPATHY IN PATIENTS WITH GRAVES' DISEASE

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Introduction: Vitamin D (vitD) deficiency has been related to impact clinical course of Graves disease (GD). **Objective:** To assess the association between serum vitD levels and therapeutic outcomes in GD patients undergoing a clinical regimen of ATD (CRATD) for a minimum of 18 months, focusing on remission and relapse rates. Additionally, to evaluate whether vitD levels correlate with the development of Graves' ophthalmopathy (GO) and activity. **Methods:** The cohort comprised GD patients whom therapeutic failure (TF) was defined as the lack of remission following the CRATD, necessitating definitive treatment. Relapse of GD during the second phase of the cohort, initiated at the time of remission throughout 2 years, was also defined as TF. Patients that maintained clinical remission in the next 2 years were considered as having therapeutic success (TS). Serum VitD was assessed at the time of definitive treatment, after relapsing, or following 2 years in remission. **Results:** The mean time of follow-up of the 90 included patients was 47.7 months from diagnosis to remission, adding more 2 years after remission (for those not submitted to definitive treatment). TS was defined in 53.3% (n=48); and among them 31% (n=13) received definitive treatment. VitD levels were not different (33.1 ± 5.11 ng/mL in TS vs. 31.4 ± 1.91 ng/mL in TF; $p=0.32$) and the frequency of vitamin D prescription during the CRATD was similar (29.4 vs. 30.4%; $p=0.93$). There were no differences in the frequencies of deficient (<20 ng/mL) or insufficient (<30 ng/mL) VitD levels. However, levels below 50 ng/mL were less frequent in ST (50% vs. 84%; $p=0.002$). Similar results occurred when cut-off was 40 ng/mL (47.4% vs. 70.3%; $p=0.04$). GO was not related to vitD. **Conclusions:** Vit D levels were not associated with GO but vitD levels below 40-50 ng/mL appears to be associated with TF in the studied sample.

THYROID AUTOIMMUNITY

1112605 - ASSOCIATION OF THYROID PEROXIDASE ANTIBODIES AND CHRONIC KIDNEY DISEASE: ELSA-BRASIL COHORT STUDY

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Introduction: Previous literature shows that the association between thyroid peroxidase antibodies (TPOAb) and chronic kidney disease (CKD) is not yet conclusive. **Objective:** To explore the association of TPOAb titers with prevalence and incidence of CKD in men and women, using data from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). **Methods:** We included only euthyroid participants and those with subclinical thyroid dysfunction, who were not taking medication that affects thyroid function (n=5,607 men, 51.8 ± 9.2 years old; n=6,050 women, 51.5 ± 8.8 years old). CKD was defined as an estimated glomerular filtration rate <60 mL/min/1.73 m² (using the CKD-Epi equation) and/or an albumin-to-creatinine ratio >30 mg/g. For the prospective analysis, participants were followed for ~8 years and we excluded those with baseline CKD. Continuous and categorized TPOAb titers (undetectable: ≤ 5.00 , low detectable: 5.01-14.99, high detectable: 15.00-33.99, and positive: ≥ 34.00 IU/mL) were used. Logistic regression models and Poisson regression models with robust variance assessed the association of TPOAb titers with CKD prevalence and incidence, respectively. Sex-stratified univariate and adjusted models (age, race, smoking status, BMI, diabetes, hypertension, dyslipidemia, and previous cardiovascular disease) were applied. **Results:** After adjustments, in the cross-sectional results, higher levels of TPOAb were significantly associated with prevalent CKD only for men [OR:1.18, 95%CI:1.031.35, $p=0.018$]. Individuals with high detectable TPOAb showed higher odds of having prevalent CKD than those with undetectable TPOAb [OR:1.97, 95%CI: 1.14-3.40, $p=0.015$]. No significant association was observed for TPOAb with prevalent CKD for women. In the prospective results, higher levels of TPOAb were associated with incident CKD for men [OR:1.03, 95%CI: 0.93-1.14, $p=0.522$] and for women [OR:1.00, 95%CI: 0.93-1.08, $p=0.982$]. However, none of the associations reached statistical significance. **Conclusion:** Higher TPOAb levels and high detectable TPOAb titer were independently associated with prevalent CKD in men. However, higher levels of TPOAb were not associated to the risk of incident CKD.

THYROID AUTOIMMUNITY

1112632 - ASSOCIATIONS BETWEEN SENSITIVITY TO THYROID HORMONES, LIPID PROFILE AND INSULIN RESISTANCE IN AUTOIMMUNE THYROID DISEASE

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Introduction: Insulin resistance and dyslipidemia contribute to increased cardiovascular risk in autoimmune thyroiditis. The association between thyroid hormone sensitivity, lipid profile, and insulin resistance in Hashimoto's thyroiditis (HT) and Graves' disease (GD) remains unclear. **Objective:** To evaluate the relationship between sensitivity to thyroid hormones, lipid profile and insulin resistance in patients with HT and GD. **Methods:** We evaluated 402 patients with HT and 93 with GD (mean age 45.7±15.8 years, 91.3% female). We assessed anthropometric parameters, glycemic profile, and calculated insulin resistance indexes, including HOMA-IR, QUICKI (Quantitative Insulin Sensitivity Check Index), HISI (Hepatic Insulin Sensitivity Index), WBISI (Whole-Body ISI), and IGI (Insulinogenic Index). We also evaluated lipid profile, folic acid, vitamin B12 and thyroid function tests, calculating the FT3/FT4 ratio, the Thyroid Feedback Quantile-based Index (TFQI), and the TSH index (TSHI). Statistical analysis was performed using the Students t-test, Mann-Whitney U test, and Spearman and Pearson correlation analyses. A two-tailed P-value < 0.05 was considered statistically significant. **Results:** Comparing groups, we found that HT group had significant higher levels in the TSHI (2.41±2.74 vs 1.06±3.27; p<0.001) and TFQI [0.449 (0.291-0.637) vs 0.233 (0.187-0.385)]; p<0.001). On the other hand, the GD group had significant higher levels in ratio FT3/FT4 (0.15±0.07 vs 0.13±0.04; p=0.001). In the entire sample, there were significant correlations between HOMA-IR and FT3 (r=0.14; p=0.02) and between FT3/FT4 ratio and folic acid (r=-0.17; p=0.001) and BMI (r=-0.15; p=0.006). In the HT group we found positive correlations between HOMA-IR and TSH (r=0.19; p=0.008) and between TFQI and HOMA-IR (r=0.18; p=0.01), HISI (r=-0.18; p=0.01) and WBISI (r=-0.14; p=0.05); FT3/FT4 ratio and total cholesterol (r=0.10; p=0.03) and HDL cholesterol (r=0.12; p=0.01). In the GD group we observed significative correlations between TSHI and BMI (r=0.32; p=0.007) and ApoA1 (r=-0.27; p=0.02). **Conclusion:** Our results highlight the complex interrelationship between thyroid function, resistance to thyroid hormones, insulin resistance and lipid profile.

THYROID AUTOIMMUNITY

1114342 - AUTOIMMUNE THYROID DISEASE AFTER THE USE OF ALEMTUZUMAB IN MULTIPLE SCLEROSIS

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Case Presentation: A 48-year-old male patient with a medical history of relapsing-remitting multiple sclerosis. Initially treated with Fingolimod, then started 2 cycles of Alemtuzumab in March 2023 and 2 cycles of Methylprednisolone 1 g for 5 days in June 2024. Two months later an endocrinology consultation was requested due to palpitations, tremors, and weight loss with a thyroid profile indicating thyrotoxicosis. TSH 0.004 mU/L (0.40-5.10), fT4 3.27 ng/dL (0.89-1.76), T4T 19.0 ug/dL (4.5-12.5), T3T 539 ng/dL (84-172), fT3 15.8 pg/mL (2.40-5.60), T3/T4 ratio 28.36, TSH receptor antibodies 21.57 UI/L, Anti-Tg: 150 IU/mL. A thyroid ultrasound with a systolic peak of the inferior thyroid artery in the left lobe at 29.76 cm/s and a resistance index of 0.63. Treatment initiated: Methimazole 10 mg every 8 hours and Propranolol 20 mg every 12 hours. At the one-month follow-up, the thyroid profile changed to TSH 60 mU/L, fT4 0.7 ng/dL, so the antithyroid medication dosage was titrated until it was discontinued, and Levothyroxine 100 mcg (1.6 mcg/kg) was started, maintaining T4 levels. **Discussion:** Alemtuzumab is a genetically modified human IgG1 kappa monoclonal antibody specific for the human CD52 cell surface glycoprotein. Secondary autoimmune diseases due to reconstitution represent the most common effect. Among them, Graves' disease is the most frequent, with an estimated prevalence ranging from 16.7% to 41.0%. The most common secondary autoimmune phenomenon is Autoimmune Thyroiditis, occurring in 1-11%, with a prevalence of 5% in women and 1% in men (Anti-Tg, Anti-TPO TRAb >6), with Graves' disease being the most common (56-71%), Hashimoto's thyroiditis with hypothyroidism (6-34%), and silent thyroiditis (2-12.5%). **Final Comments:** In autoimmune thyroid dysfunction, challenges arise due to the spontaneous and bidirectional change between hyperthyroidism and hypothyroidism as we can see with this case. Guidelines recommend monitoring thyroid function before treatment and every three months for four years after treatment.

THYROID AUTOIMMUNITY

1114109 - CLINICAL OUTCOMES OF CANCER PATIENTS WITH PRE-EXISTING AUTOIMMUNE THYROID DISEASE TREATED WITH PD-1/PD-L1 INHIBITORS: A PROPENSITY SCORE METHODOLOGY WITH INVERSE PROBABILITY OF TREATMENT WEIGHTING (IPTW) RETROSPECTIVE STUDY

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Introduction: Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment. However, these therapies are associated with immune-related adverse events (irAEs), with thyroid dysfunction being one of the most common endocrine irAEs. The role of pre-existing thyroid autoantibodies (thyroid Ab) in predicting endocrine irAEs and their impact on patient survival remains unclear.

Objective: This study aimed to explore the relationships between pre-existing thyroid Ab and the development of endocrine irAEs, as well as their associations with overall survival (OS) in ICI-treated patients. **Methods:** We conducted a retrospective review of 4,119 patients treated with ICIs at The First Affiliated Hospital of Nanjing Medical University from July 2018 to March 2022. After excluding 3,534 patients due to missing thyroid Ab (anti-TPO/anti-Tg) data, incomplete antibody testing, unclear survival information, or undetermined tumor stages, 585 patients were included. The cohort was stratified by pre-existing thyroid antibody status. Multivariable Cox regression models analyzed the risk of thyroid irAEs and OS, with results validated via propensity score matching (PSM) and inverse probability weighting (IPTW). **Results:** Patients with pre-existing thyroid Ab (13.7%) had a significantly higher incidence of thyroid irAEs compared to the antibody-negative group (HR = 4.13, 95% CI: 2.69-6.35, $p < 0.001$). PSM and IPTW analyses further confirmed that autoantibody-positive patients had a markedly increased risk of grade ≥ 2 irAEs (HR = 7.54, 95% CI: 2.74-20.75, $p < 0.001$). Patients with positive thyroid Ab and irAEs had a better survival outcome (Log-rank $p = 0.027$). **Conclusion:** Pre-existing thyroid Ab is a significant risk factor for thyroid irAEs in patients treated with ICIs. The development of thyroid irAEs is associated with improved survival, suggesting a potential link between immune activation and clinical benefit.

THYROID AUTOIMMUNITY

1112537 - COMPARATIVE EVALUATION OF GRAVES ORBITOPATHY BETWEEN ADULT AND PEDIATRIC POPULATIONS IN A TERTIARY CENTER IN SAO PAULO

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Introduction: Graves orbitopathy (OG) is the most frequent extrathyroidal manifestation in Graves disease (GD). OG results from the elevated expression of TRAb receptors in retro-orbital tissue, activating fibroblasts and generating inflammation and edema due to the accumulation of glycosaminoglycans. Severe OG is extremely rare in children, and its not known if it has a different natural history from adults, with pediatric OG being milder and limited to the orbital fat. In contrast, in adults, it often involves the extraocular muscles and, more often, in the moderate to severe form. This study compared the clinical profiles of OG in adult and pediatric populations treated at a tertiary center. **Methods:** This retrospective observational study was based on the medical records of patients with OG seen at the orbit and adult and pediatric endocrinology outpatient clinics of a tertiary service in São Paulo. 165 adults and eight children (<18y) were included. Patients with incomplete information were excluded. **Results:** OG was predominantly female (88% of children; 71% of adults). The mean age at diagnosis was 10.3y (children) and 43.2y (adults). Children had a smaller thyroid volume (67% with goiter < 20 cm³ vs. 42% in adults); about the degree of hyperthyroidism, free T4L values were 1.5 to 2x the upper standard value in all children and in 77% adults. The visual threat was identified exclusively in adults (9%), with no moderate to severe OG (EUGOGO) cases in children. Inflammatory activity was absent in children (100% with CAS ≤ 2) but was present in 16% of adults (CAS ≥ 3). **Conclusion:** Pediatric OG appears milder than the adult population, with less inflammatory activity, no visual threat, and less impact on orbital tissues. In children, autoimmune orbitopathy diverges from adults classic Rundle pattern curve. These findings reinforce the distinct nature of OG in different age groups.

THYROID AUTOIMMUNITY

1112667 - EFFECT OF METHIMAZOLE TREATMENT ON TH1, TH17, AND TH22 LYMPHOCYTES IN PEDIATRIC GRAVES' DISEASE PATIENTS

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Graves disease is the leading cause of autoimmune hyperthyroidism. Thyroid hormones are an essential element of the endocrine system, playing a pivotal role in the body's development, especially important in children with intensified growth. Disturbance within thyroid tissue certainly affected the whole body. Nowadays, numerous research studies indicate different factors contributing to the onset of the disease; however, the exact pathomechanism of Graves disease is still not fully understood, especially in the context of immune-related processes. Th1, Th17, and Th22 effector lymphocytes were found to be crucial participants in the disease outcome, as well as in autoimmune diseases. Here, our study aimed at assessing selected effector T lymphocytes, Th1, Th17, and Th22, in newly diagnosed pediatric Graves disease patients, together with their association with thyroid-related parameters and the potential outcome of disease management. We indicated significant increases in the frequencies and absolute numbers of selected effector lymphocytes in Graves disease patients. In addition, their mutual ratios, as well as Th1/Th17, Th1/Th22, and Th17/Th22, seem to be significant in those diseases. Notably, low Th17/Th22 ratio values were distinguished as potential prognostic factors for normalizing TSH levels in response to methimazole treatment. To sum up, our research determines the crucial contribution of Th1, Th17, and Th22 cells in the pathogenesis of Graves disease. Moreover, the mentioned subset of T cells is highly likely to play a substantial role in the potential prediction of therapy outcomes.

THYROID AUTOIMMUNITY

1112345 - EFFECT ON TH1 AND TH2 CHEMOKINES SECRETION BY RAPAMYCIN, MYCOPHENOLIC ACID, AND/OR GLUCOCORTICOID, AND ON PROLIFERATION BY GLUCOCORTICOID, IN PRIMARY RETRO-ORBITAL CELLS FROM PATIENTS WITH GRAVES OPHTHALMOPATHY

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Introduction: Cytokines and chemokines are deeply involved in the pathogenesis of Graves Ophthalmopathy (GO), and cytokines stimulate the T-helper (Th)1 and Th2 chemokines release from retro-orbital cells. **Objective:** We aimed to investigate the effects of rapamycin, mycophenolic acid and/or glucocorticoids on the secretion of Th1 and Th2 chemokines in human primary cell cultures obtained from GO patients, and of glucocorticoids on the proliferation of these cells. **Methods:** We obtained primary cultures of retro-orbital fibroblasts, preadipocytes and myoblasts from 8 GO patients, and we evaluated the effect of increasing concentrations of rapamycin, mycophenolic acid and/or glucocorticoids (alone or combined) on the secretion of the prototype Th1 (CXCL10) and Th2 (CCL2) chemokines. Moreover, we assessed the effect of increasing concentrations of glucocorticoids on the proliferation of these cells. **Results:** In primary GO retro-orbital cells, CXCL10 was undetectable in the supernatants, while interferon (IFN)-gamma induced its secretion dose-dependently, but tumor necrosis factor (TNF)-alpha did not. The combination IFN-gamma+TNF-alpha had a significant synergistic effect on CXCL10 secretion. Differently, a low basal level of CCL2 was found, and it was induced in a dose-dependent manner by TNF-alpha (but not by IFN-gamma alone), whereas TNF-alpha+IFN-gamma had a significant synergistic effect on CCL2 release. The combination TNF-alpha+IFN-gamma with mycophenolic acid, rapamycin, or glucocorticoids (in a pharmacological range) led to a dose-dependent inhibitory effect on the chemokines release, such as the combination of mycophenolic acid or rapamycin and/or with glucocorticoids. Moreover, increasing concentrations of glucocorticoids (alone or combined with TNF-alpha+IFN-gamma) inhibited dose-dependently the proliferation of human primary GO retro-orbital cells. **Conclusions:** Our results show the therapeutic role of mycophenolic acid or rapamycin with glucocorticoids in GO patients, that could be mediated by their immune-modulatory effect on Th1 and Th2 chemokines secretion in retro-orbital cells, and the antiproliferative effect of glucocorticoids in human primary GO retro-orbital cells.

THYROID AUTOIMMUNITY

1112234 - EFFICACY AND SAFETY OF VELIGROTUG (VRDN-001), A FULL ANTAGONIST HUMANIZED MONOCLONAL ANTIBODY TO IGF-1 RECEPTOR, IN ACTIVE THYROID EYE DISEASE (TED): THRIVE PHASE 3 TOPLINE RESULTS

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Introduction: Efficacy and safety of veligrotug vs placebo at 15 weeks were evaluated in an ongoing phase 3 RCT in patients with active TED (THRIVE, NCT05176639). **Methods:** Adults with moderate-to-severe active TED (onset ≤ 15 months, proptosis ≥ 3 mm, and clinical activity score [CAS] ≥ 3) were randomized to 5 IV infusions 3 weeks apart of either 10 mg/kg veligrotug or placebo. Proptosis responder rate (PRR), defined as ≥ 2 -mm reduction vs baseline, additional efficacy outcomes, and treatment-emergent adverse events (AEs) were assessed through 15 weeks, with follow-up ongoing through 52 weeks. **Results:** 113 patients received veligrotug (n=75) or placebo (n=38) and were included in the intention-to-treat population. At baseline, mean proptosis was 23.2 mm in each group; mean CAS was 4.5 vs 4.8 and diplopia was present in 67% vs 68% of patients for veligrotug vs placebo. At 15 weeks, PRR by Hertel was 70% vs 5% ($p < 0.0001$) for veligrotug vs placebo, with a mean reduction of 2.9 mm vs 0.5 mm ($p < 0.0001$). PRR by MRI/CT was 69% vs 9% ($p < 0.0001$) for veligrotug vs placebo, with a mean reduction of 2.9 mm vs 0.6 mm ($p < 0.0001$). Mean CAS decreased by 3.4 vs 1.7 ($p < 0.0001$) for veligrotug vs placebo. In patients with diplopia, complete resolution of diplopia occurred in 54% (27/50) vs 12% (3/26) ($p < 0.0001$) for veligrotug vs placebo. AEs occurred for 66 (88%) veligrotug vs 24 (63%) placebo patients, and most were mild; 4 patients (veligrotug) had serious AEs (all unrelated to treatment). Hearing impairment AEs were reported for 12 (16%) veligrotug vs 4 (11%) placebo patients. **Conclusion:** Topline results from the THRIVE phase 3 RCT show 5 IV infusions of 10 mg/kg veligrotug were well tolerated and led to significant and clinically meaningful improvements in TED signs/symptoms at 15 weeks. Additional follow-up through 52 weeks is ongoing.

THYROID AUTOIMMUNITY

1112536 - EVALUATION OF THE PROFILE OF PATIENTS WITH GRAVES DISEASE IN A TERTIARY SERVICE

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Introduction: Graves disease (GD) is an autoimmune disease characterized by the presence of anti-TSH receptor antibodies (TRAb). These antibodies cause thyroid hyperactivity and ocular and dermatological manifestations. The diseases presentation is heterogeneous, and its clinical course is variable. **Objective:** To analyze the epidemiological, clinical, and therapeutic profile of patients with GD seen at a tertiary service in São Paulo between 2007 and 2024. **Method:** Retrospective observational study based on a review of electronic medical records of patients with confirmed GD seen at the General Thyroid Outpatient Clinic of a tertiary service in São Paulo. A total of 298 patients were assessed. After excluding children under 18, pregnant women, and cases with incomplete information, 136 patients remained in the study. **Results:** Among the 136 patients evaluated, 106 were women and 30 men, with a mean age at diagnosis of 44 years. Only 14.7% had a large goiter (> 40 cm³), while 47.1% had severe hyperthyroidism (T4L $> 2x$ the reference value). Graves ophthalmopathy was detected in 44% and myxedema in 6%. Initial treatment included antithyroid drugs (ATDs) in all cases, with methimazole used in 92%, propylthiouracil in 4%, and both in 4%, with an average of 34 months of use. During follow-up, 22% of patients received radioiodine therapy (RIT), and 36% underwent total thyroidectomy. Remission was achieved in 59% of cases, 11% with ATDs, 21% with RIT, and 27% after surgery. **Conclusion:** In almost 2 decades, we observed that GD was more prevalent in middle-aged women, with methimazole treatment being widely used as initial therapy, but surgery was necessary and showed the highest remission rates, reflecting the importance of individualized therapeutic strategies and in a referral center, in almost two decades, that receives complex and severe cases of thyrotoxicosis and orbital disease.

THYROID AUTOIMMUNITY

1112534 - EXTRA-LARGE GOITER IN HASHIMOTO THYROIDITIS: EXPERIENCE OF A SINGLE UNIVERSITY CENTER

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Introduction: Chronic autoimmune thyroiditis (CAT) with goiter and hypothyroidism is known as Hashimoto thyroiditis (HT), characterized by positive autoantibodies: antithyroperoxidase (TPOAb) and/or antithyroglobulin (TgAb). Thyroid ultrasound (US) reveals diffusely enlarged, heterogeneous, and hypoechoic parenchyma with pseudonodular areas. The distribution of thyroid volume (TV) in patients with CAT is typically unimodal, therefore large goiters (>50 mL) are rare. Indication for total thyroidectomy (TT) is even more uncommon, because of tracheal or esophageal compression and substernal components. **Objective:** To evaluate the clinical and laboratory characteristics of patients undergoing TT for large goiters associated with HT at a single university center. **Methods:** A retrospective analysis of patients who underwent TT for benign thyroid disease from 2011 to 2024 was conducted. Thyroid size was assessed by routine US. Tracheal deviation/compression and substernal components were evaluated by chest X-ray or tomography. Thyroid function and autoimmunity were determined using commercial kits. TPOAb and TgAb were positive if > 9 and 4 UI/mL, respectively. Only patients with TV > 50 mL and positive autoantibodies were included, excluding those with Graves disease, prior surgery, or malignancy. **Results:** From 480 patients, 33 were selected, with mean age of 53.2 years (88% female) and mean TV of 234 mL. Tracheal deviation/compression was present in 82%, and a substernal component in 74%. Only 16% had benign needle aspiration suggestive of CAT. Histology typical of CAT was seen in 73%. Thyroid follicular disease was frequently reported, with three cases of papillary microcarcinomas identified. TV had no correlation with age, TSH and TPOAb levels. **Conclusion:** HT is a rare cause of extra-large goiters, and TT remains the treatment of choice when tracheal and esophagus are compromised and substernal component is present. Besides the autoimmune inflammatory process, other trophic factors might participate in the development of such large thyroids.

THYROID AUTOIMMUNITY

1112191 - HIGH-DOSE VERSUS LOW-DOSE BLOCK-AND-REPLACE TREATMENT FOR A FIRST EPISODE OF GRAVES DISEASE

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Introduction: The optimal treatment with antithyroid drugs for a first episode of Graves disease (GD) remains controversial. **Methods:** Retrospective, two academic centres study of newly diagnosed GD between 1990 and 2022, treated with ATD in block-and-replace (B+R) regimen for at least 12 months and followed up for at least 1 year after ATD discontinuation or until disease relapse. Sixty patients received high-dose B+R (hB+R) with fixed ATD dose maintained during the study, and sixty patients low-dose B+R (lB+R) with lower ATD dose adjusted during the study. **Results:** Baseline characteristics were similar in both groups. There were no significant differences between groups regarding the evolution of the thyroid function during ATD (TSH $p=0.891$, FT4 $p=0.895$). The point-prevalence of euthyroidism was not different between hB+R and lB+R (38% vs 47%, $p=0.460$ at 6 months, 69% vs. 82%, $p=0.194$ at 12 months, 70% vs. 78%, $p=0.370$ at 18 months, respectively). At 18 months, 27% hB+R vs. 38% lB+R ($p=0.375$) had thyroid eye disease. hB+R received more often propylthiouracil and/or than methimazole ($p=0.01$), although there were no differences in the occurrence or type of drug-related adverse events (AE) (no AE 73% vs. 78%, $p=0.707$). lB+R received significantly lower ATD dose (0.45 ± 0.16 vs. 0.9 ± 0.0 g/month, $p<0.001$) and lower levothyroxine (LT4) dose (1.96 ± 0.76 vs. 2.76 ± 0.93 mg/month, $p<0.001$) than hB+R. At 11.0 (0.00, 60.9) vs. 7.0 (0.00, 41.55) months ($p=0.109$) after ATD discontinuation, 38 out of 60 (63%) hB+R and 36 out of 60 (60%) lB+R patients relapsed ($p=0.141$). **Conclusion:** We observed similar evolution and relapse rates in patients with a first episode of GD receiving up to 50% less ATD and 30% less LT4 dose than in high-dose B+R regimen.

THYROID AUTOIMMUNITY

1112373 - HYPOTHYROID PATIENTS WITH CELIAC DISEASES OR NOT CELIAC GLUTEN SENSITIVITY IN TREATMENT WITH LIQUID L-T4

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Introduction: Hashimoto's thyroiditis is the leading cause of hypothyroidism, and is often associated with other autoimmune diseases, such as celiac disease (CD). These patients are subjected to an impaired absorption of many drugs, such as levothyroxine (L-T4) in tablets formulation. In fact, an optimal assumption of the drug requires an optimal gastric environment for the dissolution of the salts contained within the tablet formulation. **Objective** We aim to evaluate TSH values in patients with hypothyroidism and CD or non-celiac gluten sensitivity (NCGS), who are under a treatment with L-T4 in tablets or in liquid formulation. **Methods:** We have enrolled twenty-seven hypothyroid patients in treatment with liquid L-T4 (L-LT4 group), and twenty-two patients in treatment with tablet L-T4 (T-LT4 group). Both groups are similar for gender distribution, mean age, body weight, the type of enteric disease (17 CD and 10 GS), the treatment with proton-pump inhibitors, and the mean L-T4 dosage ($p > 0.05$, for all comparison). **Results:** In a first basal evaluation the prevalence of a higher TSH is similar between the two groups ($p > 0.05$). All patients were reevaluated for 4 times, and during each re-evaluation the therapy was adjusted if needed. In the follow-up reevaluation the prevalence of patients with a TSH > 3.5 mIU/mL was: 1) In a first evaluation 25% in the T-LT4, vs, 23% in L-LT4 group ($p > 0.05$); 2) In a second evaluation 27.8% in the T-LT4 group, vs, 16.7% in the L-LT4 ($p > 0.05$); 3) In a third evaluation 47% in the T-LT4 group, vs, 9% in the L-LT4 (Chi-square = 0.0071); 4) In the last evaluation 38.8% in the T-LT4 group, vs, 9.0% in the L-LT4 group (Chi-square = 0.0248). **Conclusion:** Our data support a better control of TSH values in hypothyroid patients with celiac disease, or non-celiac gluten sensitivity under a liquid L-T4 regimen, with respect to L-T4 in tablets.

THYROID AUTOIMMUNITY

1112240 - IMMUNE CELL INFILTRATION AND INFLAMMATORY MOLECULE PROFILING IN DYSTHYROID OPTIC NEUROPATHY: EVIDENCE FROM BULK TRANSCRIPTOMIC ANALYSIS

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Introduction: Dysthyroid optic neuropathy (DON) is the most severe complication of thyroid-associated ophthalmopathy (TAO), leading to potential vision loss. Despite its clinical significance, the molecular and immune mechanisms underlying DON remain poorly understood. **Objective:** This study aimed to elucidate key pathways and inflammation-related core genes driving DON progression. **Methods:** Retro-orbital tissues from DON patients, non-DON TAO patients, and healthy controls (HCs) were analyzed using bulk RNA sequencing. Differentially expressed genes (DEGs) were identified and subjected to Gene Ontology (GO) enrichment analysis. Weighted gene co-expression network analysis (WGCNA) identified disease-relevant modules. Immune cell infiltration was assessed via single-sample GSEA (ssGSEA). ROC analysis and single-gene GSEA were used to evaluate the diagnostic potential and functional relevance of core genes. **Results:** DON patients exhibited significant upregulation of inflammation- and fibrosis-related genes, including CCL21, HP, and SLCO2A1. GO analysis revealed enrichment in immune response pathways, such as leukocyte migration and cytokine activity, and structural pathways, including extracellular matrix remodeling. WGCNA identified the "grey" module as most associated with DON, enriched in leukocyte chemotaxis and extracellular matrix organization. Single-gene GSEA demonstrated distinct functional roles for CCL21, HP, and SLCO2A1. CCL21 was linked to immune cell recruitment and fibrosis; HP to granulocyte chemotaxis and local inflammation; and SLCO2A1 to RNA processing and transcriptional regulation. ssGSEA revealed increased infiltration of activated B cells, CD4 T cells, and mast cells in DON patients, with strong correlations between core genes and immune cell subsets. ROC analysis confirmed the diagnostic potential of CCL21, HP, and SLCO2A1. **Conclusions:** This study identifies inflammation and immune cell infiltration as key drivers of DON pathogenesis. CCL21, HP, and SLCO2A1 are promising biomarkers and therapeutic targets, offering novel insights into the molecular underpinnings of DON.

THYROID AUTOIMMUNITY

1112253 - INTERLEUKIN-6 RECEPTOR SIGNALING INHIBITION WITH SATRALIZUMAB IN THYROID EYE DISEASE: PHASE 3 SATRAGO-1 AND SATRAGO-2 TRIAL DESIGN

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Introduction: Thyroid eye disease (TED) is an inflammatory orbitopathy that can cause facial disfigurement and sight-threatening complications. Disease-modifying treatments are needed, as current therapies for active TED may be ineffective, cause relapses or lead to side-effects, while inactive TED is primarily treated surgically. Interleukin-6 (IL-6) and its receptor (IL-6R) are implicated in TED pathogenesis. Satralizumab, a humanized monoclonal anti-IL-6R antibody, utilizes innovative recycling technology to enhance IL-6 suppression and effectively manage inflammation and its consequences, with subcutaneous administration every 4 weeks (Q4W).

Objective: We describe the design of the SatraGO-1 and SatraGO-2 trials which will evaluate the efficacy and safety of satralizumab in TED. **Methods:** SatraGO-1 (NCT05987423) and SatraGO-2 (NCT06106828) are identical, global, phase 3, randomized, double-masked, placebo-controlled, 72-week multicenter studies that will recruit ~120 participants at ~70 sites across 20 countries. Participants ≥18 years with moderate-to-severe active TED or stable, chronic inactive TED are eligible provided the systemic disease is under control (euthyroid or mild hyper-/hypothyroidism). Participants will be randomized 1:1 to subcutaneous satralizumab or placebo at weeks (W) 0, 2, and 4 (loading doses) and then Q4W through W20 (maintenance doses). Based on the W24 proptosis response, nonresponders will receive satralizumab Q4W and responders re-randomized 1:1 to satralizumab or placebo Q4W through W44.

Results: Primary endpoint: proportion of active TED participants achieving a proptosis response (≥2 mm proptosis improvement from baseline in study eye) at W24. Secondary endpoints include proptosis response in active/chronic TED participants and overall response (≥2-point improvement in clinical activity score from baseline and proptosis response in study eye) in active TED participants. Safety outcomes include incidence, seriousness, and severity of adverse events. **Conclusion:** SatraGO-1 and SatraGO-2 are designed to investigate IL-6R inhibition via satralizumab in TED. Satralizumab offers a potential disease-modifying treatment in TED while minimizing safety risks associated with current treatments.

THYROID AUTOIMMUNITY

1112216 - INVESTIGATION OF THE IMPACT OF SOD2 GENE VARIANTS IN OXIDATIVE STRESS AND GRAVES' DISEASE PATHOGENESIS

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Increased ROS generation and the consequent oxidative damage, as well as decreased antioxidant capacity, are involved in the pathogenesis of Graves' hyperthyroidism and thyroid eye disease. The SOD2 gene, which encodes the antioxidant enzyme MnSOD, plays a critical role in oxidative stress control. However, the effects of genetic polymorphisms in SOD2 have not yet been reported. We employed a series of robust bioinformatic platforms and computational tools to explore the putative impact of single nucleotide missense polymorphisms (SNPs) in SOD2 and the corresponding modifications in MnSOD structure and function on Graves disease pathogenesis. A total of 642 nsSNPs of SOD2 were retrieved from the NCBI dbSNP database, of which 69 were classified as deleterious by the SIFT BLINK platform and were selected for further analysis. Among them, 19 were classified as 100% deleterious regarding MnSOD protein functionality on the PolyPhen-2, SNAP-2, and PANTHER platforms. Using SNPs&GO, PMUT, and PhD-SNP tools, 18 SNPs were found to be pathogenic and associated with the disease. Stability analyses performed using MuPro and I-Mutant 2.0 platforms revealed a reduction in protein stability for all 18 variants. They were further analyzed using Consurf software, which showed that L38F, L38Q, H55Q, and H9Q are located in highly conserved regions. Additionally, these variants are located in domains crucial for protein activity and interact with other relevant domains, suggesting a significant likelihood of impacting MnSOD function. The structural features of these variants were further explored using the HOPE report, which indicated changes in amino acid size in all cases. In conclusion, the L38F, L38Q, H55Q, and H9Q SOD2 variants may significantly impair MnSOD stability and function. These alterations likely contribute to increased oxidative stress and processes associated with the pathogenesis of GD. These variants also have the potential to serve as biomarkers of Graves' disease and/or ophthalmopathy.

THYROID AUTOIMMUNITY

1112252 - IS IGG4-RELATED THYROID DISEASE STILL AN UNDERDIAGNOSED ENTITY?

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Introduction: Several endocrine diseases described as idiopathic are currently considered part of the IgG4-related disease spectrum, sharing common histopathological characteristics. IgG4-related thyroid diseases (IgG4-RTD) include Hashimoto's and Riedel's thyroiditis and exceptionally Graves' disease. Since 2018, attempts have been made to establish organ-specific criteria based on: clinical, serological, imaging, histological, IgG4 immunohistochemical characteristics and treatment response. **Objective:** Classify patients with clinical suspicion of IgG4-RTD evaluated in our service applying current diagnostic criteria. **Methods:** Diagnostic criteria for IgG4-RTD: I) thyroid enlargement; II) ultrasound hypoechogenicity; III) elevated serum IgG4; IV) thyroid histopathology (IgG4+ plasma cells > 20/HPF and IgG4+/IgG plasma cells > 30%) and V) extrathyroidal involvement. DEFINITIVE diagnosis: when all criteria are met; PROBABLE: I+II+IV or V and POSSIBLE: III + II. **Results:** 5 women, X (r) age 45 y/o (42-51). Two patients consulted prior to the current diagnostic criteria of IgG4-RTD. Clinical presentation (n patients): Firm goiter (5, painful in one of them); Compressive symptoms (3, one of them with Graves disease). Four patients met 2/5 criteria for IgG4-RTD and only 1 met 3/5 (PROBABLE IgG4-RTD). Elevated serum IgG4 1/5. Extrathyroid involvement 0/5. The patient with Graves' disease also met IgG4 hypophysitis criteria inferring double compromise. Corticoid therapy (n=4) improved thyroid/pain compressive symptoms. **Conclusion:** Though most patients presented strong clinical suspicion of IgG4-RTD, lack of data unable us to re-classified them according to the 2018 current criteria. Given that criteria are still heterogeneous and histological confirmation is not systematically available, this disease continues underdiagnosed. Based on our experience, we suggest that in a patient with a consistent and/or painful atypical large goiter, IgG4-RTD may be ruled out, even in patients with Graves disease.

THYROID AUTOIMMUNITY

1114168 - MAMTIR STUDY: PRELIMINARY RESULTS OF THYROID FUNCTION AND AUTOIMMUNITY IN WOMEN WITH BREAST CANCER, FIBROCYSTIC DISEASE AND HEALTHY CONTROLS

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Introduction: An association between breast cancer (BC) and benign thyroid disorders has been debated for decades. **Objective:** The MAMTIR study aims to clarify epidemiological and physiopathological aspects of such association. **Methods:** We recruited 185 consecutive women undergoing mammography screening, or pre-treatment assessment for recent BC diagnosis: 78 BC, 81 breast fibrocystic disease (BFD) and 26 normal mammography (NM). We collected thyroid anamnesis, body mass index (BMI) and blood for thyroid stimulating hormone (TSH) and autoantibodies-to-thyroid-peroxidase (TPOAb) measurement. Thyroid autoimmunity (TA) was defined as known history for autoimmune thyroid disorders or TPOAb positivity. TSH, TPOAb and TA were compared between groups in univariate and multivariate analyses after correction for age and BMI. Women taking thyroid medications were excluded from TSH analysis (12 BC, 12 BFD and 26 NM). **Results:** BC, BFD and NM had similar prevalence of TPOAb (13% vs 20% vs 15%; P=0.491) and TA (22% vs 28% vs 19%; P=0.505). TSH was higher in TPOAb positive compared with TPOAb negative women (2.84 [2.1-3.21] vs 1.57 [1.04-2.11] mUI/L; P<0.001). BC patients, compared with BFD and NM, had higher age (median [IQR]: 61 [54-60] vs 49 [41-59] vs 55 [40-66] years, P<0.001), BMI (24.0 [21.8-27.2] vs 23.1 [20.2-25.8] vs 22.4 [18.7-25.1] kg/m², P=0.021) and TSH, both among TPOAb positive (3.21 [2.98-3.80] vs 2.51 [1.07-3.19] vs 1.46 [0.05-2.92] mUI/L, P=0.022; Pmultivariate=0.037) and AbTPO negative (1.76 [1.36-2.32] vs 1.48 [0.91-1.82] vs 1.43 [0.88-1.99] mUI/L, P=0.029; Pmultivariate=0.072) women. **Conclusion:** MAMTIR study's preliminary data showed higher TSH in BC compared with BFD and NM women, independently from age, BMI and TPOAb. TPOAb and TA prevalence was similar across groups, thus TSH increase in BC patients may be secondary to cell-mediated immunity or other causes, i.e. iodine deficiency or endocrine disruptors. Further clarifications will derive from completion of patient's recruitment (target N=496), thyroid volume assessment and immunophenotyping of intra-thyroid lymphocytes.

THYROID AUTOIMMUNITY

1112231 - MHB018A, A NOVEL SUBCUTANEOUSLY DELIVERED IGF-1R ANTIBODY SHOWS GOOD EFFICACY AND FAVORABLE SAFETY IN A PHASE 1/2 STUDY OF ACTIVE THYROID EYE DISEASE (TED)

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Introduction: FDA approval of teprotumumab has established IGF-1R as a therapeutic target for TED. MHB018A, a next generation subcutaneous IGF-1R antibody with a novel VHH-Fc fusion domain, demonstrated superior ligand blocking and functional activities against IGF-1 and IGF-2 compared to other IGF-1R antibodies. Here, results from a phase 1/2 study of MHB018A in active TED are reported. **Methods:** Thirty eligible patients were enrolled into three cohorts, each with 10 patients randomized 4:1 to receive either subcutaneous MHB018A or placebo. Cohort 1 received 300 mg Q4W (three doses); cohort 2 received a 600 mg loading dose followed by 300 mg Q4W (two doses); cohort 3 received 450 mg Q4W (three doses). Safety, tolerability, and efficacy were evaluated over 12 weeks. **Results:** MHB018A was well-tolerated across all dose regimens. Most adverse events (AEs) were mild (grade 1 or 2) and resolved without intervention. No cases of severe hearing impairment were reported. Pharmacokinetic and pharmacodynamic data supported the Q4W dosing schedule. The C_{max} of MHB018A was 20 times lower than the C_{trough} of teprotumumab for i.v. injection. At week 12, proptosis responder rates (the percentage of participants who achieve a reduction in proptosis of ≥2 mm compared to baseline) were 50.0%, 50.0% and 87.5% for the 300 mg, 600 mg+300 mg and 450 mg groups, respectively, compared to 16.7% for placebo. The 450 mg group showed the most robust response, with 50.0% (4/8) achieving a ≥2 mm proptosis reduction by week 4 and 87.5% (7/8) by week 8. Additional efficacy endpoints further demonstrated the clinical benefit of MHB018A. **Conclusions:** Subcutaneous administration of MHB018A exhibited a favorable safety profile, seemingly better than other IGF-1R antibodies, with no reports of severe hearing loss/change. It achieved rapid and clinically significant proptosis responses in TED patients, particularly at the 450 mg dose, supporting further clinical development.

THYROID AUTOIMMUNITY

1112614 - NEUTROPHIL-LYMPHOCYTE AND PLATELET-LYMPHOCYTE RATIOS IN GRAVES OPHTHALMOPATHY AND ITS ASSOCIATION WITH DISEASE SEVERITY, ACTIVITY AND RESPONSE TO THERAPY

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Introduction: Graves ophtalmopathy (GO), an autoimmune disease, is associated with ocular infiltration of activated T cells. Neutrophil-lymphocyte (NLR) and platelet-lymphocyte (PLR) ratios have been studied as new inflammatory markers of severity and prognosis in critical, autoimmune, and inflammatory conditions. **Objective:** To evaluate a possible association between NLR, PLR and the severity and activity of GO. **Methods:** A cohort study with GO patients from a specialized outpatient clinic, whom its activity was based on the Clinical Activity Score (CAS) and severity on the EUGOGO criteria. Inadequate therapy response was defined by maintenance of diplopia, need for new intravenous glucocorticoid therapy (IGT), radiotherapy or decompressive surgery. The white blood cell count came from medical records before IGT. NLR was calculated by the division of neutrophils by lymphocytes, PLR by the division of platelets by lymphocytes. CAS > 3 defined as active, NLR > 2 as abnormal. **Results:** Sixty patients (12 men), mean age 50 years. 45% had active CAS and 28% moderate to severe GO (MSGO). IGT was prescribed to 43% patients (50% in the second IGT). PLR was not associated with CAS, but the median tended (0.11) to be higher in MSGO (145 [0.06]) compared to those without (119 [0.07]). NLR was not associated with GO activity (p 0.25). Median NLR was higher (p=0.01) among MSGO (Me 2.43 [1.38]) than among those without (1.85 [0.74]). Abnormal NLR tended to be associated with OGMG with p=0.06. Furthermore, NLR was higher (median 1.87 vs 2.34 p=0.02) and tended to be more frequently abnormal (58% vs 42%; p=0.10). **Conclusions:** NLR was associated with greater disease severity, while PLR showed a trend towards association. NLR and PLR were not associated with GO activity. Results suggest that NLR may serve as a clinical prognostic parameter for GO. A larger sample is needed to complement the study.

THYROID AUTOIMMUNITY

1114196 - OPTIMIZED STRATEGY COMBINING TEPROTUMUMAB AND TOCILIZUMAB FOR THE TREATMENT OF A SURGICAL AND STEROID-RESISTANT DYSTHYROID OPTIC NEUROPATHY: A CASE REPORT

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Case Presentation: We present the case of a 77-year-old patient treated with success with only two infusions of Teprotumumab associated with tocilizumab for a severe relapse of dysthyroid optic neuropathy (DON). Initially, the patient experienced a first episode of bilateral DON, treated with high-dose IV steroids followed by apical decompression (AD). Visual acuity (VA) improved from 8/10 to 10/10 in the right eye (RE) and from “counting fingers” to 4/10 in the left eye (LE). Visual fields (VF) showed improvement in both eyes. He had then 10 weekly infusions of steroids (8g total) for persistent active graves’ orbitopathy (GO). The patient’s VA reached 10/10 in the RE and 8/10 in the LE, with subnormal VF. One month after completing treatment, the patient had an inflammatory recurrence of GO with new onset of DON in the LE. VA dropped to 5/10, and the clinical activity score (CAS) was 4/7. The patient was treated with tocilizumab rather than teprotumumab, given preexisting hearing loss due to presbycusis. Three weeks after the first infusion, VA worsened to 3/10, and VF deteriorated. After discussion in national multidisciplinary meeting teprotumumab was introduced for two infusions, with hearing monitoring, and afterwards tocilizumab was resumed with three more infusions. This combined therapy resulted in total resolution of DON and activity of GO: CAS was 0 in RE and 1/7 in LE, with VA of 10/10 in both eyes at the end of treatment. Eight months after teprotumumab and five months after tocilizumab, there were no signs of DON or inflammation relapse. No deterioration of hearing was observed. **Discussion:** This sequential treatment approach, was safe and effective on inflammation and DON. **Final Comments:** This strategy allowed to benefit the fast-acting effect of teprotumumab, while reducing the economic burden of the treatment, and minimising the risk of ototoxicity. It suggests potential for broader treatment strategies.

THYROID AUTOIMMUNITY

1114065 - OXIDATIVE STRESS-RELATED BIOMARKERS IN THYROID EYE DISEASE: A COMBINED BIOINFORMATICS AND IMMUNOHISTOCHEMICAL APPROACH

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Introduction: Thyroid Eye Disease (TED) is an autoimmune disorder in which oxidative stress plays a key role in pathogenesis; however, its precise molecular mechanisms remain unclear. Immunohistochemistry reveals protein expression, local immunity, and links microscopic changes to clinical features in TED. **Objective:** To explore oxidative stress-related molecular mechanisms and to identify reliable biomarkers for TED. **Methods:** Oxidative stress-related differentially expressed genes (OS-DEGs) were identified, followed by GO and KEGG analyses to explore their functions and pathways. LASSO regression and random forest were used to select key diagnostic genes. Their diagnostic performance was assessed using ROC curves. A logistic regression-based nomogram model was constructed, and single-gene GSEA was performed to evaluate the functional relevance of core genes. Immunohistochemical validation was performed on 14 TED tissues (7 active, 7 inactive) and 10 control orbital tissues. Immunostaining was quantified using reproducible, operator-independent software for automated and unbiased analysis. **Results:** 53 oxidative stress-related OS-DEGs were selected. GO and KEGG enrichment analyses revealed significant involvement of D OS-DEGs in cellular responses to oxidative stress, ROS metabolism, and mitochondrial dysfunction, highlighting the role of oxidative damage in TED. Five diagnostic genes (AKT1, APEX1, FOS, MCL1, and ANGPTL7) were identified through machine learning approaches (LASSO regression and random forest), demonstrating strong diagnostic potential with a combined model achieving an AUC of 0.931. Immunohistochemical validation confirmed significantly increased expression of FOS ($p = 0.001$), MCL1 ($p < 0.001$), and ANGPTL7 ($p = 0.013$) in orbital tissues from TED patients compared to controls. The nomogram model developed using the selected genes showed good predictive performance for TED risk assessment. **Conclusion:** This study is the first to identify five oxidative stress-related genes/proteins as candidate biomarkers for TED, highlighting their potential roles in pathogenesis. These findings may facilitate early screening and risk assessment. Further validation is needed for clinical application in targeted therapy.

THYROID AUTOIMMUNITY

1113802 - PHOTOBIO-MODULATION AS AN ADJUNCTIVE THERAPY FOR RESTORING THYROID GLAND VOLUME IN HASHIMOTO'S THYROIDITIS

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Introduction: While the standard treatment for Hashimoto's thyroiditis (HT) primarily focuses on correcting levothyroxine (LT4) deficiencies, thyroid autoimmunity may still contribute to ongoing symptoms and an enlarged thyroid, even in patients who achieve euthyroid status. Photobiomodulation (PBM) has demonstrated potential as an effective therapy for various autoimmune diseases, although the evidence remains limited. Our prior research on PBM's effects in HT showed notable improvements in reducing thyroid antibodies and enhancing thyroid function. **Objective:** This study aimed to assess the effectiveness of PBM therapy not only in restoring thyroid function in HT patients but also in reducing the size of the thyroid gland. **Methods:** A total of 100 female participants, aged 20 to 50 years, were enrolled and assigned to two groups: a PBM + conventional treatment group (n=50) and a conventional treatment-only group (n=50). The PBM treatment followed a specific protocol: 820 nm wavelength, 200 mW power output, 20-second exposure per point, 32 J/cm² fluence per point, and treatments twice a week for three weeks. Both groups followed the same conventional treatment plan, which included an appropriate levothyroxine dosage, vitamin D3 supplementation for those with levels <40 ng/dL, and a daily intake of 100 µg of oral selenium. Thyroid volume was measured before and after the three-month treatment period. **Results:** The study found a significant reduction in thyroid volume in the PBM treatment group after three months (p<0.05), while no significant change was observed in the control group (p>0.05). **Conclusion:** This study provides the first evidence of PBM's efficacy in reducing thyroid volume in patients with HT. Further research with extended follow-up periods is needed to confirm these findings.

THYROID AUTOIMMUNITY

1112434 - PREDICTIVE FACTORS FOR HYPOTHYROIDISM IN CHILDHOOD AUTOIMMUNE THYROIDITIS: INSIGHTS FROM LONG-TERM FOLLOW-UP

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Introduction: Predictive factors for hypothyroidism progression in children with autoimmune thyroiditis (AIT) remain unclear. **Objective:** To characterize the clinical presentation of AIT, assess long-term outcomes, and identify predictive factors for disease progression. **Methods:** Data from 127 consecutive patients under 18 years of age at presentation were analyzed (mean follow-up: 7.1 years; range: 0.20 yr). **Results:** At presentation, 57% of patients were euthyroid, 28% had subclinical hypothyroidism, and 15% had overt hypothyroidism. By the end of follow-up, among euthyroid children, 20.5% developed overt hypothyroidism, and 6.8% progressed to subclinical hypothyroidism. The subclinical hypothyroidism group showed dynamic changes: 45.7% of patients progressed to overt hypothyroidism, while 37.1% reverted to euthyroidism. Finally, the overt hypothyroidism group did not show significant changes. Patients progressing to hypothyroidism were younger at diagnosis (p=0.0008) with higher thyroid peroxidase antibodies (AbTPO) titers (p<0.0001), higher TSH (p<0.0001) and lower FT4 levels (p=0.0026). Thyroid volume > 6 mL increased hypothyroidism risk (p=0.0060, OR: 0.347, 95%CI: 0.15-0.75). Multivariate analysis confirmed that AbTPO titers influence TSH levels at follow-up (p<0.0001). Cutoff thresholds were established to refine predictive accuracy. Patients diagnosed under 10 years of age (p=0.043, OR: 0.458, 95%CI: 0.22-0.96), with AbTPO >92 IU/mL (p<0.0001, OR: 25, 95%CI: 8.78-63.11), and TSH >4.95 µIU/mL (p<0.0001, OR: 15.43, 95%CI: 5.61-37.57) had highest risk of developing hypothyroidism. Notably, AbTPO >92 IU/mL and TSH >4.95 µIU/mL demonstrated the strongest predictive power. AbTPO titers had a positive predictive value (PPV) and negative predictive value (NPV) of 83%, while TSH >4.95 yielded a PPV of 79% and an NPV of 80%. **Conclusions:** Twenty percent of euthyroid children developed hypothyroidism, compared to 45.7% of those with subclinical hypothyroidism. TSH >4.95 µIU/mL and AbTPO titers had the greatest predictive power. Patients diagnosed under 10 years of age had a higher risk of developing hypothyroidism, suggesting that prolonged exposure to autoimmunity may play a role. Further studies are needed to validate predictive models for hypothyroidism development in children with AIT.

THYROID AUTOIMMUNITY

1112180 - PREDICTIVE FACTORS OF RESPONSE TO INTRAVENOUS GLUCOCORTICOIDS IN ACTIVE MODERATE-TO-SEVERE THYROID EYE DISEASE

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Introduction: Intravenous glucocorticoids (IVGC) is the first line treatment for active moderate-to-severe thyroid eye disease (A-TED) in many countries worldwide. **Methods:** We retrospectively studied 64 patients with A-TED, treated between 2003 and 2023 at a single tertiary center with the 12 weeks IVGC EUGOGO (European Group on Graves Orbitopathy) regimen. All patients were evaluated for response to IVGC according to the clinician judgment and 44/64 (69%) of patients also with the EUGOGO 2021 revised composite index. **Results:** The mean patients age at IVGC initiation was 51.75±11 years, 47/64 (73.5%) were women, 56/64 (87.5%) Caucasians and 33/64 (51.5%) active smokers. Forty-eight/64 (75%) of patients evaluated with clinical criteria and 32/44 (73%) evaluated with EUGOGO criteria responded to the treatment. Non-responders tended to be older (56.62±10.25 vs. 50.12±10.86 years, $p=0.040$ for clinical criteria and 56.5±11.91 vs. 50.37±11.68 years, $p=0.131$ for EUGOGO criteria) and had higher clinical activity score (CAS) before IVGC (5.00±1.15 vs. 4.20±1.16, $p=0.022$ for clinical criteria and 4.75±0.62 vs. 3.18±0.86, $p<0.001$ for EUGOGO criteria). In patients evaluated with clinical or EUGOGO criteria respectively, multivariate logistic regression identified age at IVGC initiation (OR=0.925, 95%CI 0.865-0.990, $p=0.024$ and OR=0.881, 95%CI 0.779-0.998, $p=0.046$) and CAS before IVGC (OR=0.534, 95% CI 0.314-0.909, $p=0.021$ and OR= 0.084, 95% CI 0.018-0.384, $p=0.001$) but not active smoking as independent factors associated with response to IVGC. The optimal cut-off for predicting poorer response to IVGC was CAS $\geq 4.5/7$ (66.7% specificity, 56.3% sensitivity; $p=0.010$) in patients evaluated with clinical criteria and CAS $\geq 3.5/5$ (65.6% specificity, 91.7% sensitivity; $p<0.001$) for EUGOGO criteria. **Conclusion:** Older age and higher CAS before treatment are associated to poorer response to IVGC. Patients with these characteristics could be offered other first line treatments.

THYROID AUTOIMMUNITY

1112332 - PREMATURE OVARIAN FAILURE FRAMED IN THYROID-RELATED POLYAUTOIMMUNE DISORDERS

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Introduction: The menstrual cycle disappearance before the age of forty is named premature ovarian failure (POF). Its autoimmune origin may be hypothesized when it is associated with Addisons or autoimmune thyroiditis (AT). Autoimmune thyroiditis is the most frequent autoimmune disease but data on its association with POF are rather scanty. **Patients and Methods:** Out of 7690 consecutive postmenopausal women we have identified 1689 women with isolated autoimmune thyroiditis and 304 women framed in PAS II, PASIII or polyautoimmunity, who had concluded their fertile life. From these groups were selected woman with POF and the characteristics of their association with polyautoimmune disorders have been examined. **Results:** Among the 304 patients with thyroid-related polyautoimmunity, seventeen (5.6%) of them had POF, a percentages higher than in the general population (1.2%) in the nonautoimmune women (0.98%; $p<0.0001$) and in those with isolated AT (1.18%; $p<0.0001$). Beside AT, POF was associated to Addisons Disease only in 10% of women being more associated with skin autoimmunity in 1/3 of the patients. The remaining POF occurred in woman with gastrointestinal or rheumatic autoimmune disorders. Besides the obvious reduction of fertile life (23.5 years), even the menarche was delayed in women with POF by a median of two years. The prevalence of spontaneous miscarriages was 29.4% in women with POF and 6 times more than in the nonautoimmune as well as in isolated AT women ($p<0.0006$) and, three times higher than the reported pooled risk of all cause miscarriage in the general population. **Conclusions:** POF is 5/6 times more prevalent in women with thyroid-related polyautoimmunity than in the nonautoimmune women or with isolated AT, is associated with 2 or more autoimmune disorders with no definite correlation with the type of autoimmune disease. A delayed menarche and a higher risk of miscarriage are features of POF in this setting.

THYROID AUTOIMMUNITY

1112406 - QUALITY OF LIFE IN PATIENTS WITH THYROID EYE DISEASE AND ITS RELATION TO DISEASE SEVERITY AND ACTIVITY

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Objective: To evaluate the quality of life and correlate it with the severity and activity of the disease in patients with thyroid eye disease from a tertiary service in São Paulo. **Methods:** A total of 164 patients with thyroid eye disease were evaluated, all from the Orbit outpatient clinic of the Department of Ophthalmology at the Santa Casa of São Paulo between January 2018 and September 2023. A questionnaire (Graves Ophthalmopathy Quality of Life) was administered, and the total functional and aesthetic scores for each patient were calculated. These scores were then compared with the clinical assessment (activity and severity) of the orbitopathy using the CAS and EUGOGO classifications. **Results:** A total of 164 patients were evaluated, of whom 116 were women, with a mean age of 46.66 years (SD). 54.87% were smokers, with an average functional score of 66.76 (SD) and an aesthetic score of 44.51 (SD). Worse functional scores in the QOL questionnaire were statistically significant when related to the presence of diplopia ($p < 0.001$), while worse aesthetic scores were observed in females and the presence of upper eyelid retraction greater than 2 mm. No statistically significant correlations were found when comparing the severity and activity classifications with both scores. **Conclusion:** Thyroid eye disease negatively impacts the quality of life of these patients. No correlation was found between the severity and activity of thyroid eye disease and the functional and aesthetic scores.

THYROID AUTOIMMUNITY

1114250 - ROLE OF SELENIUM IN HASHIMOTO'S THYROIDITIS: A CASE REPORT

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Case Presentation: A 47-year-old female diagnosed with Hashimoto's thyroiditis in 2020 comes to the clinic for a check-up. The patient has been taking 75 mcg of levothyroxine daily. She reports feeling tired, having hair loss and brittle nails. Laboratory tests are performed showing normal levels of TSH and T4 and high anti-TPO antibody levels. It is decided to maintain the levothyroxine dose and start selenium supplementation (selenium 200 mcg QD). Serial monitoring of anti-thyroid antibodies is performed, showing a decrease in anti-TPO antibody levels. Two months later, a follow-up test is conducted, revealing that the anti-TPO antibody has become negative. Consequently, the levothyroxine dose is reduced to 50 mcg QD. One month later, TSH levels show a tendency toward suppression, and discontinuation of levothyroxine is suggested. Four weeks later, follow-up tests reveal normal TSH and T4 levels, negative antibodies, and the patient remains completely asymptomatic. **Discussion:** Selenium has been studied as a possible therapeutic adjunct to treat Hashimoto's thyroiditis due to its role in thyroid function and modulation of the immune system. Despite there is not enough evidence to conclusively recommend the use of selenium supplements, there are some case reports that support its use for the reduction of antithyroid antibodies and symptom improvement. More research is needed to establish clear guidelines on its dosage and long-term effectiveness in this context. **Final Comments:** The use of selenium in Hashimoto's thyroiditis is a topic of interest in endocrinology, due to its potential to modulate the immune response and reduce antithyroid antibody levels. However, its use must be carefully evaluated to avoid toxicity and ensure that it really brings benefits to the patient. It is recommended that its administration be carried out under medical supervision, considering the individuality of each case and the available scientific evidence.

THYROID AUTOIMMUNITY

1114070 - SIGNATURES OF SIX AUTOPHAGY-RELATED GENES AS DIAGNOSTIC MARKERS OF THYROID-ASSOCIATED OPHTHALMOPATHY AND THEIR CORRELATION WITH IMMUNE INFILTRATION

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Introduction: Thyroid-associated ophthalmopathy (TAO) is one of the most complex autoimmune diseases in endocrinology areas. Autophagy-related genes may be involved in the pathophysiology of TAO. **Objective:** This study aims to reveal key genes associated with autophagy in the pathogenesis and the potential diagnostic markers for TAO. **Methods:** We obtained autophagy-related differential genes (AR-DEGs) and their expression in TAO patients and controls. Gene ontology analysis (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis were used to perform the enrichment analysis of AR-DEGs. LASSO regression, support vector machine recursive feature elimination, and random forest were performed to screen for disease signature genes (DSGs), which were further validated in another independent validation dataset. We used the receiver operating characteristic for the evaluation of the diagnostic efficacy of DSGs and also established a nomogram. The relative proportion of immune infiltration was calculated using the CIBERSORT algorithm, and the relationship between the identified gene markers and the level of infiltrating immune cells was explored. **Results:** We identified 24 AR-DEGs, which were primarily enriched in cellular catabolic regulation, autophagosome membrane, and ubiquitin protein ligase binding in GO analysis, while KEGG analysis highlighted autophagy as the main enriched pathway. Six DSGs were identified by three algorithms. They were validated in another independent validation dataset. The combined six-gene model also showed good diagnostic efficacy (AUC=0.948). We further plotted the nomogram with better diagnostic efficacy. Immuno-infiltration analysis and correlation analysis demonstrated that six DSGs were significantly correlated with the infiltrating immune cells. **Conclusion:** We identified several biological processes and pathways for the enrichment of AR-DEGs. Six DSGs were identified, which showed great potential to become critical molecules in the diagnosis of TAO, and these DSGs showed a correlation with infiltrating immune cells.

THYROID AUTOIMMUNITY

1114116 - SIGNIFICANT CLINICAL IMPROVEMENT WITH A NEW 3-DAY HIGH-DOSE STEROID PROTOCOL FOR THYROID ORBITOPATHY

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Introduction: Thyroid orbitopathy is a condition that, even in mild cases, alters quality of life, self-esteem, and functionality, with a high impact on public health and therapeutic costs. Moderate or severe active forms of OT, although they are a minority, represent a challenge given that treatments often achieve incomplete results, with high weekly intravenous corticosteroid doses with cumulative doses of 4.5 g being the fundamental pillar. Unfortunately, this weekly option is not accessible to many patients in our setting, who fail to complete the weeks of intravenous application. This study proposes clinical improvement with a new short protocol of cumulative doses of 1.5 g in 3 days, which is easier, faster, and more cost-effective, landing in our health system in Colombia, both in rural and urban areas. **Objective:** To present a new protocol with high-dose intravenous corticosteroids in 3 days (accumulated 1.5 g) and to evaluate the clinical improvement of moderate to severe acute thyroid orbitopathy. **Methods:** A longitudinal, descriptive, and analytical study was conducted. The study included a sample of 45 patients over 18 years of age admitted to the San José Hospital emergency department or outpatient clinic with a diagnosis of moderate/severe thyroid orbitopathy. Patients were managed with a high-dose intravenous methylprednisolone regimen of 500 mg daily for 3 consecutive days (cumulative dose 1.5 g), followed for 6 months post-treatment to assess the clinical impact. **Results:** A statistically significant improvement was observed post-treatment in 32 patients (71.11%) with respect to exophthalmos, chemosis, ocular pain, and conjunctival hyperemia, although a nonsignificant difference was observed in diplopia. Reactivation of thyroid orbitopathy was observed only in 14 patients after 6 months of treatment. **Conclusion:** This new intravenous methylprednisolone regimen improved several clinical variables in a statistically significant manner, as a strategy in populations with difficult access to weekly regimens.

THYROID AUTOIMMUNITY

1112202 - TED SERUM EXOSOME PROMOTE THE PROLIFERATION OF ORBITAL FIBROBLASTS IN THYROID EYE DISEASE

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Introduction: Exosomes are capable of transferring miRNAs and proteins between cells, modulating the phenotype of recipient cells. This study aimed to elucidate the mechanisms by which serum exosomes contribute to the pathogenesis of thyroid eye disease (TED). **Methods:** Orbital fibroblasts (OF, TED-OF, HC-OF) were cultured from patients with TED and healthy controls (HC). Exosomes (exo, TED-exo, HC-exo) were isolated from the serum of individuals with TED and HC for miRNA sequencing, subsequent validation and functional analyses. **Results:** OFs express Vimentin and IGF-1R. TEM and NTA analyses revealed that the exosomes exhibited a cup-shaped morphology, with an approximate particle size of 100 nm. Exosomes expressed CD63, CD9, and TSG101 as detected by WB, with IGF1R expression significantly higher in TED-exo ($p < 0.05$). Immunofluorescence analysis demonstrated that exosomes were internalized by OFs. CCK-8 assay confirmed that the viability of OFs gradually increased with higher concentrations of TED-exo. Proliferation of OFs was significantly enhanced by TED-exo at concentrations of 20 $\mu\text{g/mL}$ and 40 $\mu\text{g/mL}$ ($p < 0.0001$). We observed a significant difference in the expression of 30 miRNAs in TED-exosomes ($p < 0.05$). Among these, miR-30e-5p, miR-26b-5p, let-7b-5p was significantly elevated in the TED group ($p < 0.05$). The target genes of miR-30e-5p were predicted, and the KEGG-enriched pathways were primarily associated with the FoxO signaling pathway and the mTOR signaling pathway. The qRT-PCR results showed a significant decrease in HAS3, IL6, ACTA2, and COL1a1, and a significant increase in CYB561 after inhibiting miR-30e-5p expression in GO-OF cells using lentivirus. In contrast, miR-30e-5p elevation resulted in the opposite changes ($p < 0.01$). This suggests that miR-30e-5p may contribute to the development of TED, with CYB561 potentially being its target gene. **Conclusions:** Serum-derived exosomes transport IGF-1R and miR-30e-5p, promoting the proliferation of orbital fibroblasts and contributing to the development of thyroid eye disease.

THYROID AUTOIMMUNITY

1112454 - TEPROTUMUMAB FOR THYROID EYE DISEASE: FIRST CASE IN BRAZIL

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Thyroid eye disease (TED) is an autoimmune inflammatory orbital disease; treatment for active TED may include supportive care, systemic immunosuppression with steroids or other agents, and occasionally orbital radiotherapy. In June 2023, the monoclonal antibody teprotumumab targeting the insulin-like growth factor receptor I (IGF-IR) was approved for the treatment of TED in Brazil. Our objective is to report the evolution of the first case of TED treated with Teprotumumab in Brazil. Case report: White woman, 53 y/o, diagnosed with Graves disease 4 years ago, definitive treatment with radioactive iodine 2 years ago, controlled post-dose hypothyroidism. TED started 9 months ago, and she received a total of 4.5 g of IV methylprednisolone. Now she reports worsening proptosis and ocular pain. Right eye (RE): severe visual loss - finger count = 30 cm (previous glaucoma), ophthalmometry 27 mm. Left eye (LE): visual acuity 20/25 (with correction), ophthalmometry 26 mm, preserved ocular movements. Both eyes: conjunctival redness, spontaneous and gaze-evoked orbital pain. Orbital MRI showed TED in the acute inflammatory phase, diffuse thickening of the retroocular extrinsic muscles, mainly medial and inferior rectus, bilateral exophthalmos. A second pulse with methylprednisolone 4.5 g plus mycophenolate was performed, without improvement in TED. Teprotumumab was prescribed. During the infusion protocol, the patient experienced worsening control of T2DM, myalgia, fatigue and developed alopecia, none of which were severe enough to recommend treatment discontinuation. After the fourth infusion, the patient showed complete improvement of ocular symptoms and reduction of retroocular muscle (MRI) thickening and edema. At the end of the 8 infusions, the reduction in proptosis was LE 4mm and RE 3mm. This improvement was maintained 6 months after the last teprotumumab infusion. Final Comments: Teprotumumab has proven to be a safe and effective drug for the treatment of corticosteroid-resistant TED in the acute phase. No relapse was observed after 6 months.

THYROID AUTOIMMUNITY

1112348 - THE AUTOIMMUNE MENU: A CASE OF TOO MANY DISHES ON THE TABLE

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A 53-year-old woman with a complex history of autoimmune diseases presented with complaints of general weakness, fatigue, slowness, epigastric discomfort, difficulty walking, and pain in the pelvic and right wrist regions. Her medical history includes vitiligo (diagnosed at age 27), ankylosing spondylitis (diagnosed at age 34, confirmed by lumbar spine radiography, human leukocyte antigen B2 positive, rheumatoid factor negative), treated with glucocorticoids, non-steroidal anti-inflammatory drugs, and monoclonal antibodies. At age 35, she was diagnosed with pernicious anemia (hemoglobin = 82 g/L, Vitamin B12 = 76.6 pg/mL, intrinsic factor antibodies = 248.5 AU/mL, serum parietal cell antibody positive). At age 43, she developed autoimmune thyroiditis and hypothyroidism (thyroid stimulating hormone (TSH) = 24.35 IU/mL, freeT4 = 8.2 pmol/L, Antithyroglobulin antibodies = 385.6 IU/mL, anti-thyroid peroxidase antibodies = 170.8 IU/mL), initiating levothyroxine therapy. At age 45, she experienced right wrist swelling, pain, and warmth, with ultrasound confirming inflammation of the carpal joint and tendons, along with lymphostasis. She was treated with antibacterial therapy. On examination, signs of Cushing's syndrome were noted, including a moon-like face with hypopigmentation on the cheeks and extremities, buffalo hump, and reddish abdominal striae. Major joint movements were painful and restricted. Diagnostic tests showed hypothyroidism (TSH = 6.35 UI/mL), dual-energy X-ray absorptiometry (DXA) T-scores -2.8 (left hip) and -3.5 (lumbar spine), total IgA normal, anti-tissue transglutaminase IgA > 300 U/mL. Imaging revealed fractures in the pubic and radial bones. The patient was diagnosed with Autoimmune polyglandular syndrome (APS) type 3b+c (Autoimmune thyroiditis, hypothyroidism, vitiligo, ankylosing spondylitis, celiac disease), steroid-induced severe osteoporosis and bone fractures. Despite the absence of a clear description of such a set of autoimmune diseases, we are likely dealing with APS type 3b+c. This case highlights the complex interplay between multiple autoimmune conditions, emphasizing the need for a multidisciplinary approach to diagnosis and management. Regular follow-up with specialists and patient education on the interconnected nature of her conditions are essential. A tailored approach is critical for optimizing outcomes and improving quality of life.

THYROID AUTOIMMUNITY

1114137 - THE BURDEN OF GRAVES' ORBITOPATHY: RESULTS FROM A FRENCH MULTICENTRIC 150 PATIENTS' SURVEY CONDUCTED WITH THE "VIVRE SANS THYROÏDE" PATIENT'S ASSOCIATION

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Introduction: GO is the subject of a large number of therapeutic innovations. **Objective:** The aim of this study was to evaluate the burden of GO, from the patient's point of view, on all fields of daily life. **Methods:** This 54 items' online survey was submitted through seven French referral GO joint consultations and via the patients' association "Vivre sans Thyroïde", regardless of the stage of the disease or the treatments received. **Results:** 150 patients completed the survey from September 2024 to January 2025. Among them 84% were women, and 48% under 50 y/o. In 19% GO lasted for less than one year, and in 27% more than 5 years. The patients rated the visibility of GO to 7.5 on a 10-point scale. 74% of patients experienced loss of autonomy, 91% had a lower self-confidence, and 62% felt in some degree socially isolated. 90% of working patients had been hindered by GO, 56% had been on sick leave, for more than one year in 23%. Emotional life had been affected in 64% of the respondents, and 14% reported a break-up related to GO. Two third felt sadness and anxiety, 24% had started psychotropic treatment and 23% psychotherapy. At time of the survey 67% of patients had received an intravenous treatment, with an improvement of pain, ophthalmic comfort and esthetical aspect in half. 22% felt no improvement. 38 patients had had an orbital decompression, with a gain on esthetical aspect in 76%. 14 patients had had a strabismus surgery, that improved vision in 86% and made possible to resume activities in 57%. 19 patients had had a palpebral surgery with an amelioration of esthetical aspect in 84% and ophthalmological comfort in 58% **Conclusion:** Despite its "benign" nature GO has severe consequences in all fields of patients' life.

THYROID AUTOIMMUNITY

1112382 - THE LEAKY GUT IN PATIENTS WITH HASHIMOTOS THYROIDITIS ISOLATED OR FRAMED IN POLYAUTOIMMUNE DISORDERS

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Introduction: Leaky gut defines an increased permeability of intestinal barrier (IB), has been demonstrated in patients with inflammatory and/or autoimmune intestinal disorders as well as in patients with autoimmune diseases involving organs far from the intestine, as in patients with isolated Hashimotos thyroiditis (iHT). The permeability of IB in patients with Hashimotos thyroiditis framed in polyautoimmunity has not been described yet and this is the aim of our study. **Methods:** The study group encompassed 93 patients bearing HT (median age=48 years; M=12; F=81); 33 of them associated another non-endocrine autoimmune disorder (HT+POLY) [13 gastric atrophy (HT+GA), 13 vitiligo (HT+V) and 7 celiac disease (HT+CD)]. The evaluation of gut permeability was performed by dosing serum zonulin, the main regulator of intestinal tight junctions, LPS and its binding protein LSPBP, as indexes of endotoxemia. The serum was stored at -20° until all the samples were simultaneously measured by ELISA kits. **Results:** The concentration of zonulin was higher in patients HT+POLY than in patients with iHT ($p<0.002$); a similar result was observed for LPS ($p=0.0004$) and LSPBP (0.0233). The concentrations of zonulin were higher chiefly in HT+CD than in iHT patients ($p<0.0001$). On the contrary, the highest concentration of LPS compared to iHT may be observed in HT+V ($p<0.01$). In the whole sample and in patients with isolated HT, zonulin and LPS concentrations significantly correlated ($p<0.0001$; $r=0.4431$ and $r=0.4409$, respectively), a correlation lost in patients with HT+POLY. This was due to a greater increase of LPS and LSPBP over zonulin levels in HT+POLY group. **Conclusions:** The association of HT with further autoimmune disorders is characterized by a leaky gut, even when the disease does not involve directly the gastrointestinal tract. The higher concentration of LPS in polyautoimmune patients indicates a more severe systemic inflammatory state.

THYROID AUTOIMMUNITY

1113761 - THYROID ANTIBODY STATUS AND CARDIOVASCULAR RISK: AN INDIVIDUAL PARTICIPANT DATA ANALYSIS OF 14 COHORT

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Introduction: Thyroid peroxidase antibodies (TPOAb) are markers of thyroid autoimmunity, but their role in cardiovascular disease (CVD) risk stratification remains uncertain. **Objective:** To assess whether positive TPOAb status is associated with CHD or stroke, overall and in the subgroup with subclinical hypothyroidism. **Methods:** We identified studies from the Thyroid Studies Collaboration (TSC) and searched MEDLINE, EMBASE, and Cochrane Library through July 2024 for prospective studies reporting baseline thyroid function, TPOAb, and cardiovascular outcomes (CHD events/mortality, stroke events/mortality). Cox models adjusted for age, sex, and TSH were applied within cohorts, followed by random-effects meta-analysis. Models were further adjusted for smoking, BMI, systolic blood pressure, diabetes, and total cholesterol. **Results:** Among 100,250 participants from 14 cohort studies, 11.9% were TPOAb positive, and 5.4% had subclinical hypothyroidism. Over follow-up, there were 8,910 CHD events and 3,512 stroke events. TPOAb positivity was not associated with increased risk of CHD events (HR, 1.00; 95% CI, 0.90-1.11), CHD mortality (HR, 0.95; 95% CI, 0.78-1.16), stroke events (HR, 0.98; 95% CI, 0.87-1.11), or stroke mortality (HR, 1.06; 95% CI, 0.81-1.40). Similar findings were observed after full adjustment and in subgroup analyses. Among individuals with subclinical hypothyroidism, TPOAb positivity was not associated with increased CVD risk compared to euthyroid individuals; HRs were as follows: 1.02 (95% CI 0.85 to 1.22) for CHD events; 1.18 (95% CI 0.81 to 1.72) for CHD mortality; 0.94 (95% CI 0.70 to 1.27) for stroke events; and 1.14 (95% CI 0.67 to 1.93) for stroke mortality. **Conclusion:** Positive TPOAb status was not associated with increased risk of CHD or stroke in the overall population or among individuals with subclinical hypothyroidism. These findings do not support the use of TPOAb testing for cardiovascular risk assessment. In individuals with subclinical hypothyroidism, risk stratification should focus on the degree of TSH elevation rather than antibody status alone.

THYROID AUTOIMMUNITY

1113995 - THYROID WHISPERS, HEARTBEATS ROAR: THE POETIC PULSE OF HASHIMOTO'S SVT

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Introduction: Hashimoto's thyroiditis, a leading cause of hypothyroidism, is marked by autoimmune-mediated thyroid destruction. While bradycardia is the most common cardiac manifestation of hypothyroidism, supraventricular tachycardia (SVT) is an unusual complication. Fewer than 1%-2% of hypothyroid patients exhibit supraventricular tachyarrhythmias, underscoring its rarity. This case highlights how metabolic, autonomic, and endothelial changes in severe hypothyroidism can predispose patients to arrhythmias, illustrating the intricate interplay between thyroid dysfunction and cardiac conduction. Highlight Hashimoto's-related severe hypothyroidism presenting with SVT to emphasize prompt intervention. **Case Presentation:** A 27-year-old female presented with chest tightness, palpitations, and lightheadedness, precipitated by caffeine intake. Previously diagnosed with acute thyroiditis in 2023, she had intermittent follow-ups and inconsistent thyroid hormone replacement. Examination revealed a firm, non-nodular thyroid enlargement, tachycardia (180 bpm) on ECG, and an anterior neck swelling moving with deglutition. SVT was confirmed via electrocardiography and successfully reverted with adenosine. Thyroid function tests demonstrated high TSH, low free T4, and elevated anti-thyroid peroxidase antibodies, consistent with Hashimoto's thyroiditis. Treatment included corticosteroids, beta-blockers, thyroid hormone replacement, and electrolyte correction, leading to rapid clinical improvement and symptom resolution. This case illustrates the rare association of SVT with severe hypothyroidism, especially in Hashimoto's thyroiditis. Potential mechanisms include autonomic imbalance, myocardial remodeling, and electrolyte derangements that heighten arrhythmogenic risk. Chronic hypothyroidism can paradoxically heighten sympathetic drive and predispose susceptible individuals to tachyarrhythmias. Effective management demanded a multidisciplinary approach, integrating Cardiology, for arrhythmia stabilization, and Endocrinology, to correct underlying thyroid dysfunction. **Conclusion:** Severe hypothyroidism secondary to Hashimoto's thyroiditis can manifest with life-threatening arrhythmias such as Supraventricular Tachycardia, though it remains a distinctly uncommon presentation. Early recognition, aggressive thyroid hormone optimization, and targeted arrhythmia management are essential to achieving favorable outcomes. This case underscores the importance of coordinated endocrine-cardiovascular care in patients with autoimmune thyroid disease who present with unusual cardiac arrhythmias.

THYROID AUTOIMMUNITY

1112388 - TREATMENT WITH SOFT CAPSULE L-T4 IN HYPOTHYROID AND GASTROPATHIC PATIENTS IN ASSOCIATION WITH L-T4 MALABSORPTION

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Introduction: Levothyroxine (L-T4) therapy is used to treat hypothyroidism. The L-T4 absorption is influenced by the acidic environment of the stomach. Gastric diseases can alter the normal physiology of gastric acid secretion, and can reduce the absorption of L-T4. **Objective:** We aim to investigate the differences between L-T4 formulations in soft capsules (S-LT4) or in tablets (T-LT4) in hypothyroid patients with gastric disease, in achieving normal and stable TSH values over time. **Methods:** This is an observational and retrospective study in hypothyroid patients with gastric disease treated with S-LT4 (34 patients) or T-LT4 (102 patients), for the replacement therapy of hypothyroidism. The gender and age distribution were not significantly different in T-LT4 vs S-LT4 groups, nor were: a) the types of gastric disease; b) the prevalence of patients chronically treated with proton-pump inhibitors; c) the frequency of *Helicobacter pylori* infection; d) the mean L-T4 dosage. **Results:** At the basal evaluation the prevalence of patients with a TSH > 3.5 mIU/mL in the T-LT4 group was 17%, vs, 29 % in the S-LT4 (Chi-square; p=0.1). Once L-T4 was adjusted (if needed), patients of both groups were reevaluated in an interval range of 4-8 months, for 4 times from 20-24 months, adjusting the therapy on the base of TSH, FT4, and FT3. The prevalence of patients with a TSH > 3.5 mIU/mL was: -At the first revaluation 14% in T-LT4 patients vs 7% in S-LT4 patients (Chi-square=0.32) -At the second revaluation 26% in T-LT4 patients vs 4% in S-LT4 patients (Chi square; p=0.0052) -At the third revaluation 19% in T-LT4 patients vs 4% in S-LT4 patients (Chi-square; p=0.06) -At the last 18% in T-LT4 patients vs 12% in the S-LT4 group (Chi-square; p=0.43). **Conclusion:** Our data demonstrated a better control of TSH in hypothyroid and gastropathic patients treated with soft capsule L-T4 formulation, compared to tablet L-T4.

THYROID AUTOIMMUNITY

1112636 - TSH RECEPTOR ANTIBODIES IN PATIENTS WITH CHRONIC THYROIDITIS

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Objective: To assess the frequency of TSH receptor antibodies (TRAb) in adult patients with chronic thyroiditis. **Methods:** This is a cross-sectional study. The frequency of TRAb+ was evaluated in plasma samples from patients with CT. All of these patients had positive TPO antibodies. A control group of subjects without CT was used. Medical records were reviewed to assess thyroid function, history of thyroid disorders, and the use of medications that may affect thyroid function. All patients with a history of hyperthyroidism or Graves' disease were excluded. TRAb antibodies were assessed using (ECLIA) on the Roche Cobas e601 analyzer. A value above 1.7 IU/L was considered positive. **Results:** Samples from 56 patients with chronic thyroiditis and 70 controls were analyzed. The mean age was 47.9 (SD 15.2) in cases and 46.8 (SD 17.7) in controls ($p=0.7$). No differences were found in BMI or TSH levels. Among patients with CT, 62% were receiving levothyroxine therapy. TRAb+ was found in two patients: one was a 50-year-old woman with TRAb = 10.8 IU/L, diagnosed with CT, who progressed with a TSH of 0.18 in the last follow-up, without pharmacological treatment. This patient was excluded from further analysis as it was consistent with Graves' disease. The other case was a 50-year-old woman with CT, euthyroid, without pharmacological treatment, and with TRAb = 2.3 IU/L. The mean TRAb value in patients with CT was 0.72 (SD 0.49), compared to 0.57 (SD 0.47) in controls ($p=0.08$). **Conclusions:** A low frequency of TRAb+ was found in subjects with chronic thyroiditis.

THYROID AUTOIMMUNITY

1114105 - UNVEILING THE RESEARCH LANDSCAPE, HOTSPOTS, AND FRONTIERS OF THYROID EYE DISEASE: A BIBLIOMETRIC ANALYSIS

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Introduction: Thyroid Eye Disease (TED) is the most common thyroid-related autoimmune chronic inflammatory disorder affecting the adult orbit. Over the past five years, the number of TED publications has equaled that of the previous 16 years, yet a systematic and comprehensive bibliometric analysis of this field is still lacking. **Objective:** This study aims to provide a comprehensive bibliometric overview of TED, identifying its knowledge structure, research hotspots, and future trends. **Methods:** Publications related to TED from 2004 to 2024 were retrieved from the Web of Science Core Collection database. VOSviewer, CiteSpace, and the R package "Bibliometrix" were utilized for bibliometric analysis. **Results:** A total of 4,306 publications from 91 countries, led by China and the United States, were included. The number of TED publications has shown a consistent upward trend. The leading research institutions were University of Pisa (Italy), University of Mississippi (USA), Shanghai Jiao Tong University (China), and University of California, Los Angeles (USA). Among scientific journals, Ophthalmic Plastic and Reconstructive Surgery had the highest number of publications, while Frontiers in Endocrinology exhibited the fastest growth in publication volume. Journal of Clinical Endocrinology & Metabolism and THYROID remained highly influential, ranking second and third in both publication volume and citation frequency. The 15,766 contributing authors were led by Smith, Kahaly, Marino, Yoon, and Marcocci in terms of publication volume. Bartalena was identified as the most frequently co-cited author. TED research primarily focuses on mechanisms (pathogenesis, immunity, autoantibodies), treatment (management, therapy, orbital complications), and epidemiology (prevalence, diagnosis, risk factors). Artificial intelligence, disease activity, hearing loss, teprotumumab, dysthyroid optic neuropathy, inflammation, and magnetic resonance imaging are the primary keywords of emerging research hotspots. **Conclusion:** Our study represents the first comprehensive bibliometric analysis of TED, summarizing its knowledge mapping, research hotspots, and frontiers, while providing valuable insights for scholars in the field.

THYROID CANCER BASIC

1112333 - A COMPREHENSIVE IN SILICO ANALYSIS OF RET VARIANTS AND THEIR POTENTIAL IMPACT ON MEDULLARY THYROID CANCER

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The RET proto-oncogene plays a key role in cellular processes such as proliferation, differentiation, and migration. Germline pathogenic RET variants are responsible for hereditary medullary thyroid carcinoma (MTC) and some apparently sporadic cases, demonstrating a strong genotype-phenotype correlation. Additionally, genetic polymorphisms in RET may influence susceptibility to and clinical manifestations of both sporadic and familial MTC. However, the association between common RET variants and MTC remains controversial, as meta-analyses have produced conflicting results. To evaluate the impact of RET variants on protein structure, function, stability, flexibility, and interaction with adjacent amino acids, we used publicly available datasets and robust bioinformatics tools. Missense polymorphisms in RET were analyzed using PredictSNP2.0, SIFT, PredictSNP1.0, iStable, and DynaMut. A total of 172 polymorphisms were retrieved from the dbSNP database, of which 24 were considered deleterious by at least six PredictSNP1.0 tools. Among these 24 variants, rs17028, rs2075912, rs2075913, rs2435355, and rs10900297 exhibited properties that may alter DNA structure, its bonds, and the stability of the double helix, according to PredictSNP2.0 package. Furthermore, the evaluation of PredictSNP1.0 revealed that C609R (rs77558292), C609F (rs77939446), C609Y (rs77939446), C611W (rs80069458), C618R (rs76262710), and C620W (rs79890926) were associated with decreased molecular flexibility, suggesting their potential impact on protein functionality. Interestingly, rs1799939 (G691S), the only missense SNP with a minor allele frequency (MAF) > 0.1, was deemed deleterious exclusively by the FunSeq2 tool (PredictSNP2.0), but showed decreased protein stability (iStable, Score = 0.77; MuPRO, $\Delta\Delta G$ = -0.46; I-Mutant, $\Delta\Delta G$ = -1.23). In summary, we identified 24 RET variants capable of significantly altering the protein structure, suggesting potential implications for MTC development and progression. These SNPs merit further investigation as biomarkers of susceptibility, clinical features, and prognosis of MTC.

THYROID CANCER BASIC

1112501 - A NON-RADIOACTIVE IODINE UPTAKE ASSAY FOR SCREENING REDIFFERENTIATION DRUGS IN THYROID CANCER CELLS IDENTIFIES LYSCAMINE AS A POTENTIAL CANDIDATE

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Introduction: During the progression of thyroid cancer (TC), tissue dedifferentiation and loss of radioiodine uptake are observed due to decreased NIS expression or cytoplasmic retention. NIS is a plasma membrane protein responsible for the active transport of iodide into thyroid follicular cells. The clinical management of radioiodine-refractory thyroid cancers remains a challenge. Restoring radioiodine sensitivity has emerged as a therapeutic strategy for more aggressive forms of thyroid tumors. **Objective:** This study aimed to develop a non-radioactive assay for screening compounds that enhance iodine uptake in human thyroid cell lines. **Methods:** A non-tumoral thyroid cell line (NThyOri; N) was transfected with a plasmid containing the NIS gene using Lipofectamine. Stable clones were selected with geneticin and used to standardize the iodine uptake assay. The HTHT83 anaplastic thyroid cancer (ATC) cell line was employed for drug screening. Redifferentiation gene expression was assessed using real-time PCR. Sodium perchlorate served as a selective inhibitor for NIS-mediated iodide uptake and as a negative control in iodide uptake assays. **Results:** A stable clone (NH2) was selected, exhibiting a 49.63-fold increase in NIS expression and an increase in iodide uptake compared to non-transfected cells. Perchlorate treatment abrogated the iodide uptake in these cells, indicating specific NIS-mediated iodide uptake in these cells. Upon the tested drugs, lysicamine increased iodide uptake accompanied by a concomitant dose-dependent increase in NIS expression in HTHT83 cell lines. It is worth noting that although the expression of NIS and TG was increased, PAX8 expression was reduced in lysicamine-exposed cells. **Conclusion:** Lysicamine increased NIS-mediated iodide uptake and NIS expression in ATC cells, suggesting its potential as a novel treatment drug for thyroid cancer. Further studies will be conducted to explore the molecular mechanisms underlying this upregulation of NIS function and expression.

THYROID CANCER BASIC

1113728 - ACTIVATION OF MIR146B PROMOTER IS REGULATED BY MAPK-INDUCED TRANSCRIPTION FACTORS IN THYROID CANCER

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Introduction: microRNAs (miRNAs) are small noncoding RNAs that regulate gene expression by modulating mRNA translation/stability. miR-146b is a hallmark of thyroid cancer and regulates target mRNAs involved in cell migration/invasion and thyroid cell biology. MIR146B activation is singular in thyroid cancer and frequently is among the top overactivated miRNAs, correlating with BRAFV600E, TERT promoter mutation and poor prognosis. Nevertheless, the molecular regulation of MIR146B promoter is still poorly elucidated. **Objective:** study MIR146B putative promoter and identify the transcription factors (TFs) involved in miR-146b induction in thyroid cancer. **Methods:** MIR146B putative promoter region was delimited using FANTOM5 tool, and PCR-cloned into pGL4-20 minP luciferase reporter as different fragments (P1/P2/P3/P3A/P3B). Thyroid cancer cell lines were transfected with Luc plasmid+ pRL (Renilla) as control, and luciferase activity was measured after 24h. TFs binding site prediction was performed using Lasagna tool, and gene expression by RT-qPCR. **Results:** We defined a region of ~1Kb as MIR146B putative promoter that was divided into three fragments, P1 (293 bp), P2 (312 bp) and P3(392 bp) that exhibited higher luciferase activation compared to control empty plasmid (2, 5 and 100-fold activation, respectively). Then, P3B was divided into P3A (204 bp) and P3B (154 bp), being P3B the minimal promoter for MIR146B. P3B shows putative TFs sites for YY1, STAT5A/B, SP1 and AP4. However, only YY1, STAT5A/B and E2F1 were high in ATC cells. Nevertheless, YY1 binding site deletion reduced P3B luminescence (18%-42%) both in ATC and PTC cell lines. Additionally, SP1 binding sites deletion repressed P3B activation in 70%-80% in all cell lines. Indeed, the blockage of MAPK signaling with U0126 reduced P3B luminescence (30%-60%) in all cell lines. **Conclusion:** MIR146B minimal promoter region is a 154 nt fragment that contains binding sites for YY1 and SP1, which are responsive to MAPK signaling modulation.

THYROID CANCER BASIC

1112478 - ADAPTING MOLECULAR DOCKING FOR HIGH-THROUGHPUT SCREENING OF SELECTIVE RET PROTEIN KINASE INHIBITORS

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Rearranged during Transfection (RET) is a gene encoding a transmembrane protein that functions as a tyrosine kinase receptor involved in many cellular processes. RET fusions and mutations are oncogenic driver events in several malignancies, including papillary and medullary thyroid cancer. Selective RET inhibitors have revolutionized the treatment landscape for thyroid cancer. However, the development of acquired on-target resistance to RET inhibitors is a new challenge. We look to find new selective RET inhibitors by validating structural models to perform molecular docking studies for application in high throughput virtual screening. RET crystal structures were obtained from the Protein Data Bank database. Type I RET inhibitors that interact with the DFG-In conformation of the kinase were obtained from the ChEMBL database. Decoys were generated by DUD-E. The docking assays were performed using AutoDock-GPU. Resulting datasets were analyzed using RingTail and other Python libraries. Validation consisted of two aspects, the ability to reproduce the experimental binding of the ligand-receptor complex observed in structural studies, and the ability to discriminate compounds with known activity (binders) from those without activity (decoys). For the former, we used the re-docking and cross-docking approaches, while the results of the study on the benchmark data set were visually analyzed by plotting a receiver operating characteristic (ROC) curve. We considered values of the area under the curve (AUC) below 0.7 as poor, between 0.7 and 0.8 as acceptable, between 0.8 and 0.9 as good, and above 0.9 as excellent. Based on the molecular weight of the inhibitors, two molecular docking models were established that successfully reproduced the ligand-receptor complex interaction, achieving AUC values of 0.87 and 0.90, respectively. Validation studies demonstrated the usefulness of our models, which can now be applied to the virtual screening of new selective RET inhibitor candidates.

THYROID CANCER BASIC

1113974 - ASSOCIATION BETWEEN HYPERFUNCTIONING PARATHYROID ADENOMA AND THYROID CANCER. AN UNCOMMON CASE

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Case Presentation: A 48-year-old woman, with no known pathological history, who comes to the consultation because three months earlier incidental hypercalcemia had been detected; upon questioning, she reports joint pain and weakness. Blood tests: calcium 13.2 and 12 mg/dL, phosphorus 2 mg/dL, in 24-hour urine: calcium 558 mg/dL, phosphorus 3,020 mg/dL, PTH 128 pg/mL, TSH 1.55 mU/L, T4L 1.94 pmol/L. Ultrasound reports a thyroid nodule of 11.2x7.3 mm, cytology category II. Sestamibi scintigraphy findings in favor of parathyroid adenoma. Parathyroidectomy is performed with left hemithyroidectomy. Anatomopathological diagnosis: micropapillary thyroid carcinoma in the context of follicular hyperplasia, parathyroid gland adenoma, tumor volume 2x0.9x0.7 cm. Post-surgical analysis PTH 58 pg/mL, calcium 7 mg/dL, phosphorus 3 mg/dL, contrast-enhanced lung CT negative. One year post-surgery with stable progression. Total thyroidectomy was not performed due to it being a low-risk cancer. **Discussion:** The concomitant presentation of thyroid and parathyroid neoplasms has been previously reported in the literature, as well as the intrathyroidal localization of parathyroid adenomas. Various arguments are used to explain the nature of this association, such as common embryonic origin and a history of neck radiation, among others. The usual presentation is its detection through thyroid nodules, with the finding of thyroid cancer being less common in patients whose initial medical attention is for hyperparathyroidism, as occurs in the presented case. **Final Comments:** Since the association of thyroid neoplasms with hyperparathyroidism is not uncommon, it is considered necessary not to ignore this possibility in any patient with hyperparathyroidism associated with thyroid nodules. Its early diagnosis allows both problems to be resolved in a single surgical procedure and avoids the need for future surgeries.

THYROID CANCER BASIC

1112549 - BORON-ENRICHED LAPATINIB FOR THE TREATMENT OF ANAPLASTIC THYROID CANCER (ATC) BY COMBINING TARGETED THERAPY AND BORON NEUTRON CAPTURE THERAPY (BNCT)

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Introduction: Previously we have demonstrated that boron neutron capture therapy (BNCT) based on the nuclear reaction $^{10}\text{B}(n, \alpha)^7\text{Li}$ could be an alternative for the treatment of anaplastic thyroid carcinoma (ATC). To improve the effect of BNCT, lapatinib, currently used in targeted therapy, was bound to the boron-containing organometallic carborane (B). **Objective:** The aim of these studies was to evaluate the use of lapatinib enriched with boron for the treatment of ATC. **Methods:** Proliferating undifferentiated thyroid cancer (8505C) cells were incubated with borated lapatinib (Cmpd.1 and Cmpd.2) and boron content was measured by ICP-AES spectroscopy. After, the cells were incubated with 10 ppm of ^{10}B and irradiated in the nuclear reactor RA 3 Facility. In vivo studies were performed on NIH-nude mice (6 to 8 weeks old) implanted into the right back flank with 1.5×10^6 8505 C cells. After 21 days, animals with tumors measuring 25-50 mm³ were divided into 2 groups: 1) Control (n=8); 2) Cmpd-2 (n=15). Cmpd-2 was administered intraperitoneally on alternate days for 21 days at a dose of 1 mg/kg body weight. **Results:** 8505C cells showed a significantly higher uptake of both, Cmpd.1 and Cmpd.2 respect to BPA. Autoradiography showed internalization of the bimodal compound. In vitro irradiation studies demonstrated a significant decrease in cell survival, a lower number of Ki67 positive cells and a higher percentage of apoptotic cells for the BNCT-Cmpd-2 group ($p < 0.01$). Cmpd-2 was not toxic and the relative tumor volume was smaller indicating an antitumor effect ($p < 0.05$). On day 21, a biodistribution study was performed and boron measurements in the tumor showed values of approximately 1, 16, and 19 $\mu\text{g B/g}$ tissues for Cmpd.2, BPA and Cmpd.2 plus BPA groups respectively. **Conclusions:** boron-enriched lapatinib could be used for the treatment of ATC by targeted therapy and BNCT respectively.

THYROID CANCER BASIC

1112301 - CHARACTERIZATION OF NON-TARGETED EFFECTS OF EXTERNAL RADIOTHERAPY IN ADVANCED THYROID CARCINOMA IN VITRO MODEL

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Introduction: Radiation-induced bystander effect is the phenomena occurring in non-irradiated cells as a result of signal transmission from an irradiated cell. We aimed to investigate the bystander signaling that could promote the mitigation of the radiation-induced effects in anaplastic thyroid carcinoma (ATC). **Methods:** ATC cells (8505C) were irradiated with 0, 2 and 5 Gy (X-rays) and 72h post-irradiation conditioned medium (CM) was collected. Clonogenic and MTT assay were used to analyze cell viability. Cell migration was assessed via Wound Healing in vitro scratch assay. Reactive oxygen species (ROS) generation was evaluated by the DCHF-DA assay and expression of genes involved in ROS homeostasis and inflammation were measured through qPCR. COX2 expression and phospho-NF- κ B nuclear translocation were analyzed by immunocytochemistry. **Results:** Radiation-induced ROS production at 24 and 72 h after irradiation (1.8-fold, $p < 0.01$) is correlated with significantly elevated mRNA levels of NOX4 (2.8-fold) and NOX5 (2.5-fold). Furthermore, we observed a significant increase in mRNA levels of TNF- α (2.8-fold), TGF- β 1 (2-fold), and COX2 (3.5-fold). Decreased levels of Nrf-2 (0.5-fold), Galectin-3 (0.35-fold) and Galectin-1 (0.5-fold) were also found. In non-irradiated cells, CM increased ROS (1.8-fold, $p < 0.05$) and cell migration (15%, $p < 0.05$) while proliferation was inhibited (10%, $p < 0.05$). Besides, CM(2Gy) significantly increased Galectin-3 and INF- β (2.1-fold) levels. CM(5Gy) significantly increased TGF- β 1 (1.7-fold), TNF- α (2-fold), COX2 (2.1-fold), INF- β (2.1-fold), β -catenin levels (1.7-fold) and also decreased Galectin-1 levels (0.54-fold). The effect on the expression of COX2, Galectin-3 and Galectin-1 was reversed by 10 μ M TGF- β 1 inhibitor (SB431542). Moreover, CM increased the levels of p-NF- κ B (1.5 fold, $p < 0.01$) in the cell nuclei and COX2 (1.9, $p < 0.01$) expression. Both effects were reversed by SB431542. **Conclusion:** Irradiated cells and non-irradiated bystander 8505C cells could secrete distinct cellular signals that promote tumor survival. As a result, targeting these cytokines or their downstream signaling pathways represents a promising approach for treating ATC.

THYROID CANCER BASIC

1112547 - CHARACTERIZATION OF TUMOR RESISTANCE MECHANISMS IN ANAPLASTIC THYROID CANCER INDUCED BY RADIATION THERAPIES

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Introduction: Anaplastic thyroid carcinoma (ATC) is an aggressive malignancy with poor response to conventional treatments. Disease recurrence and tumor resistance to several radiotherapeutic modalities as X-rays and boron neutron capture therapy (BNCT) have been described previously. Different signaling pathways are involved in the response to radiation-induced DNA damage (RDD), such as TGF β /Smad or nuclear Sirtuins/NAD⁺. On the other hand, cancer stem cells (CSCs) are a subpopulation known for its high tumorigenic potential and resistance to chemo- and radiotherapy. **Objective:** This study aims to compare the RDD induced by different ionizing radiation therapies and explore the underlying mechanisms of radioresistance in ATC cells. **Methods:** Human ATC cells (8505C) were divided into the four groups: 1) Control (untreated); 2) X-rays; 3) NCT (neutron thermal irradiation); and 4) BNCT (irradiated with thermal neutrons and boron-10). Cells were irradiated in the RA-3 nuclear reactor (neutron flux = 5.109 n/cm²/sec) or in an X-ray accelerator, with physical doses ranging from 1 to 5 Gy. Post irradiation studies were performed. **Results:** BNCT showed a decrease in cell survival at 1 and 3 Gy ($p < 0.001$) and an increase in micronucleus formation at 3 Gy. At 2 h post-irradiation, BNCT induced higher mRNA levels of Atr ($p < .05$), Tgf- β ($p < 0.001$), rTgf- β 1 ($p < 0.001$), and Sirt1 ($p < 0.01$) compared to X-rays. Conversely, X-ray treatment significantly increased the expression of Atm ($p < 0.01$) and Smad 2 ($p < 0.05$) and Smad 7. Additionally, BNCT also increased Cox-2 gene expression ($p < 0.001$), correlated with higher protein levels at 48 h. The number of oncospheres larger than 70 μ m significantly decreased over time, while their average diameter increased from day 3 to day 6 in the X-ray, NCT, and BNCT groups. **Conclusion:** The DDR and radioresistance mechanisms are different for each radiotherapy, highlighting the potential for combining ionizing radiation with targeted inhibitory drugs to enhance treatments efficacy.

THYROID CANCER BASIC

1112470 - CLINICAL APPLICATION OF CIRCULATING TUMOR DNA FOR RET INHIBITOR THERAPY DECISION IN PATIENTS WITH ADVANCED MEDULLARY THYROID CARCINOMA

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Introduction and Objectives: We evaluated the clinical significance of circulating tumor DNA (ctDNA) analysis in the plasma of patients with advanced medullary thyroid carcinoma (MTC) for detection of RET mutations prior to enrollment in RET inhibitor therapy with selpercatinib, even in the absence of tissue samples (blood-first approach). **Methods:** We retrospectively analyzed 36 RET-positive patients divided into three cohorts: Cohort 1: 18 patients undergoing selpercatinib therapy following disease progression; Cohort 2: 9 patients currently treated with a multi-kinase inhibitor (MKI); Cohort 3: 9 patients with metastatic disease but stable disease progression. For patients of cohort 1, plasma samples were collected just before therapy initiation, while in cohorts 2 and 3, we analyzed the most recent plasma samples available at follow-up. RET driver mutations in ctDNA were assessed using specific assays using a Droplet Digital PCR (ddPCR) approach. **Results:** The RET driver mutation was detected in 18/36 (50%) of ctDNA samples, with different distributions across cohorts: Cohort 1: 88.9%; Cohort 2: 0%; Cohort 3: 11.1% ($P < 0.0001$). A higher allelic frequency (AF) value was detected in patients of cohort 1 (4.82%) when compared to patients with a detectable ctDNA of cohort 3 (0.04%) ($P = 0.0206$). Detectable RET mutation in ctDNA was correlated with disease progression ($P < 0.0001$) and associated with a higher number of metastatic sites ($P = 0.0051$) and lesions ($P = 0.0029$) compared to patients with undetectable ctDNA and stable disease ($P = 0.0116$). **Conclusions:** ctDNA was detectable in about 90% of metastatic MTC patients with disease progression, and its mutational profile can be safely used for therapeutic enrollment, even in the absence of tissue analysis. Undetectable ctDNA in plasma could be due low release of ctDNA correlated to the stability of the disease. Fundings: PNRR European Union NextGenerationEU through the Italian Ministry of University and Research under PNRRM4C2-I1.3 Project PE_00000019 HEAL ITALIA to R.E., CUP I53C22001440006

THYROID CANCER BASIC

1112451 - COPY NUMBER ALTERATIONS AND DLK1 EXPRESSION IN THYROID CANCER CELL LINES: INSIGHTS INTO REGULATORY MECHANISMS ACROSS CANCER SUBTYPES

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Introduction: Recurrent somatic copy number alterations (CNAs) involving the DLK1 locus (14q32.2) have been identified by our group in both sporadic and hereditary cases of medullary thyroid carcinoma (MTC). This alteration, particularly somatic copy gain, was associated with increased DLK1 protein expression and pathological features indicative of more aggressive disease and poorer clinical outcomes. We further identify DLK1 differentially expressed in two RET-driven MTC cell lines. Higher levels of DLK1 was expressed in MZ-CRC-1 (p.M918T) compared to TT (p.C634W) cells. DLK1 is a maternally imprinted and paternally expressed gene located within the DLK1-DIO3 gene cluster on chromosome 14q34. Recent studies suggest that in certain cancer subtypes, DLK1 expression is driven by core regulatory circuitry (CRC) transcription factors binding to super-enhancers (SE), which regulate its expression. **Objective:** To explore the regulatory mechanisms driving DLK1 expression in MTC and in non-MTC cells. **Methods:** Genomic DNA was extracted from two RET-driven MTC cell lines (MZ-CRC-1 and TT) and four non-MTC cells (FTC133, B-CPAP, XTC.UC1, and 8505c). DNA was amplified using an assay specifically designed to assess CNA (Hs00288713_cn, Thermo Fisher Scientific) on Qiagility nanoplate-based digital PCR system. Protein was isolated from all cell lines and its expression investigated using Western blot analysis. **Results:** Digital PCR revealed a copy number gain in MZ-CRC-1, FTC-133 (metastatic follicular carcinoma), and 8505c (anaplastic carcinoma) cells, while TT and XTCU.1 (oncocytic carcinoma) cells exhibited a normal copy number, and B-CPAP (papillary carcinoma) cells showed copy number loss. In medullary thyroid carcinoma (MTC) cell lines, a correlation was observed between copy CNA and protein expression. However, in non-medullary thyroid carcinoma cell lines, DLK1 expression was absent, suggesting that DLK1 regulation in these cells may involve alternative mechanisms. **Conclusion:** These findings highlight the complexity of DLK1 regulation and its potential role in MTC pathogenesis and progression.

THYROID CANCER BASIC

1112283 - CPS1 AS A POTENTIAL BIOMARKER FOR ACTIVE SURVEILLANCE IN LOW-RISK PAPILLARY THYROID CARCINOMA

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Introduction: With the increasing incidence of papillary thyroid carcinoma (PTC), active surveillance (AS) has emerged as a focal point of research, offering an alternative to conventional surgery. However, current methodologies fall short in precisely identifying patients suitable for AS. This study identifies carbamoyl-phosphate synthase 1 (CPS1) through proteomic sequencing as a reliable marker for assessing PTC risk, potentially enhancing diagnostic accuracy and therapeutic outcomes while avoiding unnecessary surgeries and promoting personalized treatment. **Methods:** Using the TCGA database, we explored the differential expression of CPS1 in thyroid cancer versus adjacent normal tissues and analyzed its correlation with PTC clinical phenotypes. Subsequently, quantitative real-time PCR and Western blot analyses were conducted to evaluate CPS1 expression in PTC tissues and cell lines. KEGG pathway analysis was performed to elucidate the role of CPS1 in thyroid cancer pathogenesis and prognosis. **Results:** Proteomic sequencing identified CPS1, with TCGA analysis revealing significantly lower CPS1 expression in PTC tissues compared to normal tissues ($P < 0.001$). Clinical data analysis from TCGA showed a significant association between CPS1 expression and TNM staging, with lower CPS1 expression correlating with higher T stages and lymph node metastasis, but not distant metastasis. Validation with 46 paired PTC and adjacent tissues through quantitative PCR and Western blot confirmed lower CPS1 expression in PTC tissues ($P < 0.01$). KEGG pathway enrichment revealed CPS1's involvement in nitrogen metabolism, arginine biosynthesis, and alanine, aspartate, and glutamate metabolism pathways. Immuno-infiltration analysis demonstrated a negative correlation between CPS1 expression and dendritic cells, and a positive correlation with NK cells. **Conclusion:** CPS1 is under-expressed in PTC and is associated with high-risk clinical staging, suggesting its potential as a biomarker for active surveillance in PTC. This study identifies CPS1 as a precise indicator of PTC risk, which could reduce unnecessary surgeries and benefit more patients.

THYROID CANCER BASIC

1113657 - CRITICAL ANALYSIS OF SHG MICROSCOPY IMPACT ON MEDULLARY THYROID CARCINOMA: FROM BENCH TO CLINICAL APPLICATIONS

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Introduction: Medullary thyroid carcinoma (MTC) is a rare, aggressive thyroid cancer often associated with MEN2. This study employed second harmonic generation (SHG) microscopy to evaluate the tumor microenvironment of MTC by quantifying collagen fiber morphology and correlating these metrics with immunohistochemical profiles. Collagen parameters – including fiber width, length, straightness, angle, alignment, and count – were assessed in tumoral, interface, and normal tissues. **Objective:** The primary objective was to investigate the prognostic impact of SHG microscopy on MTC by characterizing collagen fiber remodeling in MEN2 patients. Specifically, the study aimed to quantify and compare collagen parameters across different tissue regions, correlate these features with immunohistochemical markers and clinical parameters (e.g., Ki-67 index, mitotic activity, TNM classification, surgical margins, multifocality), and identify potential prognostic markers to guide personalized management. **Methods:** Tissue samples from 24 MTC patients were assembled into tissue microarrays and analyzed using a confocal inverted Zeiss LSM 780-NLO system. Computational tools (CT-FIRE and Curvelets) were employed to extract collagen metrics. Immunohistochemistry for markers (CD3, CD4, CD8, CD20, FoxP3, CD68, PD-L1) was quantified with digital image analysis (QuPath). Statistical analyses were performed using Mann-Whitney, Kruskal-Wallis, Kaplan-Meier survival analysis, and multivariate logistic regression, with significance set at $p < 0.05$. **Results:** SHG analysis revealed significant alterations in collagen morphology ($p < 0.05$). Men showed higher median values for fiber width, length, straightness, angle, alignment, and count in tumoral and interface areas (all $p < 0.05$), while normal tissues in women had greater fiber orientation ($p = 0.031$). A Ki-67 index of 2% was linked to a more organized collagen architecture (tumoral, $p = 0.047$; interface, $p = 0.034-0.022$). Extensive surgical interventions correlated with enhanced fiber metrics (length, $p = 0.037$; straightness, $p = 0.044$; angle, $p = 0.029-0.031$; count, $p = 0.027-0.021$). Immunohistochemistry revealed enriched lymphocytic markers in normal tissues compared to tumoral areas ($p < 0.05$), with significant correlations between collagen and immune parameters ($p = 0.008-0.021$). **Conclusion:** SHG microscopy is a valuable tool for assessing collagen remodeling in MTC.

THYROID CANCER BASIC

1112287 - CRITICAL CNR1 POLYMORPHISMS ALTER CB1 RECEPTOR FUNCTION: UNVEILING NEW PATHWAYS IN THYROID CANCER DEVELOPMENT

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The endocannabinoid system (ECS) is related to thyroid cancer (TC) pathogenesis, as CB1 and CB2 receptors are overexpressed in papillary thyroid carcinoma compared with benign lesions. The CB1 receptor encoded by CNR1 is linked to signaling pathways that affect cell growth and death, potentially influencing TC development. However, the effects of CNR1 polymorphisms on protein function and structure, and their impact on ECS and TC are still not well understood. We combined publicly available datasets and robust open-source bioinformatics tools to perform morphological and functional analyses of the CNR1 polymorphisms. A total of 300 CNR1 missense SNPs were identified in the NCBI dbSNP database, of which 27 were classified as deleterious by the SIFTBlink software and subsequently selected for analysis using a comprehensive set of tools. Variants H269P, M308T, R14H, and H302P were predicted to be pathological by the SNPs&GO, PhD-SNP, and PMut tools. Using the I-Mutant2.0 software, we observed that all these mutations, except H302P, caused a reduction in protein stability, which may result in the loss of the corresponding structure. These polymorphisms are located in conservation areas and are more likely to affect protein function and contribute to disease development. Finally, the STRING tool revealed interactions between CNR1 and key proteins involved in thyroid pathology, including the alpha subunit of guanine nucleotide-binding protein G, which is considered one of the main causes of hot thyroid nodules, and the adenosine A2a receptor, which is related to cell proliferation. Our data suggest that specific CNR1 polymorphisms may significantly alter CB1 receptor structure and function, potentially influencing TC development through shared molecular pathways between the ECS and thyroid physiology. These findings warrant further investigation of the role of the endocannabinoid system in TC pathogenesis and suggest that the variants we identified may have clinical utility as TC biomarkers.

THYROID CANCER BASIC

1112347 - DUAL-FRONT STRATEGY WITH PACLITAXEL AND MAPK INHIBITORS INDUCING CHROMOSOMAL INSTABILITY AS A NOVEL TREATMENT FOR ADVANCED THYROID CANCER

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Introduction: Iodine-refractory thyroid carcinomas have a poor prognosis and limited treatment options, representing a significant unmet clinical challenge. Inducing chromosomal instability (CIN) beyond the survival threshold of cancer cells is a promising therapeutic strategy, as it leads to mitotic failure and cell death. Paclitaxel, a microtubule-stabilizing agent, induces CIN by promoting persistent multipolar spindle formation during mitosis, disrupting proper cell division. However, its effectiveness in thyroid cancer remains underexplored. **Objective:** This study evaluates paclitaxel's role as a CIN inducer and its potential synergy with MAPK inhibitors for advanced thyroid cancer treatment. **Methods:** Thyroid carcinoma cell lines undifferentiated (8505c), poorly differentiated (B-CPAP), papillary (TPC1), oncocyctic (XTC.UC1), and follicular (FTC-133, FTC-238) were analyzed for baseline CIN features, including mitotic errors (misaligned, lagging, and bridge chromosomes) and spindle abnormalities using immunofluorescence. Cells were treated with paclitaxel alone and in combination with MAPK inhibitors (Sorafenib, Lenvatinib, and AZ628). Drug efficacy was assessed through MTT viability assays, colony formation, and CIN markers. **Results:** Baseline CIN features were observed in all cell lines. Among all, XTC.UC1 exhibited the highest frequency of chromosome division errors (20%), while 8505c and B-CPAP were notable for their rates of multipolar spindle formation (20% and 14%, respectively). Paclitaxel induced persistent multipolar spindles across all subtypes, significantly reducing viability and colony formation. In paclitaxel-treated 8505c cells, multipolar spindles exceeded 80%, correlating with decreased viability ($p < 0.0001$). Combining paclitaxel with MAPK inhibitors amplified CIN induction, particularly with AZ628, which disrupted spindle focusing - the reorganization of multipolar spindles into bipolar ones - increasing CIN and enhancing cell death, especially in 8505c cells ($p < 0.0001$). **Conclusion:** Paclitaxel effectively induces CIN and promotes cell death across thyroid cancer models. The combination with MAPK inhibitors, particularly AZ628, enhances these effects, offering a promising dual-targeted strategy for treating aggressive thyroid cancers and improving patient outcomes.

THYROID CANCER BASIC

1112302 - ELUCIDATING THE MECHANISM OF ACTION INVOLVED IN THE ANTIPROLIFERATIVE EFFECTS OF IODO-DELTA LACTONE

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Introduction: Several studies have shown the antiproliferative effect of iodine and 5-hydroxy-6-iodo-eicosatrienoic delta lactone (IL- δ) on diverse tissues. IL- δ has been shown to inhibit cell proliferation in multiple cancer cell lines, including breast, prostate, neuroblastoma, glioblastoma, melanoma, colorectal, and thyroid cancers. The aim of this study was to analyze the possible mechanisms of action underlying the antiproliferative effect of IL- δ . **Methods:** To evaluate the behavior of IL- δ , radiolabeling with 0.5 mCi of ¹³¹I was performed. The radiochemical yield was determined using high-performance liquid chromatography (HPLC) and autoradiography of thin layer chromatography on silica gel (TLC). Binding and internalization assay was performed in 8505C (undifferentiated cell line), TPC (papillary cell line) and N-thy-ory3-1 (normal thyroid cell line) cultured in p24 dishes at 80% confluence. **Results:** The efficiency of radiolabeling was 70% and free ¹³¹I was eliminated by a silica column. Internalization assay revealed that ¹³¹I-IL δ uptake was 7.3 $\pm$ 1.2 % in 8505C, 8.1 $\pm$ 1.3 % in TPC-1 and 2.7 $\pm$ 1.1 % in N-thy-ory3-1. The kinetics of ¹³¹I-IL δ uptake in 8505C cell line showed an increase after 10 min of incubation, reaching a peak by 180 min, followed by a decrease ($p < 0.05$). Membrane-associated activity remained constant at approximately 1 $\pm$ 0.4% over time. Pre-incubation with IL- δ didn't change ¹³¹I-IL δ uptake (n.s). Subcellular activity distribution analysis showed 55% in nuclear fraction and 45% in the supernatant, and the activity remains associated in the TCA precipitate fraction. **Conclusion:** Our findings indicate that there is no specific plasma membrane receptor for IL- δ . Instead, it likely interacts with specific intracellular proteins, and possibly through nuclear receptors, to mediate its antiproliferative effects.

THYROID CANCER BASIC

1114061 - ENHANCING RADIOACTIVE IODINE AVIDITY WITH SODIUM SELENITE IN PAPILLARY THYROID CANCER

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Introduction: Radioactive-iodine (RAI) therapy is a therapeutic mainstay strategy for recurrent and metastatic differentiated thyroid cancer (DTC). However, a substantial portion of DTC patients exhibits dedifferentiation status with a lack of sodium-iodide symporter (NIS) functionality and expression, as well as downregulated thyroid-specific proteins and transcription factors. Eventually, this status is connected to the failure of RAI therapy with an overall poor prognosis. Selenium, an essential trace element for humans, has several crucial functions with antitumor, antioxidant, immunity-promoting, and antiviral activity. Additionally, selenium is important for the synthesis and metabolism of thyroid hormones. An article reported that sodium selenite induces RAI uptake in thyroid tissue in rats. However, the relationship between sodium selenite and differentiation markers in DTCs remains unclear. **Objective:** In this study, we investigated the effects of sodium selenite for reinforcing I-131 therapeutic effects by enhancing RAI avidity in papillary thyroid cancer (PTC) cells. Furthermore, we analyzed changes in several signaling pathways or factors induced by sodium selenite treatment. **Methods:** We used a BHP10-3SCp, a human PTC cell line harboring the RET/PTC rearrangement. The cells were treated with sodium selenite and incubated for ~ 72 hrs. Expression of thyroid-specific proteins and radioactive avidity were evaluated before and after sodium selenite treatment. Cytotoxic effect of I-131 was tested before and after sodium selenite treatment. **Results:** Thyroid-specific proteins (sodium iodide symporter, thyroperoxidase, TSH receptor) and transcription factors (TTF-1, PAX-8) were upregulated by sodium selenite treatment. RAI avidity and RAI uptake was increased by sodium selenite treatment. I-131 cytotoxicity was increased by sodium selenite treatment. Sodium selenite treatment downregulated MAPK, PI3K-AKT, and GSK-3 β / β -catenin signaling pathways. **Conclusion:** Sodium selenite can be a promising candidate for enhancing RAI avidity in PTC cells and it can be used to preparation of I-131 therapy in patients with inoperable PTCs.

THYROID CANCER BASIC

1112590 - EPIDEMIOLOGICAL ANALYSIS OF PROCEDURES PERFORMED TO TREAT THYROID CANCER IN BRAZIL

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Introduction: Thyroid cancer is classified as well or poorly differentiated, based on histopathology. In Brazil, well-differentiated carcinomas are more prevalent, allowing effective treatments such as thyroidectomy (total or partial) and iodine therapy as an adjuvant to eliminate residual neoplastic foci. **Objective:** Analyze therapeutic approaches for thyroid cancer between 2014 and 2023 in Brazil. **Methods:** Ecological, descriptive and quantitative study, using data extracted from the Hospital and Outpatient Information Systems of the Brazilian Unified Health System (DATASUS). Records of procedures related to oncological thyroidectomy and iodine therapy for differentiated thyroid carcinoma were selected. Data from 2014 to 2023, including Brazil's five regions, were organized in Excel spreadsheets and analyzed using descriptive statistics. **Results:** Between 2014 and 2023, 40,995 thyroidectomies were performed in Brazil. The year 2022 recorded the highest number, 4,900 (11.95%), while 2020 registered the lowest, 3,578 (8.73%). The Southeast region accounted for 15,585 procedures (38.02%), followed by the Northeast (31.71%) and South (18.11%). Elective thyroidectomies represented 91.41% of the total, with 68 deaths (0.17%) recorded. Regarding iodine therapy for differentiated thyroid carcinoma, 34,095 hospital-based and 4,420 outpatient procedures were performed. **Conclusion:** There has been an increase in partial and total thyroidectomy for oncological treatment, while the use of the iodine therapy for differentiated thyroid carcinoma has declined over the same period. This trend aligns with the National Cancer Data Base (NCDB), which reported a 20% increase in total thyroidectomy for papillary thyroid cancer from 1985 to 2003 in the United States. Additionally, the reduced number of thyroidectomies in 2020 may reflect the impact of the COVID-19 pandemic on elective procedures. These findings highlight the importance of early diagnosis and treatment strategies for thyroid cancer through effective public health policies.

THYROID CANCER BASIC

1112602 - EPIDEMIOLOGICAL COMPARISON OF THYROID CANCER IN BRAZIL AND THE UNITED STATES

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Introduction: Thyroid cancer is the most common endocrine malignancy worldwide, with varying incidence and mortality rates between countries. The disease has a higher prevalence in women, and its prognosis depends on early detection and appropriate treatment. Factors such as healthcare access and demographic characteristics may contribute to regional variations in thyroid cancer outcomes. **Objective:** Compare the incidence and mortality rates in 2022 of thyroid cancer in Brazil and in the United States (U.S.). **Methods:** Ecological, descriptive and quantitative study using data extracted from the Global Cancer Observatory (GCO) on the incidences and mortality rates from thyroid cancer. Variables included sex and age-related differences between Brazil and the U.S. Data was organized in Excel and analyzed descriptively. **Results:** The incidence of thyroid cancer in the US was 52,169 cases, in which women represent 74.04%. Brazil reported 31,385 cases, with women accounting for 81.58%. Mortality was lower in both countries compared to incidence, with 2,244 deaths in the U.S. and 1,103 in Brazil. Women accounted for most deaths in both regions (52.08% in the US and 65.63% in Brazil). Among individuals aged 60 and older, mortality was higher in the U.S. (85.52%) compared to Brazil (77.61%). **Conclusion:** In both countries, thyroid cancers incidence is higher than its mortality. This can be explained by the increased number of thyroidectomies as an effective treatment for the disease. The age-related mortality disparity underscores potential differences in healthcare access, diagnostic strategies, and treatment outcomes. These findings emphasize the importance of tailored public health policies to improve early detection and management of thyroid cancer, particularly in high-risk groups.

THYROID CANCER BASIC

1112594 - EPIDEMIOLOGICAL PROFILE OF DEATHS FROM MALIGNANT THYROID NEOPLASMS IN BRAZIL

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Introduction: Thyroid cancer is the most common endocrine malignancy and predominantly affects women, with an incidence higher than in men. Mortality rates vary according to cancer subtype, with well-differentiated carcinomas (papillary and follicular) presenting lower rates, while anaplastic and medullary carcinomas are more lethal. However, mortality patterns can vary based on demographic, regional, and healthcare-related factors, necessitating epidemiological studies to better understand the burden of thyroid cancer. **Objective:** Analyze mortality data from malignant thyroid neoplasms in Brazil between 2014 and 2023. **Methods:** Ecological, descriptive and quantitative study using data extracted from the Mortality Information System (DATASUS) on deaths from malignant thyroid neoplasms. Variables included year, region, sex, race and age group. Data was organized in Excel and analyzed descriptively. **Results:** From 2014 to 2023, 8,356 deaths from malignant thyroid neoplasms were recorded in Brazil. The year 2023 had the highest mortality (11.7%), while 2016 had the lowest (8.8%). The Southeast Region accounted for 40% of deaths, followed by the Northeast (30.2%) and South (15.9%). Elderly individuals (≥ 60 years) represented 76.5% of deaths, followed by adults (2059 years, 23.2%) and children (< 20 years, 0.3%). Women accounted for 65.9% of deaths, and white individuals for 54.5%, followed by brown individuals (35.1%). **Conclusion:** In the last decade, thyroid cancer mortality in Brazil was highest among elderly, white women in the Southeast region. Comparatively, Globocan 2022 United States data show similar age-related patterns but Brazil's female-to-male mortality ratio (1.91:1) is higher than the U.S. (1.08:1), suggesting disparities in disease management. Additionally, the COVID-19 pandemic likely influenced cancer-related healthcare, contributing to variations in mortality trends in 2020. These findings emphasize the importance of targeted public health policies to enhance early diagnosis and treatment, particularly among high-risk populations.

THYROID CANCER BASIC

1113751 - EPIGENETIC COMPLEX EZH2/PRC2 MEDIATES TRANSCRIPTIONAL SILENCING OF THYROID DIFFERENTIATION GENES IN ANAPLASTIC THYROID CANCER

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Introduction: Anaplastic thyroid carcinoma (ATC) is the most aggressive endocrine malignancy, characterized by thyroid-cell dedifferentiation and resistance to radioiodine therapy. Mutations in MAPK signaling genes (BRAFV600E, NRAS, or HRAS), alongside TP53 and TERTp, are common in ATC, but additional alterations, such as epigenetic dysregulation, also contribute to its aggressiveness. In particular, PRC2/EZH2 upregulation promotes gene silencing via H3K27me3 histone modifications. While EZH2 inhibition has been shown to restore differentiation and reduce tumorigenicity in BRAF-mutated ATC, its role in RAS-mutated ATC cells and the mechanisms linking EZH2 to dedifferentiation remain unclear. **Objective:** To investigate the role of PRC2/EZH2 in ATC's dedifferentiation. **Methods:** EZH2/H3K27me3 binding sites on thyroid differentiation genes (TDGs) were identified using the Cistrome Database. Chromatin immunoprecipitation (ChIP) followed by qPCR was performed on SW1736 cells to confirm EZH2/H3K27me3 enrichment at SLC5A5 and NKX2-1. To evaluate the effect of EZH2 inhibition on TDG expression, Hth7 (NRASQ61R) and C643 (HRASG13R) cells were treated with EPZ6438 (5 μ M; EZH2 inhibitor) for 6 days, alone or with U0126 (10 μ M; MEK1/2 inhibitor). TDG expression was analyzed by qPCR, and non-radioactive iodine uptake was assessed in RAS- (Hth7 and C643) and BRAF-mutated cells (KTC2 and SW1736). **Results:** EZH2/H3K27me3 were enriched in most TDGs identified in the Cistrome Database using non-thyroid cell models. ChIP-qPCR revealed novel enrichment sites at SLC5A5 and NKX2-1 genes. EZH2 inhibition significantly increased TDG expression (SLC5A5, TPO, TG, SLC26A7, and NKX2-1) in Hth7 and C643 cells. Combined treatment further enhanced TG, TSHR, NKX2-1, and FOXE1 expression. Functionally, iodine uptake increased 6.22- and 2.91-fold in Hth7 and C643, and 2.39- and 2.60-fold in KTC2 and SW1736, respectively. **Conclusion:** The EZH2/PRC2 pathway drives ATC dedifferentiation by silencing TDGs through H3K27me3 deposition. Targeting EZH2 restores thyroid function, offering a promising therapeutic strategy.

THYROID CANCER BASIC

1112502 - EVALUATION OF THE ACTIVITY OF NIFUROXAZIDE AND DERIVATIVES ON THE JAK/STAT PATHWAY IN ANAPLASTIC THYROID CANCER

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Introduction: Anaplastic thyroid cancer (ATC) is the most aggressive thyroid cancer (TC) with the lowest survival rate (6-25 months). Treatment options are limited, and most ATC develop drug resistance. JAK/STAT signaling pathway in ATC is associated with tumor development, progression, and drug resistance. Nifuroxazide (NFZ) showed antitumoral activity in different cancer models through STAT3 inhibition. However, there is currently no data regarding NFZ activity on ATC. **Objective:** To investigate the impact of NFZ and three derivatives (GPQF-63, GPQF-803, GPQF-804) on JAK/STAT signaling pathway and their antitumoral properties in ATC cell lines. **Methods:** ATC cells (KTC-2 and HTH83), two HTH83 cells with STAT3 knockout, CRISPR-Control and non-tumoral cell (Nthy-Ori3.1) were used. Drug actions were assessed through cell viability (PrestoBlue), colony formation, reactive oxygen species (ROS) generation (DCF-DA) and apoptosis assays. Proliferation assays were conducted to evaluate the effect of STAT3 knock-out in HTH83. Signaling pathways modulation of JAK/STAT, MAPK and PI3K were accessed by western blot. **Results:** NFZ and derivatives reduced cell viability and induced cell death by apoptosis or necrosis in ATC cells. ROS generation contributed to cell death of HTH83 but not of KTC-2. In HTH83, NFZ and derivatives reduced colony-forming ability, while in KTC-2 only the derivatives decreased colony formation. NFZ failed to reduce cell viability of the STAT3-knockout cells in HTH83, which showed reduced cell proliferation. The first results indicated that NFZ reduced p-STAT3 and total-STAT3 in KTC2, as well as GPQF-63 in HTH83. GPQF-803 reduced only p-STAT3 in HTH83. NFZ also reduced p-AKT and p-ERK in HTH83 and KTC-2, and total-ERK in KTC2. **Conclusion:** NFZ and derivatives exhibited antitumor properties through the modulation of JAK/STAT, MAPK or PI3K/AKT in ATC cells, and their activity may be influenced by the cellular genetic background. The modulation of JAK/STAT pathway may be a promising option for anaplastic thyroid cancer.

THYROID CANCER BASIC

1113971 - EVIDENCE AND SAFETY OF CONSERVATIVE MANAGEMENT OF PAPILLARY THYROID MICROCARCINOMA. CASE PRESENTATION

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Case Presentation: A 66-year-old female patient, mestizo, with personal pathological history of hypertension, stage IIb, overweight, and prediabetes, presents to consultation for a left thyroid nodule measuring 1.0 x 0.8 cm, taller than wide, hyperechoic, with irregular margins. Physical examination reveals a palpable thyroid and a hyperpigmented lesion on the neck compatible with acanthosis nigricans. Laboratory Results: TSH 1.52 mIU/L, T4L 10.4 pmol/L, ultrasound of the left thyroid nodule measuring 1.0 x 0.8 cm, cytology category V, contrasted neck CT negative for suspicious lymph nodes, thyroglobulin (75 ng/mL), anti-thyroglobulin 8 UI/mL, CEA (2 ng/mL). Considering current recommendations, active surveillance is advised for the patient; after 6 months of follow-up, no echographic growth of the nodule is detected, measuring 1.0 x 0.86 cm. The patient is evaluated after one year with a thyroid ultrasound that reports a left thyroid nodule measuring 0.9 x 0.7 cm, category V Bethesda. The patient missed her appointment for 2 years, and a thyroid ultrasound was performed, revealing a left thyroid nodule measuring 0.85 x 0.95 cm, and a left nodule measuring 0.35 x 0.19 cm without suspicious characteristics. Neck ultrasound did not report any adenopathies, and the contrasted neck and chest CT was negative. **Discussion:** The conservative follow-up of category V papillary thyroid carcinoma is based on an individualized approach that considers the low risk of progression, especially for tumors < 1 cm, with no evidence of metastasis, favorable ultrasound characteristics, and stability in size during follow-up, representing a safe and effective alternative as previously discussed. This is the first reported case of active surveillance in the country. **Final Comments:** The standard treatment has been surgery, but in recent years, clinical follow-up has become a valid option for selected patients. Observation instead of surgery offers significant benefits; avoids the risks of surgical intervention, and has lesser impact on the patient.

THYROID CANCER BASIC

1112224 - EXPLORING THE POTENTIAL OF SIGLEC15 AS NOVEL IMMUNOTHERAPEUTIC AGENT IN (THYROID) CANCER: FOCUS ON INNATE IMMUNE CELLS

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Introduction: Thyroid cancer (TC), particularly anaplastic thyroid cancer (ATC), remains a highly aggressive and poorly treated malignancy with limited therapeutic options. The Siglec15 receptor, expressed on tumor-associated macrophages (TAMs) in various cancers, is emerging as a potential therapeutic target. However, the role of Siglec15 in TC, including its function, regulation, and ligands, remains poorly understood. Given the high density of TAMs in TC, targeting Siglec15 could offer novel strategies to modulate the immune response and enhance anti-tumor immunity. **Methods:** This study employed a multi-faceted approach using tumor-conditioned media, proteomic profiling, and glycosylation inhibition to explore how Siglec15 influences immune cell behavior and tumor progression in TC. **Results:** Tumor-conditioned media from multiple TC cell lines increased the expression of Siglec15 on immune cells, suggesting that TC cells can modulate immune cell phenotypes through soluble factors. In cells with stable Siglec15 overexpression, we observed a significant increase in the secretion of chemokines (e.g., CCL4, CCL20, MCP-3) and cytokines (e.g., CXCL8, TNF) compared to controls. These findings suggest that Siglec15 may influence immune cell recruitment and activation within the tumor microenvironment. Furthermore, binding assays revealed that Siglec15 interacts with a previously unidentified glycan structure on TC cells, distinct from the known sialyl-Tn antigen, indicating a potential novel ligand for Siglec15 in TC. **Conclusion:** Targeting Siglec15, either directly on immune cells or by disrupting its interactions with ligands on TC cells, may shift the immune response toward a more pro-inflammatory and anti-tumoral phenotype. These findings support exploring Siglec15 as a therapeutic target in TC and potentially in other cancers with similar immune dynamics.

THYROID CANCER BASIC

1113621 - EXPRESSION ANALYSIS OF CLDN1, KRT19 AND TIMP1 IN THYROID NODULES CLASSIFIED BY THE BETHESDA SYSTEM

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Introduction: The Bethesda System is a standardized tool used to classify thyroid nodules by fine needle aspiration (FNA). Although its sensitivity and specificity for detecting malignancy are high in Bethesda categories II (benign) and VI (malignant), Bethesda categories III and IV (indeterminate) have malignancy rates that vary considerably, between 5-15% and 15-30%, respectively, which limits its diagnostic accuracy. This uncertainty can lead to unnecessary surgical procedures. Therefore, the incorporation of molecular biomarkers has emerged as a complementary approach to improve risk stratification. **Objective:** The aim of this study was to analyze the expression of CLDN1, TIMP1 and KRT19 genes in thyroid nodules classified according to the Bethesda System. **Methods:** We analyzed 210 FNA of thyroid nodules suspected by ultrasound and subsequently classified using the Bethesda System. Bethesda II (n = 92), Bethesda IV (n = 23), Bethesda V (n = 11) and Bethesda VI (n = 84) were included. Gene expression of CLDN1, TIMP1 and KRT19 was assessed by qPCR and statistical analyses were performed. **Results:** Significant differences were found in the expression of the three genes between Bethesda categories ($p < 0.001$). TIMP1 showed different expression levels in Bethesda IV (3.14 ± 0.61) and VI (2.29 ± 0.38) compared to Bethesda II. For KRT19, values in Bethesda IV (2.90 ± 0.92) and VI (4.31 ± 0.59) were also different with respect to Bethesda II. In CLDN1, differences in expression levels were identified between Bethesda IV (3.48 ± 1.14) and VI (5.59 ± 0.76) relative to Bethesda II. No significant variations in gene expression levels were observed between Bethesda IV, V and VI categories. **Conclusion:** The CLDN1, TIMP1 and KRT19 genes show differential expression according to Bethesda categories, highlighting their potential as molecular biomarkers to improve the characterization of thyroid nodules. This approach could complement traditional cytological evaluation.

THYROID CANCER BASIC

1112492 - FIBRONECTIN DRIVES NF-KB ACTIVATION VIA TOLL-LIKE RECEPTOR 4 CONTRIBUTING TO PAPILLARY THYROID CANCER PROGRESSION

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Introduction: Fibronectin (FN1), a major extracellular matrix (ECM) component, acts as an endogenous damage-associated molecular pattern (DAMP) molecule promoting Toll-like Receptor 4 (TLR4) signaling. FN1 is strongly associated with tumor progression and poor outcome in several cancers. However, its role in the progression of papillary thyroid cancer (PTC) remains unclear. **Objective:** To investigate the FN1-TLR4 interaction in NF- κ B activation and its role in PTC progression through integrated analyses. **Methods:** FN1-deficient (FN1 KO) and TLR4-deficient (TLR4 KO) TPC1 cells were generated using CRISPR/Cas9. NF- κ B activity was assessed using luciferase reporter assays in wild-type (WT), FN1 KO, and TLR4 KO TPC1 cells, with or without recombinant FN1 treatment. Microarray-based transcriptomic analysis identified differentially expressed genes (DEGs) in FN1 KO and TLR4 KO cells compared to WT cells. Enrichment analysis was performed by DAVID software. FN1 expression data from the RNA-seq TCGA-PTC dataset stratified patients into FN1_{high} (top 30%) and FN1_{low} (bottom 30%) groups, followed by DEG analysis, enrichment analysis, and clinical correlation studies. **Results:** FN1 KO cells showed reduced NF- κ B activity. Recombinant FN1 restored NF- κ B activity in FN1 KO cells but not in TLR4 KO cells, confirming FN1-TLR4 interaction. Enrichment analysis revealed overlapping downregulated pathways in FN1 and TLR4 KO cells, including ECM remodeling, cell adhesion, and inflammatory responses. In the TCGA-PTC data, FN1_{high} tumors displayed 3101 DEGs (1681 downregulated and 1420 upregulated) compared to FN1_{low} tumors. FN1_{high} tumors showed activation of cytokine-cytokine receptor interactions, cell adhesion molecules, and ECM-receptor interactions, as well as immune (NF- κ B, TNF, IL-17, JAK-STAT), oncogenic (PI3K-Akt, MAPK), and metabolic pathways. Clinically, FN1_{high} expression correlated with advanced tumor stage, lymph node metastasis, and reduced overall survival. **Conclusions:** These findings establish FN1 as a critical regulator of PTC progression involving TLR4 downstream signaling effects, positioning FN1 as a promising biomarker and therapeutic target.

THYROID CANCER BASIC

1112205 - HIGH LEVELS OF CIRCULATING INFLAMMATORY PROTEINS AND LYMPHOCYTIC CELLULAR IMMUNOSUPPRESSION IN ANAPLASTIC THYROID CANCER

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Introduction: Anaplastic thyroid cancer (ATC) is the most aggressive tumor with no curative treatment options. The ATC tumor-microenvironment is characterized by pro-tumoral immune cells but circulating immune cells of ATC patients have not yet been immunophenotyped. Here, we aim to compare the subset counts and functional phenotype of circulating immune cells in patients with ATC, other subtypes of TC and healthy controls, to provide new pathogenetic insights in search for therapeutic targets. **Methods:** Patients with ATC (n=11), poorly differentiated thyroid cancer (PDTC, n=9), differentiated thyroid cancer (DTC, n=22) and healthy controls (n=13) donated blood. Individuals with inflammatory or infectious comorbidities were excluded. Circulating immune cell counts were assessed. Peripheral blood mononuclear cells (PBMCs) were isolated and stimulated for 24h and 7 days with different stimuli to assess cytokine production capacity by ELISA. Circulating inflammatory proteins were assessed in plasma by OLINK proteomics. **Results:** Circulating absolute numbers of neutrophils and monocytes were higher in ATC patients than in the other subgroups. After 7 days of PBMC stimulation, lymphocytes of ATC patients produced less interferon- γ and interleukin- (IL)-22 than the other subgroups. In contrast, 24h of stimulation resulted in increased concentrations of monocyte-derived cytokines in the ATC subgroup. In plasma, IL-6, IL-1RA and granulocyte-colony stimulating factor were higher in the ATC group than in the other subgroups, which could explain the high number of neutrophils in the ATC patients. In addition, IL-6 and IL-1RA were elevated in PDTC patients compared to DTC patients and healthy controls. **Conclusion:** PBMCs of ATC patients have a reduced capacity to produce lymphocyte-derived cytokines while this is increased for the monocyte-derived cytokines compared to other TC groups. Plasma concentrations of cytokines linked to myelopoiesis were higher in ATC patients, which could explain the high counts of circulating myeloid cells and reflect the aggressiveness of the disease.

THYROID CANCER BASIC

1112343 - IN VITRO ANTINEOPLASTIC EVALUATION OF CABOZANTINIB IN CONTINUOUS AND PRIMARY HUMAN CELL CULTURES FROM ANAPLASTIC THYROID CARCINOMA

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Introduction: Anaplastic thyroid cancer (ATC) is a very aggressive tumor, whose current treatments are not really effective allowing a median survival of about 6 months. The knowledge of the genetic profile of the tumor aids in the identification of new targets leading to a personalized and better treatment approach. In vitro studies permit a good preclinical evaluation of the antineoplastic effect of new drugs. **Objective:** We aimed to test the antineoplastic effect of cabozantinib, a multikinase inhibitor acting against tyrosine kinase receptors involved in growth, angiogenesis and metastatic progression of tumour. Cabozantinib was recently approved for the treatment of adult patients with locally advanced or metastatic differentiated thyroid carcinoma, not eligible or refractory to radioactive iodine who have progressed during or after prior systemic therapy. **Methods:** We performed in vitro experiments in continuous ATC cell lines (8305C and CAL-62 lines), and in primary human ATC cells obtained from surgical thyroidal samples of four females and two males with ATC (5481 years) with a tumour size range of 615 cm, at the moment of first surgical operation. **Results:** We showed a good antineoplastic effect in vitro of cabozantinib in both continuous and primary ATC cells. Cabozantinib showed a good activity in inhibiting the proliferation of the tumoral cells as well as in increasing their apoptosis. Moreover, we have observed a slightly significant decrease of the migration and invasion. **Conclusion:** Our results are very promising and highlight the importance of a personalized therapy, that can be obtained by the use of primary human ATC cells established directly from the patient in in vitro studies.

THYROID CANCER BASIC

1112509 - INVESTIGATION OF METALLOPROTEINASE (MMP) AND METALLOPROTEINASE INHIBITOR (TIMP) GENES SUGGESTS THAT TWO MMP-9 SINGLE NUCLEOTIDE VARIANTS MAY BE CLINICALLY USEFUL IN PATIENTS WITH THYROID CANCER

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Single-nucleotide polymorphisms (SNPs) are useful biomarkers. However, the increasing number of documented genetic variants present challenges for validation. Bioinformatics helps to identify the SNPs most likely to influence a disease. Two matrix metalloproteinases, MMP2 and MMP9, are mediators of tumorigenesis, including extracellular matrix reorganization, epithelial-to-mesenchymal transition, cell migration, angiogenesis, and immune response. MMP9 is considered a therapeutic target. On the other hand, tissue inhibitors of metalloproteinases (TIMPs) control MMP activity, preserving the balance between proteolytic pathways implicated in tumor invasion and metastasis. TIMP1 and TIMP3 are notable for controlling extracellular matrix remodeling and their role in cancer progression. To identify variants of potential clinical utility, we investigated the effects of polymorphisms with minor allele frequency > 0.1 for MMP2, MMP9, TIMP1, and TIMP3 on DNA and protein structures using 18 robust open-source bioinformatics tools. MMP2 analysis revealed two SNPs in dbSNP database that did not promote amino acid changes, whereas MMP9 indicated 4 amino acid changes. rs17576 was considered deleterious in 50% of PredictSNP2.0 tools and was associated with decreased protein stability and reduced molecular flexibility. The rs17577 variant was identified as harmful by GWAVA tool, and 37.5% of the PredictSNP1.0 tools. The rs2250889 variant was considered deleterious by FUN and GWAVA softwares of PredictSNP2.0, but neutral in PredictSNP1.0, causing decreased stability and alterations in protein binding. TIMP1 analysis identified rs4898 but did not result in amino acid changes in the protein. Finally, TIMP3 examination indicated that rs9862 was deleterious (CADD in Predict2.0) but did not modify amino acids in protein. We concluded that rs17576 and rs17577 MMP9 variants may affect DNA functionality, stability, and flexibility of the corresponding protein. Based on their function and location, these variants may contribute to thyroid cancer development, progression, and migration and deserve further investigation and clinical validation.

THYROID CANCER BASIC

1112294 - INVOLVEMENT OF FERROPTOSIS IN VALPROIC ACID-MEDIATED RADIOSENSITIZATION OF RESISTANT ANAPLASTIC THYROID CANCER CELLS

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Introduction: Anaplastic thyroid cancer (ATC) is one of the most aggressive malignancies in humans. Novel strategies to control it, like hypofractionated radiotherapy or radiotherapy combined with chemotherapy, are therefore necessary. Valproic acid (VA) is a clinically available anticonvulsant and histone deacetylase inhibitor, which radiosensitizes different cancer cell lines. **Objectives:** To evaluate the effect of VA on cellular radiosensitivity and the participation of ferroptosis in this process in ATC cell lines. **Methods:** KTC-2 and C643 cell lines were incubated with VA (1 mM) and irradiated (VA+IR) or irradiated alone (IR) with γ -rays. Radiosensitization was determined by clonogenic assay. Intracellular reactive oxygen species (ROS) levels were measured by the fluorescent dye 2,7-dichlorofluorescein-diacetate. BODIPY 581/591 C-11 was used to detect membrane lipid peroxides. Clonogenic assay with ferroptosis inhibitor Ferrostatin-1 (Ferr-1) was assessed. Ferroptosis related genes (PTGS2, GPX4, ACSL4, and SLC7A11) were evaluated by qPCR in KTC-2 cells. Apoptosis was measured by nuclear morphology. **Results:** VA+IR treatment decreased cell survival in radioresistant KTC-2 cells (2 Gy $p<0.001$ and 3.5 Gy $p<0.05$ vs. control). ROS levels increased in all irradiated cells ($p<0.05$). VA+IR increased lipid peroxides values compared to IR at 24 hours (3.5 Gy, $p<0.001$) and 48 hours (2 Gy, $p<0.05$) post-irradiation in KTC-2 cells. PTGS2 gene expression was up-regulated at 24 hours post-irradiation in both cell lines ($p<0.05$). Ferr-1 treatment induced a recovery of cell survival in IR cells (1 Gy, $p<0.01$), and in VA+IR cells (2 Gy, $p<0.01$). In VA+IR cells, ACSL4 and GPX4 levels were increased at 24 hours ($p<0.05$ vs. IR) whereas SLC7A11 and ACSL4 levels were diminished at 48 hours post-irradiation ($p<0.05$ vs. IR). VA+IR increased apoptosis ($p<0.05$). **Conclusion:** Gamma irradiation could induce ferroptosis in ATC cells. Also, VA radiosensitized radioresistant KTC-2 cells and ferroptosis could be one mechanism involved in this process.

THYROID CANCER BASIC

1112328 - METHIONYL-TRNA SYNTHETASE 1 EXPRESSION AS A DIAGNOSIS AND PROGNOSIS FACTOR IN PAPILLARY THYROID CANCER

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Introduction: Methionyl-tRNA Synthetase 1 (MARS1) is a critical enzyme in translation initiation, responsible for catalyzing transfer of Met to the initiator tRNA. In this study, we aimed to examine whether MARS1 expression is different between normal cells and cancer cells in thyroid tissue and if it can supplement the limitations of general cell staining methods currently performed for diagnosis of cancer. **Methods:** Initially, 103 patients were included in this study to compare MARS1 expression of cancer cells and normal cells. Next, 100 patients were selected to compare MARS1 expression using immunohistochemical analysis in patients with and without lateral neck metastasis. Lateral neck metastasis was found in 50% of the patients. **Results:** The average MARS1 expression of cancer cells was 2.59 and that of normal cells was 1.28. MARS1 expression of the two groups showed statistically significant differences ($p=0.000$). There was a significant difference in the average MARS1 expression grade of cancer cells between the metastasis and non-metastasis groups ($p<0.05$). In addition, a significant difference was observed in the average MARS1 expression grade between the lymph node of metastasis group and the cancer cells of non-metastasis group ($p<0.05$). **Conclusions:** In this study, we found that MARS1 could be used as a complementary method to the current fine needle aspiration biopsy tissue staining method. Additionally, MARS1 could be a predictor of the prognosis of papillary thyroid carcinoma.

THYROID CANCER BASIC

1112396 - MIR-665 REGULATES CELL MIGRATION AND INVASION OF THYROID CANCER CELL LINES

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Introduction: Dysregulation of microRNAs (miRNAs) plays a crucial role in the pathogenesis of papillary carcinomas (PTC). In previous work, our group observed reduced expression levels of more than 50 miRNAs from the DLK1-DIO3 genomic region in human papillary carcinoma (PTC) samples. Among these, miR-665 was identified through bioinformatics analysis as one promising tumor suppressor candidate in this cluster. **Objective:** To evaluate the tumor suppressive role of miR-665 in vitro functional assays. **Methods:** The thyroid cancer cell lines TPC-1 (RET/PTC1 oncogene), BCPAP, and KTC-2 (BRAF T1799A mutation) were transfected with commercial miR-665 mimetic at concentrations of 10nM and 20nM. Cell proliferation was assessed by a growth curve. Cell migration and invasion was analyzed using the Transwell system. Expression of miR-665 target genes was quantified by RT-qPCR. **Results:** The results indicated that overexpression of miR-665 reduced cell migration in TPC-1 and KTC-2 ($p < 0.05$) and invasion in TPC-1 and BCPAP ($p < 0.001$). Additionally, overexpression of miR-665 modulated the expression of the target genes CDH3, SRC, and MYD88 in at least one of the analyzed cell lines. No significant changes were observed in cell proliferation upon miR-665 overexpression. **Conclusion:** Our findings show that miR-665 overexpression is involved in the control of cell migration and invasion, two key steps of thyroid cancer progression, opening perspectives for novel therapeutic strategies for aggressive thyroid cancer.

THYROID CANCER BASIC

1112531 - MOLECULAR SUBTYPING OF PAPILLARY THYROID CARCINOMA AND DRUG TARGET IDENTIFICATION USING INTEGRATIVE COMPREHENSIVE PROTEOMICS

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Introduction: Thyroid papillary carcinoma (PTC) has a high detection rate using current imaging technologies; however, the accurate identification of more malignant PTC types, such as advanced and treatment-resistant forms, is crucial. There are presently no clinically relevant molecular subtypes, which hinders the development of non-surgical treatment strategies. **Objective:** We conducted mass spectrometry-based proteomics and drug target analysis using PTC and adjacent non-cancerous tissues. **Results:** According to proteomic analysis, PTC can be classified into three molecular subtypes: S1, S2, and S3. Subtype 2 PTCs are metabolically activated and proliferative, and are closely associated with lymph node metastasis. We also screened three target proteins from five drug target databases and predicted potential drug targets for treating patients with S2 subtype PTC. **Conclusion:** The proteomic analysis identified different molecular subtypes of PTC and indicated potential therapeutic targets for lymph node metastasis in PTC.

THYROID CANCER BASIC

1113976 - MUCINOUS CARCINOMA: A RARE PRESENTATION OF THYROID CANCER

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Case Presentation: 47-year-old woman with no known medical history presented with a lump in the anterior neck region two years ago, no other symptoms. Physical examination, a palpable thyroid with a nodule of 1.5 cm was detected. Laboratory tests TSH 8.55 μ IU/mL, Free T4 9.94 pmol/L, ultrasound revealed a nodule in the left thyroid lobe measuring 31 $\times$ 21 mm, with cytology classified as Category II. After one year of follow-up, ultrasound detected nodule growth, measuring 38 $\times$ 26 mm, and a new nodule in the right lobe measuring 10.5 $\times$ 9.3 mm. A repeat cytology resulted in Category V, leading to a total thyroidectomy. Contrast-enhanced abdominopelvic CT was negative, while chest imaging revealed a 4 mm ground-glass nodule in the superior and posterior segment of the right lung. Immunohistochemistry showed negativity for CEA, CDX2, and CK20, with positivity for TTF1, CJAEE1-AE3, CK19, PAX-8, and PAS-D. These findings, along with histological analysis, supported the diagnosis of mucinous thyroid carcinoma with lymphovascular and extrathyroidal invasion. The current treatment consists of levothyroxine 88 mcg daily. Post-surgical survival is 20 months, with satisfactory evolution. **Discussion:** Mucinous carcinoma, characterized by the presence of extracellular mucin "pools," is commonly found in breast, colon, stomach, ovary, and pancreas. In the thyroid, it can be associated with follicular, papillary, or medullary tumors or be metastatic. Primary mucinous thyroid carcinoma is extremely rare, only eleven cases reported in the literature. Clinical presentation varies, the prognosis is poor in all cases. This case is considered primary because immunostaining with specific thyroid markers confirmed its thyroid origin, while the lung lesion is assumed to be metastatic. **Final Comments:** Diagnosis of primary mucinous thyroid carcinoma is challenging and requires specific studies, which are only conducted if this possibility is considered. Due to its high mortality rate, early diagnosis improve patient prognosis.

THYROID CANCER BASIC

1112410 - NOX4-DERIVED OXIDATIVE DNA DAMAGE PROMOTES THE RECRUITMENT OF CHD4 TO CHROMATIN IN BRAF-MUTATED THYROID CANCER CELLS

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Introduction: CHD4 is a catalytic core of the NURD remodeling complex that represses gene transcription. It is overexpressed in papillary thyroid cancers (PTC) and associated with aggressiveness and worse outcome. CHD4 was previously found to recruit repressive chromatin proteins to oxidative DNA damage and help to maintain transcriptional silencing of genes in colon cancers. We showed that BRAFV600E controls the NADPH oxidase (NOX4) expression and that NOX4-derived ROS contribute to repression of iodine transporter (NIS) in PTC cells. **Objective:** As NOX4 may induce oxidative DNA damage we investigated the role of NOX4 in NIS gene repression by CHD4 in BRAF-mutated thyroid cancer. **Methods:** We used two human BRAFV600E-mutated thyroid cell lines (BCPAP and 8505C) and evaluated the role of NOX4 in the recruitment of CHD4 and DNA repair proteins to chromatin through chromatin fractionations and western-blot analysis. We used RT-qPCR to assess the expression of NIS. We further evaluated by immunohistochemistry (IHC) the expression of NOX4, CHD4 and DNA repair proteins as potential markers of resistance to the redifferentiation strategy by using the FFPE tissue of primary tumor of 15 patients treated in the French MERAIODE phase 2 study recruiting radioactive iodine (RAI) refractory, progressive and BRAFV600E mutated PTC that underwent 6-weeks of treatment with dabrafenib (a BRAF inhibitor) and trametinib (a MEK inhibitor) followed by a 131I therapy dose of 5.5 GBq. **Results:** We show that 1- CHD4 is recruited by the DNA repair proteins to chromatin as a result of DNA damage produced by NOX4-derived ROS, 2- CHD4 cooperates with DNA methyl transferases in the repression of NIS and 3- the activity of CHD4 is regulated by TGF-beta. The quantitative IHC analysis of markers is ongoing. **Conclusions:** We provide new insights into our understanding of the epigenetic role of NOX4-derived oxidative DNA damage in BRAFV600E-mutated thyroid cancers.

THYROID CANCER BASIC

1112542 - POSSIBILITIES OF IMMUNOHISTOCHEMICAL MARKERS HBME-1, TROP-2, GALECTIN-3 AND KI-67 TO OPTIMIZE THE DIAGNOSIS OF FOLLICULAR CARCINOMAS

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Objective: To study the effectiveness of the use of (IGH) markers HBME-1, TROP-2, Galectin-3 and Ki-67 in the diagnosis of follicular adenoma (FA) and follicular carcinomas of the thyroid gland (FTC) on the histological material of patients who were operated on for nodular goiter with a cytological conclusion according to the Bethesda classification III, IV, V. **Methods:** 124 patients operated on for follicular nodular neoplasms with a cytological conclusion according to Bethesda classification III, IV, V were studied. Those pathology were: FTC - 26 (20.97%), FA - 98 (79.03%). IGH was performed using monoclonal antibodies against human HBME-1, TROP-2, Galectin-3 and Ki-67 ("Bio SB", USA). Evaluation criteria are made according to the strength of staining (from 0 to 3). **Results:** TROP-2 and Ki-67 specificity were 93.9% and 96.9%, with sensitivity 0 % and 11.5%, respectively. HBME-1 sensitivity was 88.5%: only 3 cases of 26 were missed, but it also gave false positives: 74 of 98. Galectin-3 specificity for exclusion of the disease was 79.6% (correctly identified 78 out of 98), at the same time it was ineffective in finding the disease - 9 of 26 cases of FTC. In case of simultaneous absence of the reaction of the HBME-1 and Galectin-3 markers, with a probability of approximately 0.9, it can be expected that the patient doesn't have FTC. Also, with the maximum strength of the reaction, the probability of detecting FTC reached 0.667. **Conclusion:** HBME-1 was the most significant IGH marker in the differential diagnosis between FA and FTC. Markers TROP-2 and Ki-67 were practically not useful in the detection of FTC. The combined use of HBME-1 and Galectin-3 markers proved that the absence of an IGH reaction can be interpreted in favor of the presence of FA, and the simultaneous positive reaction of both markers is a warning regarding the FTC.

THYROID CANCER BASIC

1114136 - PRIMARY SQUAMOUS CELL CARCINOMA OF THE THYROID

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Case Presentation: Initial Findings: RFN, a 49-year-old man presented with cervical swelling. A non-toxic multinodular goiter was diagnosed, and a thyroid ultrasound revealed a hypoechoic nodule with irregular contours and vascularization (Chammas III). A fine-needle aspiration biopsy suggested papillary thyroid carcinoma (Bethesda V). Pathological Findings: A right thyroidectomy was performed and histopathology confirmed a poorly differentiated carcinoma with Hashimoto's thyroiditis in the surrounding parenchyma. Immunohistochemistry confirmed squamous cell carcinoma with CK5/6 positivity. A total thyroidectomy was performed, with no residual neoplastic cells. Immunohistochemical analysis confirmed the diagnosis of squamous cell carcinoma infiltrating the thyroid, with positive CK5/6 and negative CK7, CK20, TTF-1, and PAX8. Follow-up: A first PET-CT showed mild hypermetabolism in the right cervical region, prompting cervical lymph node dissection, which revealed a benign nodular goiter. A follow-up PET-CT showed no new expansive lesions. Current Status: The patient is asymptomatic. **Discussion:** Primary squamous cell carcinoma (SCC) of the thyroid is rare and aggressive, mostly affecting older adults. A 2020 review by Lam A. identified only 117 cases, emphasizing its rarity. Possible etiology theories include: Embryonic Remnants: Squamous cells originate from embryonic structures. Metaplasia: Chronic inflammation triggers squamous metaplasia. Dedifferentiation: may arise from pre-existing thyroid carcinomas, including papillary and anaplastic forms. Diagnosis: SCC-T is characterized by infiltrating squamous cells, which can be confirmed with immunohistochemistry. TTF-1 expression is variable, and PAX-8 distinguishes primary from metastasis. Differential diagnoses include squamous differentiation in anaplastic thyroid carcinoma, mucosal carcinoma extension, and metastatic SCC. Treatment/Prognosis: There is no standard treatment. It is resistant to radiotherapy and chemotherapy, resulting in poor prognosis. However, early surgical intervention has led to a favorable clinical outcome in this case. **Final Comments:** Histopathological examination and immunohistochemistry are crucial for differentiating primary from metastasis. Molecular analysis is key to diagnosis, prognosis, and post-surgical care.

THYROID CANCER BASIC

1112571 - PRIMARY THYROID PARAGANGLIOMA: CASE REPORT

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Introduction: Primary thyroid paraganglioma is rare. **Objective:** To report the case of a patient with post-surgical diagnosis. **Method:** Review of medical records and literature. **Final considerations:** Importance of including the pathology as a differential diagnosis of neuroendocrine intrathyroid tumors.

THYROID CANCER BASIC

1113957 - PROTEOMIC ANALYSIS OF THYROID CANCER CELL LINES AND THEIR EXOSOMES FOR THE IDENTIFICATION OF NOVEL PREDICTIVE BIOMARKERS

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Introduction: Thyroid cancer is the most common endocrine malignancy, with a significant increase in incidence rates observed in recent years. Thyroid carcinoma is classified into four subtypes: papillary, follicular, medullary, and anaplastic. Differentiated thyroid carcinomas (DTC), including follicular (FTC) and papillary (PTC) subtypes, account for 90% of cases and generally have a favorable prognosis; however, up to 30% of cases experience recurrence. Poorly differentiated (PDTC) and anaplastic thyroid carcinomas (ATC) are more aggressive and have limited treatment options. The molecular characterization of thyroid cancer has positively impacted diagnosis and treatment. While specific biomarkers have been identified, the discovery of circulating biomolecules associated with different thyroid carcinoma subtypes remains crucial for patient prognostic assessment. **Objective:** To identify novel predictive biomarkers in thyroid cancer through liquid biopsy proteomics. **Methods:** In this study, we performed a comprehensive proteomic analysis of 15 thyroid cancer cell lines and their exosomes, encompassing all thyroid carcinoma subtypes. Additionally, bioinformatic analyses were conducted to identify potential subtype-specific differential markers, which were subsequently validated by western blot. **Results:** Several proteins were found to be differentially expressed across thyroid cancer cell lines and their exosomes. Specifically, four proteins were overexpressed and one was downregulated across all thyroid carcinoma subtypes. Furthermore, distinct proteins exhibited subtype-specific differential expression, with functional associations to metabolism, cell proliferation, and metastasis. **Conclusion:** We identified differentially expressed biomarkers across all thyroid follicular cancer subtypes. These markers hold promise for the stratification and prognosis of thyroid cancer through immunohistochemistry and, importantly, from circulating tumor samples in liquid biopsy assays of thyroid cancer patients.

THYROID CANCER BASIC

1112448 - REAL-TIME METABOLIC IMAGING OF ANAPLASTIC THYROID CARCINOMA WITH HYPERPOLARIZED MRI: INSIGHTS INTO TUMOR GLYCOLYSIS AND THERAPY RESPONSE

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Introduction: Anaplastic thyroid carcinoma (ATC) is an aggressive malignancy with high metabolic activity and metastatic potential. This makes ATC an ideal candidate for innovative imaging techniques like hyperpolarized MRI (HP-MRI), which enables real-time quantification of HP [1-¹³C]-pyruvate-to-lactate conversion rate by measuring the kPL. HP-MRI provides non-invasive insights into tumor metabolism, including aerobic glycolysis and oxidative stress processing, with potential for predicting therapeutic responses.

Objective: This study aims to develop real-time metabolic imaging and evaluate HP-MRIs clinical potential in monitoring tumor metabolism and guiding treatment strategies in ATC patients. **Methods:** ATC cells (Hth-83) were authenticated for Nuclear Magnetic Resonance (NMR) analysis. HP [1-¹³C]-pyruvate was prepared using the HyperSense system and diluted to concentrations of 0.5 to 10 mM. Orthotopic murine ATC tumors were imaged using HP-MRI and Dynamic Contrast-Enhanced MRI (DCE-MRI). Anatomic MRI and HP-MRI were performed on an ATC patient before and 8 days after treatment with pembrolizumab and lenvatinib. **Results:** Pharmacokinetic (PK) analysis revealed the highest kPL at 0.5 mM pyruvate, with a 150% difference between the lowest (1.185 s⁻¹) and highest (0.167 s⁻¹) concentrations. Strong correlation was found between tumor perfusion and normalized HP lactate in murine ATC tumors. HP-MRI, when integrated with DCE-MRI, improved kPL estimates. In the ATC patient, HP-MRI detected cellular lactate changes in the primary tumor, showing significant early metabolism reduction and treatment response heterogeneity. **Conclusion:** The in vitro study improved HP-MRI quantification consistency for in vivo and clinical applications. Intracellular kPL values were impacted by extracellular pyruvate concentration. Combining DCE-MRI with HP-MRI significantly enhances metabolic assessments in ATC models, supporting advancements in translational and therapeutic applications. First-in-human studies confirm that HP-MRI is safe, effective, and reproducible, offering valuable insights into tumor metabolism, therapy response, and heterogeneity, while aiding precision oncology.

THYROID CANCER BASIC

1112474 - SILVER BIONANOPARTICLES INDUCED ANTI-TUMOR EFFECTS ON ANAPLASTIC THYROID CANCER CELLS VIA AN IL-1A-DEPENDENT MECHANISM

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Introduction: Anaplastic thyroid cancer (ATC) is highly aggressive with limited effective treatment options. Silver bionanoparticles (AgNPs) have shown promises as potential agents for cancer therapy. AgNPs were previously biosynthesized by *Pseudomonas aeruginosa* culture supernatant with an important microbicide activity. However, its anti-tumor effects on ATC have not yet been investigated. **Objective:** We investigated the anti-tumor effects of biogenic AgNPs on human ATC cells and their underlying molecular mechanisms. **Methods:** ATC cells (8505C, C643, THJ-11T and THJ-16T) and non-tumor thyroid cells (NThyOri) were treated with AgNPs (0.21.25 pM), for 24h. Cell viability and reactive oxygen species (ROS) production were evaluated by MTT assay and FACS, respectively. Apoptosis was assessed by Western blot assays. Gene expression was analyzed by bulk RNA-seq, and the expression of key regulatory genes was validated by RT-PCR. **Results:** Treatment with AgNPs induced significant morphological changes in ATC cells, accompanied by a marked decrease in cell viability and an increase in ROS generation. In contrast, NThyOri cells were less susceptible to these effects, suggesting a selective effect of AgNPs on ATC cells. Additionally, AgNPs significantly upregulated apoptotic marker genes compared to untreated controls. Bulk RNA-seq analysis revealed 2242 differentially expressed genes (DEGs) in AgNPs-treated 8505C cells as compared with untreated controls. Among the top 20 upregulated genes, the upregulation of interleukin 1 alpha (IL-1A) and glutathione synthesizing genes, including GCLC, GCLM SLC7A11 was confirmed by RT-qPCR. A higher expression of IL-1A in ATC was confirmed in the single cell RNA-seq (scRNA-seq) data derived from TC patients (database GSE193581). **Conclusions:** These findings highlight the potent in vitro anti-tumor efficacy of biogenic AgNPs against ATC cells and enhance the understanding of the mechanisms underlying their effects. Thus, AgNPs represent promising candidates for further exploration as novel therapeutic agents for ATC.

THYROID CANCER BASIC

1112497 - SOMATIC MICRORNA EXPRESSION PROFILING IN A FAMILY WITH FAMILIAL NON-MEDULLARY THYROID CANCER AND NEGATIVE FINDINGS IN GERMLINE WHOLE EXOME SEQUENCING

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Introduction: Familial non-medullary thyroid carcinoma (FNMTc) is defined by thyroid cancer of follicular origin in two or more first-degree relatives, accounting for 3% of all thyroid cancers. It follows an autosomal dominant inheritance pattern with incomplete penetrance, though its genetic underpinnings remain poorly understood. **Objective:** To explore genetic predispositions and tumor profiles in individuals with FNMTc. **Methods:** A family with eight papillary thyroid carcinoma (PTC) cases (five in the first and three in the second generation) was investigated. Whole exome sequencing (WES) was performed on peripheral blood samples using the Twist Human Core Exome Kit and Illumina HiSeq4000. miRNA profiles were assessed from tumor tissues (two first-generation and one second-generation) using Nanostring nCounter[®] Human v3 miRNA Expression Assay. **Results:** WES did not identify pathogenic variants segregating with PTC. Tumor miRNA profiles were consistent with typical PTC patterns: increased expression of hsa-miR-146b-5p, hsa-miR-222-3, and hsa-miR-221-3p, and decreased expression of hsa-miR-603, hsa-miR-451a, and hsa-miR-7-5p compared to normal thyroid tissue. Notably, in familial samples compared to sporadic cases, differential expression of miR-21-5p, miR-181a-5p, miR-27b-3p, miR-24-3p, miR-126-3p, miR-145-5p, miR-148a-3p, miR-451a, and miR-7-5p was observed. No significant polymorphisms were identified in the microRNA genes analyzed. **Conclusion:** Our findings validate typical PTC miRNA expression in familial cases while highlighting distinct miRNA expression patterns unique to this FNMTc family. These differences may signify a familial-specific molecular profile, warranting further investigation.

THYROID CANCER BASIC

1112441 - STRUCTURAL AND FUNCTIONAL CONSEQUENCES OF AMINO ACID MODIFICATIONS IN VE-CADHERIN INDUCED BY CDH5 POLYMORPHISMS IN THYROID CANCER

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VE-cadherin, encoded by the CDH5 gene, is a cell adhesion molecule primarily associated with vascular biology. Studies of its expression in solid tumors have mainly focused on the tumor microenvironment and angiogenesis, and its specific relationship with thyroid cancer remains underexplored and controversial. Since the literature suggests that alterations in angiogenesis facilitated by proteins such as VE-cadherin may influence tumor progression, we aimed to evaluate the morphofunctional impacts of amino acid modifications in the VE-cadherin protein structure resulting from polymorphisms in the CDH5 gene. An in-silico approach was employed using robust bioinformatics tools to assess the structure, function, stability, and flexibility of the protein. The data for 697 SNPs were retrieved from the dbSNP database. After removing duplicates and merging the records, 99 SNPs corresponding to 102 amino acid alterations were analyzed using PredictSNP1.0. Variants rs373056526 (R207H), rs139755397 (R410H), and rs148726486 (P723S) were identified as deleterious by 87.5% (n=7) of the tools within the PredictSNP1.0 platform, demonstrating structural and functional alterations. P723S modification occurred in a highly conserved region of the protein (score=8), according to the Consurf platform, whereas R207H (score=4) and R410H (score=5) alterations were found in variable or poorly conserved regions. Additionally, iStable analysis showed that these three amino acid alterations decreased the protein stability (score=0.7611, 0.7435, and 0.7620, respectively). Furthermore, ten variants (rs145261593, rs149125818, rs140053187, rs139763470, rs144855545, rs201353685, rs200378924, rs141990946, rs146053762, and rs372602492) were classified as deleterious by 75.0% (n=6) of the tools within the PredictSNP1.0. In conclusion, analysis of genetic polymorphisms in the CDH5 gene revealed various significant amino acid substitutions that affect the structural and functional integrity of VE-cadherin. Polymorphisms rs373056526 (R207H), rs139755397 (R410H), and rs148726486 (P723S) were identified as highly deleterious and associated with reduced protein stability, highlighting their possible relevance in pathological processes and suggesting their potential utility as biomarkers for thyroid cancer.

THYROID CANCER BASIC

1112384 - TARGETING TERT WITH MIRNAS IN ANAPLASTIC THYROID CANCER

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Introduction: Thyroid cancer is the most frequent cancer of the endocrine system. A small fraction of cases, characterized as anaplastic thyroid carcinoma (ATC), is aggressive and refractory to most treatments. Mutations in the TERT (Telomerase Reverse-transcriptase) gene promoter region are frequent in ATC correlating with aggressive clinicopathological characteristics such as invasion, recurrence and death. In this context, microRNAs (miRNAs), small endogenous RNAs that target messenger RNAs and block protein translation, emerge as potential regulators of TERT expression. Thus, identifying miRNAs that target TERT mRNA may improve the understanding of TERT regulation in thyroid cancer. **Objective:** Investigate miRNA-mediated regulation of TERT in thyroid cancer. **Methods:** We used TargetScan software to identify predicted miRNA binding sites on human TERT mRNA 3' Untranslated Region (UTR). To overexpress miRNAs, we designed primers to amplify the precursor sequence of miR-143, miR-145, miR-15b and miR-16, and clone in MSCV-puro plasmid. We transfected KTC2 and C643 cells with miRNA overexpression plasmids. MiRNA and mRNA expression was assessed through qPCR, TERT protein expression was evaluated by western-blotting. To evaluate miRNA-TERT mRNA interaction, we cloned a 973 base pair segment of TERT-3'UTR in pmirGLO dual-luciferase plasmid, and generated a mutated version using site-directed mutagenesis. These plasmids were employed in dual-luciferase miRNA-target reporter assay with cotransfection of miR-200c-3p mimic. **Results:** We identified four binding sites for miR-143-3p, two for miR-145-5p, two for miR-15b-5p/miR16-5p, one for miR-200c-3p in 3'-UTR of TERT. MiRNA overexpression in KTC2 and C643 resulted in weak to moderate reduction in TERT protein. MiR-200c-3p reduced TERT 3'-UTR luciferase activity both in wild-type or mutated binding site plasmid. Functional assays in ATC cells with miRNA overexpression resulted in heterogeneous effects in cell counting and MTT. **Conclusion:** Overexpression of miRNAs reduced TERT protein levels in ATC cells, indicating that targeting TERT with miRNAs is feasible in TERT promoter-mutated ATC.

THYROID CANCER BASIC

1112311 - TEMPORAL ANALYSIS FROM 2013 TO 2024 OF DIAGNOSED MALIGNANT THYROID GLAND NEOPLASMS IN PEDIATRIC PATIENTS IN BRAZIL

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Introduction: Thyroid cancer is the most common endocrine tumor, but its occurrence in childhood and adolescence is rare. Despite this, this age group is considered at high risk for developing the disease. Young age is an important factor that can influence prognosis and treatment. **Objective:** This study aims to analyze the incidence of malignant thyroid gland neoplasms in patients under 18 years old in Brazil, identifying patterns of distribution by age and region, and evaluating the impact on public health. **Methods:** This study adopts a descriptive and quantitative approach for Brazilian regions, using data from the DataSUS platform in the section Time until the start of oncological treatment PAINEL oncology. All reported diagnoses of malignant thyroid gland neoplasms between 2013 and 2024 in patients under 18 years of age were included. The variables analyzed were the age of highest incidence, the age of lowest incidence, or age where no cases were reported. **Results:** In Brazil, between 2013 and 2024, 665 cases of malignant thyroid gland neoplasms were diagnosed. The highest incidence age was 18 years, with 138 cases (20.75%), while the lowest incidence occurred in children under 1 year, 1 year, 3 years, 4 years, and 5 years (0.30%). Regarding regions, the Southeast stood out with 247 diagnoses (37.14%). The region with the lowest incidence was the North, with 32 cases (4.81%). The discrepancy in diagnoses can be attributed to factors such as the level of knowledge about the disease, access to healthcare services, regional economic differences, and the difficulty children have in communicating symptoms. **Conclusion:** It is observed that this temporal analysis of thyroid cancer can influence public health policies, aiming to draw attention to other regions for early diagnosis in pediatric patients.

THYROID CANCER BASIC

1114001 - THE CROSSTALK OF FOXM1 AND EZH2 IN ANAPLASTIC THYROID CANCER BIOLOGY

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Introduction: Anaplastic thyroid carcinoma (ATC) is the most lethal type of endocrine cancer. Mutations in the MAPK pathway and TP53 are common, and recently TERT promoter mutation has been linked to aggressiveness. Additionally, reactivation of EZH2, the catalytic subunit of Polycomb 2 complex, promotes deposition of H3K27Me3, leading to repression of cell differentiation. We found recently that EZH2 promoter activation is controlled by several transcriptional factors induced by MAPK, including FOXM1. FOXM1 is a transcription factor that promotes cell cycle progression and proliferation, which deregulation is considered a hallmark in oncogenesis, including ATC. **Objective:** Investigate the crosstalk of FOXM1 and EZH2 activation in ATC. **Methods:** We searched for correlation between FOXM1 and EZH2 using GEPIA2 and Cistrome databases. To block FOXM1 function, we performed RNA interference and pharmacological treatment with FDI-6 inhibitor in ATC cell lines. Gene expression was analyzed by qPCR and MTT, cell counting and cell cycle analysis were performed after 24, 48 and 72 h of treatment. **Results:** We found a positive correlation between FOXM1 and EZH2 expression in GEPIA2, and Cistrome data showed FOXM1 enrichment peaks in EZH2 promoter. FOXM1 knock-down was established after plasmid transfection and G418 selection in KTC2, SW1736 and 8305C cells. FOXM1 knock-down reduced FOXM1 and EZH2 expression in ATC cell lines. Pharmacological blockage of FOXM1 with FDI-6 treatment reduced cell counting and cell viability of SW1736 cell line over 3 days of treatment. Moreover, cell cycle analysis showed an increased number of cells in sub-G1 compared to untreated cells, indicating DNA fragmentation and cell death by apoptosis. Finally, expression analysis showed upregulation of p21 gene, a cell cycle repressor, after FDI-6 treatment in SW1736 cells, indicating a cell-cycle blockage effect. **Conclusion:** FOXM1 is overexpressed in ATC and regulates cell proliferation and apoptosis while cross-talks with EZH2, an important epigenetic regulator.

THYROID CANCER BASIC

1112535 - THYROID CANCER - A SILENT DISEASE

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It's important to know how to differentiate between thyroid nodules, whether they are cystic, whether they produce hormones, whether they are firm or mobile, painful on palpation and their size. Patients may discover nodules due to changes in breathing, swallowing or even a hoarse voice, while others may first discover them due to changes in the function of thyroid hormones in the blood, which is often the case nowadays due to the high number of requests for complementary tests that were not previously recommended. Imaging tests are then ordered to determine the type of nodule and whether or not it is considered suspicious of malignancy. A fine-needle biopsy of the site can also be used to differentiate the tumor and find out how best to treat it. Treatment requires surgical removal of the thyroid. Further surgery may be necessary to determine whether the cancer has spread to the lymph nodes. According to a report by the National Cancer Institute 2022, it is estimated that every year 4,820, 760 men and 4,060 women will have a new case of thyroid cancer and 909 mortality outcomes, 338 men and 571 women, according to the Cancer Mortality Atlas 2021. Every 1 to 5 people will be affected by thyroid cancer, which is 3 times more common in women than in men, but the statistic doubles in terms of the number of deaths from it, with 1 to 9 for men and 1 to 12 for women. It is difficult to find up-to-date data on the incidence of new cases/mortality from thyroid cancer in Brazil since 2022, as the data has not been updated since 2021 in the SIM system. A silent disease that attacks the individual as a whole, altering their immune system and their perception of themselves.

THYROID CANCER BASIC

1114098 - THYROID ULTRASOUND FOR THYROID CANCER SCREENING: DIAGNOSTIC TEST ACCURACY REVIEW

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Introduction: The rising incidence of thyroid cancer, primarily attributed to increased detection through imaging, necessitates critical evaluation of screening methodologies. While ultrasound remains the primary modality for thyroid nodule assessment, its effectiveness as a screening tool in asymptomatic populations requires further investigation. **Objective:** This study aims to evaluate the effectiveness of ultrasound in the screening of thyroid cancer in relation to other imaging modalities. **Methods:** We conducted a systematic review following PRISMA guidelines with protocol registration in PROSPERO (CRD42024574934). The methodology adhered to Cochrane recommendations for systematic reviews of diagnostic test accuracy. Comprehensive searches were performed across MEDLINE, Embase, Cochrane Library, Web of Science, LILACS, and clinical trial registries without language or date restrictions. Eligibility criteria included studies evaluating ultrasound for thyroid cancer detection in asymptomatic adults or with risk factors, comparing against reference standards or alternative imaging modalities (CT, MRI, scintigraphy). Seven reviewers independently screened studies, extracted data using standardized forms, and assessed methodological quality. **Results:** Analysis of 36 studies revealed conventional ultrasound sensitivity of 47%-95% and specificity of 54%-97%, with elastography demonstrating superior performance (sensitivity 74%-100%, specificity 80%-96%). Combined approaches achieved accuracy up to 100%. Studies predominantly featured female patients (58%-96%) with average ages of 40-55 years. Malignancy rates ranged from 10%-35% of biopsied nodules, with papillary thyroid carcinoma comprising 68-99% of malignancies. Higher TIRADS scores (4-5) strongly correlated with malignancy. ACR-TIRADS prevented 52.6% of unnecessary biopsies but missed 3 malignancies, while K-TIRADS prevented 27.8% without missing any. **Conclusion:** While ultrasound demonstrates acceptable diagnostic performance for thyroid nodule assessment, its utility as a screening tool in asymptomatic populations requires careful consideration of overdiagnosis potential. Future strategies should combine ultrasound with molecular and clinical risk factors to balance early detection of clinically significant malignancies against overtreatment of indolent lesions. Continued refinement of classification systems is essential to standardize practice and improve patient outcomes.

THYROID CANCER BASIC

1114235 - TRANSCRIPTOMIC PROFILING OF PAPILLARY THYROID CANCER AND EVALUATION OF HUB GENES IN A MEXICAN COHORT

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Introduction: Papillary thyroid cancer (PTC) has experienced an increase in incidence in recent decades. Despite advances in PTC research, challenges such as understanding the molecular mechanisms persist. Moreover, Fine Needle Aspiration (FNA) cytology is commonly used for diagnosis, but indeterminate results can complicate patient management. **Objective:** This study explores the molecular profiling of PTC to identify potential differentially expressed genes (DEGs) for thyroid cancer diagnosis. **Methods:** We analyzed RNA-seq datasets obtained from the Gene Expression Omnibus (GSE197443, GSE201365, GSE171011, GSE87410, GSE153659, and GSE165724), which include FNA samples from PTC and adjacent normal tissue. DEGs were identified using the DESeq2 package (Adj p-value <0.05), and functional enrichment analysis was performed using the ClusterProfiler package in RStudio. Protein-protein interaction networks were constructed using STRING and the cytoHubba plugin to identify hub genes. Finally, gene expression of hub genes was evaluated by qPCR in FNA samples from benign thyroid nodules (BTN, n=52) and PTC (n=53) in Mexican patients. **Results:** 131 DEGs were identified (3 downregulated and 128 upregulated). Enriched biological processes included epidermis, epithelium, tissue, and animal organ development, wound healing, cell adhesion, and growth development regulation. Cellular components such as cell-cell junctions, basal part of the cell, plasma membrane region, integral component of the plasma membrane, and apical junction complex were identified. The hub genes FN1, MET, KRT19, DPP4, CLDN1, ITGA2, ERBB3, TGFA, CDH3, and SERPINA1 were identified. qPCR evaluation revealed significant overexpression of FN1, MET, CLDN1 and KRT19 (LogFC = 17.29, 12.4, 34.43 and 15.78, respectively) in PTC (p<0.001). Positive correlations between genes were observed, with the strongest correlations found between MET-FN1 (r=0.89, p<0.001) and KRT19-CLDN1 (r=0.87, p<0.001). **Conclusion:** This study identifies MET, FN1, CLDN1, and KRT19 as potential DEGs in thyroid cancer. These genes are involved in key biological processes and cellular components related to cancer progression, offering valuable insights for molecular diagnostics in PTC.

THYROID CANCER BASIC

1112489 - TRANSCRIPTOMIC-BASED MASTER REGULATORS SCREENING IN PAPILLARY THYROID CARCINOMA

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Introduction: Gene expression profiles in a cellular context reflect specific regulatory programs. A small number of master regulator-acting transcription factors coordinate the tumor phenotype. Interestingly, master regulators are increasingly emerging as optimal biomarkers and therapeutic targets. **Objective:** To uncover master regulators, whose aberrant activity is both necessary and sufficient to maintain the biological phenotype of papillary thyroid carcinoma. **Methods:** RNA-seq data were obtained from The Cancer Genome Atlas. Differential gene expression was calculated using DESeq2. Transcription factor-centered networks were inferred using the ARACNe-AP algorithm. Master regulators were predicted using VIPER analysis. **Results:** We generated a papillary thyroid carcinoma-specific transcription factor-centered gene regulatory network. Master regulator analysis considering differential gene expression in tumor and paired normal samples revealed several master regulator-putative transcription factors in BRAF- and RAS-like papillary thyroid tumors. Master regulators driving BRAF and RAS-like tumor phenotypes do not overlap. Significantly, we identified several master regulators GATAD2A, ETV5 and PROX1 previously implicated in thyroid carcinogenesis. In addition, we identified master regulators associated with a regulon controlling the NF- κ B pathway. **Conclusions:** Using high-throughput transcriptome data, we uncovered a set of master regulator-acting transcription factors that differentially coordinate BRAF and RAS-like papillary thyroid tumor phenotypes. A comprehensive understanding of the master regulators driving thyroid cancer will provide novel diagnostic and therapeutic applications.

THYROID CANCER BASIC

1112471 - WHOLE EXOME SEQUENCING (WES) OF RET AND RAS NEGATIVE SPORADIC MEDULLARY THYROID CARCINOMA (MTC) REVEALS ALTERNATIVE GENETIC ALTERATIONS RESPONSIBLE FOR PATIENTS OUTCOME

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Introduction: We previously defined mutational landscape of a large series of Sporadic Medullary Thyroid Carcinoma (sMTC) (n=181) finding mutually exclusive mutations in RET and RAS genes in about 80% of cases and no genetic driver in the remaining cases. Discovery of genetic drivers in these cases is crucial for personalized medicine. **Objective:** Aim of this study was to search for potential novel genetic drivers in RET/RAS-negative sMTC. **Methods:** We studied 21 sMTC cases previously tested negative from deep sequencing analysis. Exome sequencing was conducted both in tumoral and normal tissue. Proper filters of sequencing results were applied and potential germline and somatic drivers were annotated. **Results:** Our results confirmed the absence of RET/RAS mutations and in 7/21 (33.3%) cases we identified other genetic variations. All mutations found were pathogenic/likely pathogenic and in 4 cases were inactivating mutations occurring in tumor suppressor genes (NF1, BRIP1, VHL, ATR); in 2 cases activating mutations occurring in oncogenes (BRAF, CDK6) and in 1 case in the CHD3 gene coding for a helicase. Mutations in BRIP1 and CHD3 genes were confirmed germline on normal tissue while the remaining were somatic. NF1 and VHL inactivating mutations were reinforced by loss of heterozygosis, documented by MLPA, in chromosomes 17 and 3 respectively. When we correlated the mutational status with the outcome of patients, we found that all mutated cases were affected by biochemical/progressive disease while the remaining negative cases were all disease free (P<0.0001). **Conclusion:** This study reveals that new driver mutations can be found in RET/RAS-negative sMTC, using deeper analysis; the presence of these mutations correlates with a worst outcome and could be a precious reservoir for specific molecular targets therapies. **Fundings:** PNRR European Union NextGenerationEU through the Italian Ministry of University and Research under PNRRM4C2-I1.3 Project PE_00000019 HEAL ITALIA to R.E., CUP I53C22001440006

THYROID CANCER BASIC

1112182 - WOULD AUTOPHAGY-RELATED GENES CONTRIBUTE TO THYROID CANCER PATHOGENESIS?

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Introduction: Autophagy, a cellular process that involves degradation of intracellular proteins, is critical for carcinogenesis. However, its role in thyroid cancer pathogenesis and the role of genetic variants in the autophagy-related genes BECN1, PIK3R4, PIK3C3, and HMGB1 remain underexplored. **Objective:** To investigate whether missense single nucleotide polymorphisms (SNPs) may influence autophagy regulation and the development of thyroid cancer, we constructed a pipeline using multiple bioinformatic platforms. **Methods:** Initial data were obtained from the dbSNP database and protein sequences were sourced from UniProt. Additional tools were used to assess deleterious polymorphisms and their effects on the function, stability, and pathogenicity of the proteins. Variants predicted to be deleterious were further explored using the ClinVar and SinVar archives of human genomic variants. **Results:** A total of 312 non-synonymous SNPs for BECN1, 586 for PIK3R4, 933 for PIK3C3, and 101 for HMGB1 were found in dbSNP and analyzed using PredictSNP. Of these, four for BECN1, 14 for PIK3R4, 13 for PIK3C3, and three for HMGB1 were classified as deleterious by more than 60% of the algorithms. The variants rs375875992 (S12G), rs200762676 (G185R), rs140733016 (L367S), and rs140244450 (L366M) for PIK3C3 were predicted to be deleterious by consensus among PredictSNP, SNP&GO, PMUT, and Fathmm, suggesting a high probability of association with diseases. Stability assessments using IStable, IMutant2.0, and MuPro indicated reduced stability for all the variants. Conservation analysis in ConSurf revealed that these variants were located in conserved regions, underscoring their importance in protein function. However, no investigations of these genes variants were found in the literature or in genomic databases. **Conclusion:** Bioinformatics analysis revealed that four variants of genes involved in autophagy are potentially highly deleterious. Ongoing studies in experimental models and validation in human thyroid tumor samples may elucidate their role and possible use as biomarkers and/or therapeutic targets.

THYROID CANCER CLINICAL

1112365 - 18F-PSMA PET/CT IN PATIENTS WITH MEDULLARY THYROID CANCER: A PROSPECTIVE, FEASIBILITY STUDY

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Introduction: PET/CT imaging in medullary thyroid cancer (MTC) is challenging due to low avidity and variability in tracer uptake. As prostate specific membrane antigen (PSMA) is overexpressed in the neovasculature of MTCs, 18F-PSMA PET/CT may be valuable in MTC patients. **Objective:** To evaluate the diagnostic performance of 18F-PSMA PET/CT, compared to 18F-FDG PET/CT, in MTC patients. **Methods:** This study was conducted in a tertiary referral hospital. Inclusion criteria were: > 18 years old, MTC on histopathology, elevated calcitonin/CEA and 18F-FDG PET/CT < 8 weeks priorly. In addition to patient-, region- and lesion-based visual analyses, 18F-PSMA PET/CTs and 18F-FDG PET/CTs were quantified with SUVpeak. **Results:** In seven included patients, patient-based sensitivity was 86% and 100% for 18F-PSMA PET/CT and 18F-FDG PET/CT, respectively. Median number of positive lesions on 18F-PSMA PET/CTs and 18F-FDG PET/CT was 8 (range 351) and 6 (range 145), respectively. Of 28 regions, 13 (46%) were considered positive for tumor. 10 of these 13 regions were 18F-PSMA positive (sensitivity 77%). The 18F-FDG PET/CTs identified 12/13 regions (sensitivity 92%). Of the total of 146 lesions, 18F-PSMA PET/CT detected 84/146 lesions (sensitivity 58%) while 18F-FDG PET/CT detected 81/146 lesions (sensitivity 55%). Semi-quantitative analysis of the 43 lesions detected on both scans identified a higher SUVpeak on 18F-PSMA PET/CT ($p < 0.001$). **Conclusion:** 18F-PSMA PET/CT seems comparable to 18F-FDG PET/CT in mapping the extent of disease in MTC. The higher tracer uptake on 18F-PSMA PET/CT could facilitate visual assessment and questions the potential of PSMA-targeted radionuclide therapy.

THYROID CANCER CLINICAL

1114165 - 20-YEAR EXPERIENCE IN THYROID CANCER IN THE SUPPLEMENTARY HEALTH SYSTEM: CLINICAL, SURGICAL, AND EPIDEMIOLOGICAL PERSPECTIVES

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Introduction: Thyroid cancer is the most common endocrine malignancy worldwide but there is scarce data on thyroid cancer in Northeast Brazil and Ceará, especially with regard to patients in supplementary health who represent more than 50 million people in Brazil. **Objective:** To evaluate the clinicopathological features of patients with thyroid cancer treated in supplementary health care. **Methods:** Medical records of 240 patients diagnosed with thyroid cancer, followed in the supplementary health system in Ceará-Brazil, between 2005 and 2025, were reviewed. All ethical principles were followed. **Results:** Most patients were female (87.5%), with a mean age of 43,7 years. Clinical preoperative hypo/hyperthyroidism were detected in 6.6% and 3.3%, respectively. Total thyroidectomy alone or associated with neck dissection was performed in 92.5% of patients. Papillary thyroid carcinoma (PTC) alone was the most frequent subtype (87.1%), followed by oncocytic (2.1%), follicular (1.25%) and medullary (1.25%). Association of PTC with follicular adenoma and malignant tumor were found in 2,1% and 2.9%, respectively. Variants PTC were found in 27.5% of cases and follicular variant was the most frequent. Tumor size was less than 2 cm in 78,3% and larger than 4 cm in 2.9% of cases. Multifocality and lymphocytic thyroiditis were detected in 23,7% and 20.4% of cases, respectively. Lymph nodes and distant metastasis occurred in 16.7% and 2.5%, respectively and 63.75% of patients underwent radioiodine. **Conclusion:** Socioeconomic differences have effects on the epidemiological profile of thyroid cancer as regards incidence, morbidity, mortality, recurrence, survival and quality of life. This study underscores the relevance of epidemiological analysis for a better understanding and management of thyroid cancer, encouraging further research especially in regions where data is not available.

THYROID CANCER CLINICAL

1112246 - A 18-YEAR STORY OF A PATIENT WITH MEN2A-SYNDROME

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Introduction: Multiple endocrine neoplasia type 2A (MEN2A) is an autosomal dominant inherited disease with an incidence of 1 in 2.000.000, caused by a proto-oncogenic mutation in REarranged during Transfection (RET) gene. In MEN2A syndrome medullary thyroid carcinoma is associated with pheochromocytom and hyperparathyroidism. **Case Presentation:** A 59-year-old male patient in the Department of Endocrinology, 1st Department of Internal Medicine, underwent surgery for bilateral medullary thyroid carcinoma and parathyroid adenoma in 2006 and right pheochromocytoma in 2008. Genetic testing confirmed a RET Cys634Arg mutation. During the follow-up period, the tumour markers remained abnormal. In 2010, cervical block dissection was performed due to lymph node metastases, followed by percutaneous ethanol injection (PEI) to manage recurrent lymph node metastases in 2016. In 2020, bone metastasis was confirmed, so a multikinase inhibitor, vandetanib was started. A significant therapeutic response was achieved, but due to severe gastrointestinal side effects at the effective dose, a change in therapy was necessary. In July 2022, a full-dose of highly selective RET kinase inhibitor, selpercatinib was initiated with excellent results. In June 2024, laboratory and imaging results indicated stable disease. **Summarize:** Treatment and care of patients with MEN2A syndrome requires a coordinated multidisciplinary approach, involving endocrinology, oncology, radiology and surgical expertise. For primary tumours, surgical intervention remains the cornerstone of treatment. Compared to earlier therapeutic approaches such as radiotherapy, chemotherapy and multikinase inhibitors, selective RET kinase inhibitors have emerged as a preferred first-line treatment for distant metastases in the context of confirmed RET mutations.

THYROID CANCER CLINICAL

1112214 - A COMPARATIVE ANALYSIS OF OUTCOMES AND SIDE EFFECTS IN METASTATIC DIFFERENTIATED THYROID CANCER PATIENTS PREPARED FOR RADIOACTIVE IODINE THERAPY WITH THYROID HORMONE WITHDRAWAL VERSUS RECOMBINANT HUMAN THYROTROPIN: A MULTICENTER RETROSPECTIVE COHORT

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Introduction: There is a lack of data regarding the appropriate thyroid stimulation method (TSM) for radioactive iodine (RAI) therapy in patients with metastatic differentiated thyroid cancer (MDTC). **Objective:** Our study aimed to compare the outcomes and side effects of RAI therapy in MDTC patients according to TSM: thyroid hormone withdrawal (THW) or recombinant human thyrotropin (rhTSH). **Methods:** A total of 371 patients enrolled from 13 hospitals underwent 678 cycles of RAI therapy prepared with THW (551 cycles) or rhTSH (127 cycles). We defined progression as progressive disease (PD) according to the RECIST criteria. Cox proportional-hazards regression analysis was performed to evaluate clinical factors related to disease progression for the cycles of RAI therapy. We used Pearson's Chi-square test to analyze the incidence of side effects. **Results:** Age at RAI (HR = 1.0271, $P < 0.001$) and stimulated thyroglobulin at RAI (HR = 1.0001, $P < 0.001$) were statistically significant predictor of disease progression. However, TSM was not related to disease progression ($P = 0.197$). Other variables including sex, RAI cycle number, cumulative RAI dose, number of metastasized organ were not significant for the prediction of disease progression. There was no significant differences in the incidence of side effects according to TSM. **Conclusion:** Our study suggested that TSH stimulation methods for RAI therapy did not affect therapeutic effect in MDTC patients. Therefore, rhTSH could be considered equivalent for the preparation of RAI therapy especially in MDTC patients with difficult long-term THW.

THYROID CANCER CLINICAL

1113991 - A SENSITIVE LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY METHOD (LC-MS/MS) FOR PLASMATIC LENVATINIB MEASUREMENT IN PATIENTS WITH THYROID CANCER

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Introduction: No data are available regarding the pharmacokinetics (PK) and bioavailability of Lenvatinib in patients with radioiodine-refractory thyroid cancer (RAIR-TC) treated with Lenvatinib. **Objective:** This preliminary retrospective study aims to assess the PK profile of Lenvatinib in a real-world setting, with the aim of validate the clinical applicability of the method. **Methods:** Twenty-three patients with radioiodine-refractory thyroid cancer (RAIR-TC) were enrolled, having been treated with Lenvatinib for an average duration of 45 months (range 6-96 months). At the time of sampling, the daily doses were as follows: 4 mg in 3 patients, 10 mg in 8 patients, 14 mg in 4 patients, 18 mg in 1 patient, 20 mg in 4 patients, and 24 mg in 3 patients. Lenvatinib was administered to all patients between 8:00 pm and 11:00 pm, and plasma samples were collected the following morning before 9:00 am. Plasma samples were obtained at multiple time points for each patient, yielding a total of 51 samples. Samples were collected in sodium heparinized tubes and stored at -80°C until analysis. Lenvatinib levels were quantified using liquid chromatography-tandem mass spectrometry (LC-MS/MS) with 250 µL of plasma, following analytical assay validation. **Results:** The steady-state exposure to Lenvatinib increased in direct proportion to the dose, indicating linear pharmacokinetics (PK), with a plateau phase observed at doses exceeding 20 mg ($R = 0.8038$, $P < 0.0001$). The analysis revealed comparable Lenvatinib plasma concentrations among patients receiving the same dose, regardless of age or body mass index. Median Lenvatinib concentrations were 37 ± 17.1 ng/mL in patients on 4 mg, 85.4 ± 20.6 ng/mL in patients on 10 mg, 128.5 ± 31.4 ng/mL in those treated with 14 mg, and 208.6 ± 48.9 ng/mL in patients receiving 20/24 mg. **Conclusion:** This is the first demonstration that plasma Lenvatinib concentrations can be accurately measured using an LC-MS/MS assay in RAIR-TCs.

THYROID CANCER CLINICAL

1114324 - ACTIVE SURVEILLANCE FOR LOW-RISK THYROID MICROCARCINOMA: PERSPECTIVES FROM PATIENTS AND TREATING PHYSICIANS AT A BRAZILIAN REFERRAL CENTER

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Introduction: Active surveillance (AS) is an established alternative for low-risk papillary thyroid microcarcinoma (mPTC). **Objective:** This study aimed to evaluate the perspectives of patients and treating physicians regarding AS and assess the impact of an educational intervention on their decision-making process. **Methods:** A cross-sectional study was conducted at a Brazilian tertiary referral center. Patients with thyroid disorders (n=102) and physicians (n=105), including endocrinologists, head and neck surgeons (HNS), and oncologists, completed structured questionnaires before and after an educational intervention. The intervention consisted of educational pamphlets detailing AS eligibility criteria and outcomes. **Results:** Before the intervention, 83.3% of patients were unaware of AS, and 77.5% did not recognize it as a management option. After receiving educational materials, 28.4% of patients who initially preferred surgery shifted to AS, reducing the proportion of surgery preference to 15.7%. Among physicians, 55.2% did not routinely recommend AS. Post - For Review Only intervention, 59.6% of endocrinologists and 100% of oncologists reported increased confidence in recommending AS, whereas only 11.1% of head and neck surgeons did so (valor-p=0.006). Concern about living many years while carrying a malign cancer was the main reason between younger patients (<52 years) compared to the older ones (>63 years). **Conclusion:** Besides, the fact that endocrinologists feel more confident when recommending a non-surgical approach may explain why only 29.8% of them cited patient refusal as a limitation to AS success, compared to 77.8% of HNS (valor-p=0.014). This study underscores the importance of epidemiological surveys in assessing patient and physician perspectives on AS.

THYROID CANCER CLINICAL

1112174 - ACTIVE SURVEILLANCE IN ARGENTINA: A TEN-YEAR PROSPECTIVE STUDY WITHOUT CHANGES IN ACCEPTANCE AND DISCONTINUATION RATES

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Introduction: Active surveillance (AS) for low-risk papillary thyroid carcinoma (PTC) has been practiced for over 30 years with encouraging results globally. However, its adoption remains limited in certain contexts. **Objective:** This study aimed to evaluate the long-term oncological outcomes of patients undergoing AS and compare changes in the acceptance and discontinuation rates in Argentina over the past decade. **Methods:** This prospective, observational cohort study (2014-2024) included 358 patients diagnosed with low-risk PTC ≤ 1.5 cm across two university hospitals and private practices. Of these, 104 patients (30%) opted for AS and were followed up with thyroid ultrasounds and function tests annually for at least 24 months. Surgery was recommended if tumors grew ≥ 3 mm, new tumor foci developed, or metastases occurred. Outcomes were analyzed in two periods: 2014-2019 (A) and 2020-2024 (B). **Results:** Of the 104 patients under AS, 10.6% developed a tumor growth, and 7.6% developed new PTC foci. The 5- and 10-year cumulative incidence of tumor growth was 7% and 8%, respectively. Lymph node metastases occurred in 0.9%. AS acceptance rates remained stable between periods A (25%) and B (30%, p=0.82). AS discontinuation rates were also similar: 19.5% in A and 12.6% in B (p=0.63). Among patients discontinuing AS due to tumor progression, 31% underwent surgery. Anxiety prompted surgery in 66% of cases in A and 40% in B. Lobectomies increased from 1.5% (A) to 9% (B, p=0.8). An excellent response was achieved in 75% of cases. **Conclusions:** Despite persistently low acceptance and adherence to active surveillance, the long-term outcomes observed in this long-term prospective study reinforce AS as a feasible initial management option for low-risk PTC. These findings underscore the need for further efforts to improve the acceptance of AS among eligible patients.

THYROID CANCER CLINICAL

1114298 - ACTIVE SURVEILLANCE IN BRAZIL: A MULTICENTER EXPERIENCE WITH LONG-TERM FOLLOW-UP

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Introduction: Active surveillance (AS) for low-risk papillary thyroid microcarcinomas (PTMCs) was first introduced in Japan in 1993 and has since been adopted in several countries. However, limited data exist on its feasibility and long-term outcomes in Brazil, particularly in a multicenter setting. **Objective:** To evaluate the feasibility, safety, and long-term outcomes of AS in Brazilian PTMC patients from both private and public centers. **Methods:** This prospective multicenter study included 76 PTMC patients from 3 private and one public institutions between 2017 and 2025. Patients were classified as ideal, acceptable, or inadequate candidates for AS. Those deemed ideal or acceptable were enrolled in AS. Follow-up was performed every six months initially and annually after 2 years of follow-up with ultrasound and clinical evaluation, assessing tumor growth, lymph node metastasis, extrathyroidal extension, and patient adherence. Reassessment occurred at each visit. **Results:** Among 76 patients, 57 (75%) were women. Thirty-nine were considered unsuitable for AS and underwent immediate surgery (27% physician decision, 25% patient preference, 39% tumor location, 7% lymph node metastasis, and 2% extrathyroidal extension). The remaining 37 patients (81% women, median age: 51 years [44.5-64.5]) were followed for a median of 43.4 months [26.8-74]; 78% were from private centers. Seven patients required conversion surgery: two due to anxiety, four based on physician decision (tumor location), and one due to lymph node metastasis. No cases of tumor progression, life-threatening metastases, or disease-related deaths occurred during AS or after conversion surgery. **Conclusion:** AS is a feasible and safe strategy for managing low-risk PTMCs in Brazil, in both private and public settings. Long-term follow-up supports AS as a viable alternative to immediate surgery, effectively reducing overtreatment while maintaining excellent clinical outcomes.

THYROID CANCER CLINICAL

1113962 - ACTIVE SURVEILLANCE OF SMALL THYROID NODULES HIGHLY SUSPICIOUS OF THYROID MICROCARCINOMA

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Introduction: Active surveillance (AS) of micro-papillary thyroid carcinoma (mPTC) is an accepted alternative to immediate intervention. Guidelines recommend observation without fine-needle aspiration biopsy (FNAB) in appropriately selected patients with suspicious thyroid nodules <1 cm. **Objective:** To evaluate the feasibility of AS of thyroid nodules suspicious for mPTC at a center in Chile. **Methods:** Prospective observational study. Patients with thyroid nodules <1 cm, highly suspicious for microcarcinoma and who agreed to AS were included. FNAB was performed in some cases. Patients were excluded if their nodules showed any of the following: extrathyroidal extension, lymph node (LN) metastasis, proximity to the recurrent laryngeal nerve or high risk of tracheal invasion. This registry was approved by the local ethics committee. **Results:** We included 80 patients; 89% were female, median age was 48 years (range 28-80). Criteria for AS were classified as ideal in 11% and acceptable in 89%. The median nodule size was 5 mm (range 3-10 mm). Multifocality was observed in 11%, thyroiditis in 35%, and indeterminate central LNs in 21%. FNAB was performed in 45% of patients. Cytology was Bethesda IV-VI in 36% of cases. In 9%, cytology was Bethesda III with cytological and nuclear atypia; these cases were included due to highly suspicious ultrasound features. After a median follow-up of 2.6 years (range 6-132 months), progression (increase ≥ 3 mm or appearance of suspicious LNs) occurred in 2.6% of patients, and a $\geq 100\%$ increase in nodule volume was observed in 16%. Intervention was performed in 21% of patients: 6.3% due to patient anxiety, 2.5% due to progression, 8.8% due to volume increase not meeting progression criteria, and 3.8% for other reasons. All patients who underwent surgery for progression remain disease-free at last follow-up. **Conclusion:** AS of small, suspicious thyroid nodules is feasible and safe in appropriately selected patients.

THYROID CANCER CLINICAL

1112627 - ADVANCED PAPILLARY CARCINOMA AND IODINE REFRACTORINESS: CHALLENGES IN MANAGEMENT AND THE FLIP-FLOP PHENOMENON

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Case Presentation: A 76-year-old male presented with a solid, heterogeneous, and infiltrative nodule in the right thyroid lobe, measuring 3.4 x 3.0 x 2.7 cm, indicative of local recurrence. Fine-needle aspiration confirmed papillary carcinoma. PET/CT with 18F-FDG revealed hypermetabolic activity in the thyroid bed and at least seven bilateral pulmonary nodules, up to 1.0 cm. The patient declined surgery and underwent radioiodine therapy (30 mCi). Follow-up imaging showed progression of the thyroid lesion and pulmonary nodules, prompting a second dose of iodine-131 (200 mCi). Subsequent scans identified retrotracheal tissue formation and pulmonary nodules up to 1.4 cm, with no significant iodine uptake. Laboratory tests revealed Tg = 5,000 ng/mL and anti-Tg = 1.3 IU/mL, indicating refractory disease. **Discussion:** This case illustrates the challenges in managing advanced papillary thyroid carcinoma, especially with the “flip-flop” phenomenon, where high FDG uptake correlates with low iodine avidity, reflecting dedifferentiation. The lack of iodine uptake compromises radioiodine therapy efficacy, as observed in this patient despite two treatment doses. Persistent thyroglobulin elevation and disease progression confirm radioiodine refractoriness. Early recognition of iodine-refractory disease via PET/CT is essential to avoid ineffective treatments and shift toward targeted therapies, such as tyrosine kinase inhibitors (e.g., lenvatinib, sorafenib). These alternatives have shown efficacy in controlling tumor progression in advanced cases. Emerging approaches, including redifferentiation agents and immunotherapy, provide additional options, though further validation is needed. **Final Comments:** Identifying when radioiodine therapy is no longer beneficial is critical to minimize treatment-related morbidity. PET/CT with 18F-FDG plays a pivotal role in diagnosing refractory disease and guiding individualized therapeutic strategies. This case emphasizes the importance of innovative approaches to improve outcomes and quality of life in advanced, refractory thyroid cancer.

THYROID CANCER CLINICAL

1112181 - ANAPLASTIC THYROID CARCINOMA IN ARGENTINA: FACING DIAGNOSTIC LAGS AND TREATMENT BARRIERS

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Introduction: Anaplastic thyroid carcinoma (ATC) presents a high mortality rate. Approximately half of cases carry BRAF V600E mutations. In these patients, Dabrafenib-trametinib (DT) demonstrated improved overall survival (OS). This study aimed to identify diagnostic and therapeutic challenges in ATC patients. **Methods:** A multicenter, retrospective cohort study included 39 ATC patients from 11 centers in Buenos Aires (2019-2024). The study evaluated initial diagnostic methods (IDM) (fine-needle aspiration [FNA], core needle biopsy [CNB], surgical biopsy, or incidental finding after thyroidectomy) and time to confirmed ATC diagnosis. Data on BRAF testing frequency and results, DT treatment access, treatment response, and OS were collected. **Results:** The median time from symptom onset to diagnosis was 3.17 months (IQR 25.5). The IDM was FNA for 72%, followed by surgical biopsy (5%), CNB (5%), and incidental findings (18%). Diagnostic confirmation failed in 69% of cases, including 91% of those using FNA. BRAF testing was conducted in 69% of patients (n=27), revealing a 59% positivity rate (n=16); of these, 44% received DT. The median interval from sample collection to BRAF mutation result was 7.5 days (IQR 429), with a median of 39 days (IQR 2270) from diagnosis to DT initiation. The median OS was 3.18 months (IQR 1.45-11.25), which doubled to 6.86 months for 15% of patients diagnosed within the first month (p=0.25). BRAF-positive patients receiving DT showed improved OS (8.6 vs. 3.61 months; p=0.037). OS was also longer for patients undergoing surgery (11 vs. 2 months; p=0.00085), 22.5 months for R0/R1 vs. 2.33 months for incomplete resections (R2) (p=0.00089). **Conclusions:** Significant diagnostic delays were observed due to inadequate IDM, and access to molecular tests and treatments was limited. Patients receiving DT and those undergoing effective surgery experienced better OS. Rapid diagnostics and timely access to therapy are essential for improving ATC outcomes.

THYROID CANCER CLINICAL

1112195 - ANTI-THYROGLOBULIN ANTIBODY LEVELS POST-THYROIDECTOMY AND PAPILLARY THYROID CARCINOMA RECURRENCE

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Introduction: The global incidence of thyroid cancer, particularly papillary thyroid carcinoma (PTC), is rising due to more frequent incidental findings. Despite a high 10-year survival rate of 93%, up to 28% of PTC patients experience locoregional recurrence. Postoperative monitoring typically relies on serum thyroglobulin (Tg), but the presence of anti-thyroglobulin antibodies (TgAb) interferes with Tg measurement, necessitating reliable detection methods. This study aimed to assess the predictive value of postoperative TgAb levels for PTC recurrence and establish a TgAb threshold as a prognostic marker. **Methods:** A retrospective analysis was conducted on 15,620 patients who underwent bilateral total thyroidectomies at our institution between March 2004 and December 2022. After excluding patients with unmeasurable postoperative TgAb or other carcinoma types, the final cohort comprised 4,434 PTC patients (775 men and 3,659 women, median age 46 ± 11.68 years). Bilateral total thyroidectomy was performed on all patients. TgAb levels were measured 2 days post-surgery and annually, with the most recent levels used for analysis. The primary outcome was PTC recurrence, analyzed based on stratified TgAb levels. **Results:** Elevated TgAb levels were significantly correlated with increased tumor size and recurrence rates ($P < 0.001$). A TgAb threshold of 440 IU/mL was identified as a novel recurrence marker, with patients above this threshold showing higher recurrence odds. **Conclusions:** Postoperative TgAb levels are a prognostic indicator for PTC recurrence, with a proposed threshold of 440 IU/mL serving as a predictive marker, irrespective of test timing post-surgery.

THYROID CANCER CLINICAL

1112340 - ASSESSMENT OF CHANGES IN QUALITY OF LIFE AFTER THYROID SURGERY IN OLDER ADULTS. A PROSPECTIVE STUDY

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Introduction: Referral of an older adult with thyroid nodular disease to surgery remains a challenge. Potential improvement in the quality of life after surgery might help guide this decision. Aim: To prospectively measure the impact of thyroid surgery on thyroid-related quality of life in older adults with thyroid nodular disease. **Methods:** The Spanish version of the short-form Thyroid-Related Quality of Life (QoL) Patient-Reported Outcome (ThyPRO-39), expanded with the full 85-item ThyPRO scales on physical thyroid symptoms, was completed by all patients undergoing thyroid surgery during 2018-2024 for thyroid nodular disease at our Institution. The questionnaire was completed at admission and 6-12 months after surgery. The instrument consists of four physical symptoms ThyPRO scales (Goiter, Hyperthyroid, Hypothyroid, and Eye Symptoms), five mental well-being and function ThyPRO-39 scales (Tiredness, Cognitive Problems, Depressivity, Anxiety, and Emotional Susceptibility), three QoL Impairment scales (Impaired Social life, Daily Life and Cosmetic Complaints) and one overall QoL impact single-item. The mental well-being and function scales, and the QoL impairment scales (except Cosmetic Complaints) are further summarized in the ThyPRO-39 Composite scale. Histological reports were classified as benign or malignant. Wilcoxon tests were corrected for multiple testing, and linear mixed models were used in statistical analyses. **Results:** Of 88 patients (81% female, age 71 ± 6 years), 31 had malignant and 57 benign nodules. After surgery, patients showed a significant improvement ($p < 0.01$) in the four physical symptoms, one of the mental well-being scales (Anxiety), all of the QoL Impairment scales, and the ThyPRO-39 Composite scale (30 ± 17 vs 21 ± 13 , $p < 0.01$). Improvements in the physical symptoms and QoL impairment scales were observed mainly in the benign group (p for interaction < 0.05). **Conclusion:** Surgery resolved most impaired ThyPRO domains in older adults with nodular disease. Furthermore, improvement in goiter symptoms impaired daily life, and overall QoL mainly occurred in benign diseases.

THYROID CANCER CLINICAL

1112532 - ATA RISK SCORE PREDICTS TREATMENT RESPONSE IN PAPILLARY THYROID MICROCARCINOMA: AN ITCO MULTICENTER PROSPECTIVE STUDY

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Introduction: Papillary thyroid carcinomas ≤ 1 cm (microPTC) generally exhibit an excellent prognosis. To avoid overtreatment, it is crucial to identify tumor and patient characteristics predictive of treatment response. **Objective:** This multicenter prospective study aimed to describe the clinical and histological characteristics of microPTC, compared to macrocarcinomas, and to identify factors associated with biochemical and/or structural incomplete response (BIR, SIR) at 1-year after initial treatment in microPTC patients. **Methods:** The study included patients consecutively enrolled across 51 centers affiliated with the Italian Thyroid Cancer Observatory (ITCO) (NCT04031339). Inclusion criteria were histological diagnosis of PTC and complete pathological, clinical status, treatment, and 1-year follow-up data. **Results:** Of the 5038 patients enrolled, 2345 (46.5%) had microPTC and 2693 (53.5%) macroPTC. Patients with microPTC were younger and predominantly females ($p < 0.001$). Histologically, microPTC exhibited less aggressive features including variant type, multifocality, and micro- and macro-extrathyroidal extension ($p < 0.001$). Among microPTC, 3% were classified as high risk according to the ATA classification system and 1% presented with distant metastases. At 1-year, 92.7% of microPTC exhibited excellent or indeterminate response, while 5% BIR and 2.3% SIR. The presence of distant metastases emerged as the strongest SIR predictor in microPTC (OR 5.13, 95%CI 1.11-23.73, $p = 0.04$). In a subgroup of 925 patients with microPTC treated with total thyroidectomy and radiometabolic therapy, high ATA risk at diagnosis emerged as the best predictor of SIR (OR 5.47, 95%CI 1.42-21.04, $p = 0.01$). **Conclusion:** This extensive prospective study validates the ATA risk stratification as a reliable predictor of treatment response in the context of microPTC, as well. Although microPTC generally has a favorable prognosis, the presence of rare distant metastases at diagnosis significantly increases the risk of structural persistence. These results highlight the importance of tailored management strategies based on comprehensive risk stratification, rather than relying solely on tumor size.

THYROID CANCER CLINICAL

1112565 - BENEFITS OF CONTRAST ENHANCED ULTRASONOGRAPHY(CEUS) IN PREDICTING THE MALIGNANCY RISK OF BETHESDA 3,4,5 THYROID LESIONS - A PROSPECTIVE STUDY

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Introduction: Increasing incidence of thyroid malignancy has added to its diagnostic complexity. The conventional modalities have their pitfalls. Greyscale ultrasonography (US) features of benign nodules (BN) and malignant nodules (MN) are overlapping. Whereas on fine needle aspiration (FNA), 30% are indeterminate thyroid nodules (ITN)-Bethesda 3,4,5-with varying malignancy potential and are often over/undertreated. CEUS by visualizing the dynamic enhancing process of tumors, helps in predicting malignancy risk of ITN, thus aiding surgical decision making. **Objective:** Identify the CEUS parameters that predict malignancy in ITN. **Methods:** Consenting patients with ITN, who met the inclusion criteria planned for surgery were prospectively recruited, underwent greyscale ultrasonography and CEUS, final HPE considered gold standard. **Results:** Interim analysis done on 124 patients who underwent thyroidectomy, 33 were ITN. On US majority were TIRADS 3 -mildly suspicious. Final HPE had 28 BN and 5 MN. CEUS parameters studied were margin enhancement (ME), enhancement direction (ED), shape enhancement (SE), enhancement area (AE), enhancement degree (EDe), enhancement type (TE) and contrast arrival (CA). 100% (n=5) of MN had centrifugal ED as opposed to only 8.3% (n=2) of BN (p value=0.001). SE was irregular in 50% MN, contrarily 100% of BN had regular SE ($p = 0.0160$). AE was $> 50\%$ 100% of MN whereas only 20.8% of BN had AE $> 50\%$ ($p = 0.006$). 100% (n=5) of MN had high EDe whereas only 8.3% of BN had high EDe. TE was heterogenous in 100% MN as opposed to 4.1% of BN ($p = 0.000$). ME and CA did not show any statistical significance with malignant HPE. **Conclusion:** Centrifugal ED, AE $> 50\%$, high ED and heterogenous TE are significant predictors of malignancy in ITN, which is in par with other studies on CEUS. Incorporating CEUS in the diagnostic armamentarium of ITN will increase chances of distinguishing between benign and malignant nodules preoperatively.

THYROID CANCER CLINICAL

1114231 - BRAF V600E MUTATION ALLELE FREQUENCY AS A PROGNOSTIC BIOMARKER FOR AGGRESSIVE CLINICO-PATHOLOGICAL FEATURES IN PAPILLARY THYROID CANCER

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Introduction: Papillary thyroid carcinoma (PTC) is commonly associated with a favorable prognosis, however, some cases can exhibit aggressive features and poorer clinical outcomes. Recently, the allele frequency (AF) of BRAF V600E mutation has emerged as a potential biomarker for predicting aggressive clinico-pathological features of PTC, including intermediate/high American Thyroid Association recurrence risk (ATA RR), lymph node metastasis (LNM), extrathyroidal invasion (EI) and angiolymphatic invasion (AI). **Objective:** To evaluate the prognostic value of BRAF V600E mutation AF in predicting aggressive clinical-pathological features in PTC. **Methods:** A cohort of 116 PTC samples, previously characterized by comprehensive histopathological analysis to identify ATA RR, LNM, EI and AI was analyzed. BRAF V600E mutation presence and AF were determined by qPCR. Receiver Operating Characteristic (ROC) curve analysis was used to identify an optimal AF cut-off value for stratify each clinical-pathological feature associated with the risk categories: BRAF-negative, BRAF-positive AF below and above cut-off. **Results:** The presence and AF of BRAF V600E mutation significantly correlated with intermediate/high ATA RR ($p < 0.001$), LNM ($p < 0.001$) and EI ($p = 0.030$). By ROC curve analysis, an optimal AF cut-off of 16.90% was defined. Regarding ATA RR, the risk increased progressively with respectively risk categories, from 10.0% to 38.5% and 63.6%. Similarly, the risk of developing LNM rose from 13.0% to 27.3% and 61.9%. For EI, the risk increased from 3.6% in BRAF-negative or AF below cut-off, to 18.2% when AF is above cut-off. **Conclusion:** Assessing BRAF V600E mutation AF provides valuable prognostic information regarding ATA RR, LNM and EI in patients with PTC. This biomarker may facilitate improved risk stratification at diagnosis, enabling personalized management of patients.

THYROID CANCER CLINICAL

1112648 - CASE REPORT: LONG-TERM SURVIVAL OF A PATIENT WITH METASTATIC FOLLICULAR THYROID CARCINOMA AFTER MULTIMODALITY TREATMENT

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Case Presentation: The 70-year-old female patient underwent a right thyroid lobectomy in 2010 for a benign multinodular goiter. In March 2011, histology of a tumor from pathological fracture of the L1 vertebra revealed metastasis of well-differentiated follicular thyroid carcinoma. Treatment began with spinal stabilization using segmental osteosynthesis and irradiation of the thoracolumbar spine. After completion of a total thyroidectomy in April 2011, therapy with 150 mCi of I-131 was done. Uptake was observed in the spine, left femur, and left humerus. The patient was maintained on suppressive doses of L-thyroxine. From November 2011 to January 2015, five subsequent RAI treatments were administered, with doses ranging from 196 to 206 mCi. By 2015, PET/CT imaging and I-131 scintigraphy following rhTSH demonstrated stagnation of most metastatic lesions. However, disease progression was noted in the right humerus and left femur, which were irradiated with 30 Gy in 10 fractions in August 2014 and June 2017, respectively. In 2021, imaging revealed new iodine-avid metastases in both femurs, and the patient underwent subsequent RAI treatment with 202 mCi (cumulative dose: 1353 mCi). In July 2022, asymptomatic progression of femoral metastases and new iodine-refractory pulmonary lesions were detected. In June 2023, therapy with levatinib was initiated. Follow-up imaging showed a significant regression of pulmonary metastases and a marked reduction in thyroglobulin levels, indicating a good therapeutic response. **Discussion:** Radioiodine therapy plays a central role in the management of iodine-avid differentiated thyroid carcinoma. Locoregional therapies, such as spinal stabilization and external beam radiation, are effective for managing the progression of a single metastasis, while systemic targeted therapy should be used when iodine-refractory metastases progress and become symptomatic. **Final Comments:** The long-term effective control of metastatic follicular thyroid carcinoma in this patient highlights the importance of a multimodal approach.

THYROID CANCER CLINICAL

1112466 - CASE REPORT: SEPSIS SECONDARY TO THE USE OF A PENROSE DRAIN IN A PATIENT WITH MEDULLARY THYROID CARCINOMA AND CERVICAL METASTASIS

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Case Presentation: A 45-year-old black male farmer with a history of medullary thyroid carcinoma and cervical metastasis was admitted for radical cervical lymphadenectomy and neck dissection. Previous history included total thyroidectomy and recurrent neck dissection, as well as hypothyroidism under treatment with levothyroxine. On initial physical examination, the patient was stable, oriented, with normal vital signs and no significant complaints. After the surgery, he progressed well initially, remaining hemodynamically stable and with a Penrose drain in the left cervical region draining a serosanguinous secretion. After the procedure, the patient developed fever, tachycardia and hypotension. Laboratory tests showed leukocytosis with a shift to the left and an increase in inflammatory markers. Sepsis secondary to infection of the Penrose drain was diagnosed. Broad-spectrum antibiotic therapy and intensive support measures were promptly started, including volume replacement and continuous monitoring. Despite these interventions, the patient's clinical condition deteriorated rapidly, progressing to multiple organ dysfunction. The infection proved refractory to treatment, resulting in the patient's death due to the complications of sepsis. **Discussion:** This case demonstrates the potential seriousness of infectious complications associated with the use of drains in complex oncological surgeries. The rapid progression of localized infection to sepsis highlights the importance of close surveillance and early intervention in high-risk patients. Studies show that the incidence of drain-associated infections can vary from 1% to 18%, depending on the type of surgery and the patient's characteristics. The management of sepsis requires a multidisciplinary approach due to its high mortality rate in cancer patients. **Final Comments:** This report emphasizes the need for strict protocols for monitoring and managing surgical drains in order to prevent infections and their complications. Early identification of signs of infection and rapid intervention are crucial to improving clinical outcomes.

THYROID CANCER CLINICAL

1112229 - CHEMOEMBOLIZATION IN HEPATIC METASTASES OF MEDULLARY THYROID CARCINOMA

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Introduction: The liver is the most frequently affected site of distant metastases in medullary thyroid carcinoma (MTC). Transarterial chemoembolization (TACE) is used for hepatic metastases (HM) to alleviate symptoms (diarrhea or pain) or control disease progression. However, experience with TACE in MTC is limited. The objective of this study was to evaluate the efficacy and safety of TACE in patients with predominant HM from MTC. **Patients and Methods:** Patients with MTC and HM treated with TACE were included. Safety considerations, as well as clinical, biochemical (calcitonin and CEA), and imaging responses (CT and/or MRI), were assessed at 3 months post-procedure and periodically during follow-up. **Results:** Eight patients with MTC and HM were evaluated: two had disease progression under systemic treatment; the others exhibited limited extrahepatic disease. Three patients (38%) had symptomatic HM. A total of 13 procedures were performed. Post-embolization syndrome occurred in one case (16%). One of the three symptomatic patients (33%) experienced symptomatic improvement after TACE. Two cases showed $\geq 30\%$ reductions in calcitonin and/or CEA levels. On initial liver imaging evaluation, one patient (16%) had a complete response, four (50%) had a partial response, and three (38%) had stable disease. After a median follow-up of 14 months (range 3-75), one patient (16%) maintained a complete response, three (38%) a partial response, one (16%) had stable disease, and three patients (38%) experienced hepatic disease progression; two of these had disseminated disease post-systemic treatment. **Conclusions:** TACE is a safe therapeutic option for managing HM in MTC, achieving a disease control rate of 62.5% in patients with limited extrahepatic disease. However, its effectiveness was marginal in patients with advanced extrahepatic disease.

THYROID CANCER CLINICAL

1112484 - CLINICAL IMPACT OF CERVICAL LYMPH NODE MANAGERMENTS FOR PERSISTENT DISEASE IN PAPILLARY THYROID CARCINOMA

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Objective: We investigated which modalities were suitable for the detection of persistent disease (PD) in cervical lymph node and how the outcome after retreatment of PD differed according to the retreatment methods in patients with papillary thyroid carcinoma (PTC). **Methods:** Among 474 PTC patients who underwent initial surgery and radioactive iodine (RAI) therapy, 41 patients had PD on neck ultrasonography (US) or F-18 FDG PET/CT, both of which modalities were performed within two years of initial treatments. Among them, 31 patients underwent retreatment RAI therapy only or reoperation (with or without RAI therapy). Therapeutic outcomes were assessed as whether the patients had no evidence of disease (NED) or residual metastatic lesions after retreatments (subsequent PD, sPD). We evaluated whether the FDG avidity in PD lesions or retreatment methods related to therapeutic outcomes. **Results:** In 26 out of 41 patients, PD was located at the single lymph node level of the neck. Diagnostic performance for PD was 6 patients (23.1%) for PET/CT only, 7 patients (26.9%) for neck US only, and 13 patients (50.0%) for both modalities, respectively. Of 31 patients with PD, 10 patients (32.3%) had sPD after retreatments. There was no significant relationship between FDG avidity on PET/CT and NED (65.2% vs. 75.0%, $P = 1.000$). The patients who underwent reoperation regardless of RAI therapy had a higher prevalence of NED than patients who received RAI alone (76.0% vs. 16.7%, $P = 0.013$). **Conclusion:** The diagnostic performance of each modality was complementary in PD located at the single lymph node level. Although the reoperation was significantly related to therapeutic outcomes in patients with PD, therapeutic managements should be further optimized to reduce the rate of retreatment failure.

THYROID CANCER CLINICAL

1112556 - CLINICAL IMPACT OF RET GENE TESTING ON MULTIPLE ENDOCRINE NEOPLASIA TYPE 2 MANAGEMENT: A SCOPING REVIEW ANALYSIS

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Introduction: Multiple Endocrine Neoplasia Type 2 (MEN2) is a hereditary syndrome where early identification of RET gene mutations can significantly impact patient outcomes. Understanding the clinical implications of molecular testing is crucial for optimizing patient care. **Objective:** To analyze the clinical impact of RET molecular testing on disease management, prognosis, and patient outcomes in individuals with suspected or confirmed MEN2. **Methods:** A scoping review was conducted following Joanna Briggs Institute guidelines and reported according to PRISMA-ScR. Searches were performed in major databases without language or date restrictions. Studies evaluating clinical outcomes of RET molecular testing in MEN2 patients were included. Analysis focused on changes in clinical management, prognostic factors, and patient outcomes. **Results:** From 8734 references identified, 349 studies met inclusion criteria and were included. Analysis revealed that patients diagnosed through molecular screening were identified at significantly younger ages (mean difference: 12.6 years, $p < 0.001$) and earlier disease stages (32% vs 11% in stages I-II) compared to clinically diagnosed cases. Asymptomatic carriers identified through genetic screening showed better outcomes than index cases, with higher biochemical cure rates (82% vs 14%, $p < 0.001$) and lower rates of persistent disease (13% vs 28%, $p = 0.14$). Prophylactic thyroidectomy in mutation carriers led to significantly better outcomes compared to therapeutic interventions in symptomatic cases. Studies comparing pre- and post-molecular testing eras demonstrated improved disease-free survival (20% to 43%) and reduced surgical complications. However, mortality benefits were less consistent across studies. **Conclusion:** RET molecular testing significantly impacts MEN2 management by enabling earlier diagnosis and preventive interventions, particularly in asymptomatic carriers. The evidence strongly supports the clinical utility of genetic screening, though long-term mortality benefits require further investigation. These findings emphasize the importance of implementing molecular testing programs while considering their impact on clinical decision-making and patient outcomes.

THYROID CANCER CLINICAL

1112456 - CLINICAL, LABORATORY AND GENETIC PROFILE OF A SERIES OF PATIENTS WITH MEDULLARY THYROID CARCINOMA: SINGLE CENTER EXPERIENCE

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Introduction: Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor that accounts for 5% of thyroid cancers and is frequently associated with mutations in the RET proto-oncogene, particularly in multiple endocrine neoplasia (MEN) types 2A and 2B. **Objective:** This study describes the clinical and genetic characteristics of patients with MTC, focusing on presentation, treatment, and long-term follow-up. **Methods:** Of the 42 patients specifically included, 18 were analyzed after excluding those who died (n=10) or did not undergo periodic evaluations (n=14). This retrospective study evaluated clinical, laboratory, genetic, and imaging data. **Results:** The mean age at diagnosis was 42.7 years (1469 years), with 55.6% women. RET analysis revealed that 33.4% were RET-positive, with mutations at codons 634 and M918T. The mean calcitonin and CEA levels were 1510.1 pg/mL and 150.7 ng/mL, respectively. Most patients (88.8%) presented with a thyroid nodule; 11.1% diarrhea and flushing. Associations included MEN 2A (22.2%), MEN 2B (16.7%), pheochromocytoma (38.8%), and hyperparathyroidism (11.1%). All underwent total thyroidectomy. The mean referral was 9.8 years (240 years). Calcitonin and CEA doubling times were on average 18.3 (SD: 32.8) and 19.2 months (SD: 213.3), respectively. Complete biochemical and structural responses occurred in 44.4%, while 55.6% had persistent disease: 72.3% biochemical and 27.7% structural and biochemical. **Conclusion:** Our cases are in agreement with the literature data. Biomarkers and imaging are essential for long-term treatment. Despite treatment, some patients have persistent disease, highlighting the challenges to achieve complete remission or disease control.

THYROID CANCER CLINICAL

1112218 - CLINICOPATHOLOGICAL CHARACTERISTICS OF ONCOCYTIC AND FOLLICULAR THYROID CARCINOMA WITHOUT COMPLETION THYROIDECTOMY: A COHORT STUDY

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Introduction: Background The prognosis of oncocytic thyroid carcinoma (OTC) and follicular thyroid carcinoma (FTC) is poorly understood. These types of cancers are usually confirmed after diagnostic lobectomy. We aimed to evaluate the clinicopathological characteristics and prognoses of patients with OTC and FTC who did not undergo completion thyroidectomy. **Methods:** We screened 221 patients diagnosed with FTC or OTC after thyroid lobectomy at Yonsei Severance Hospital between January 2000 and December 2020. After excluding patients who underwent complete thyroidectomy, 184 patients with FTC and 37 patients with OTC were included. The mean follow-up duration was 99.2 months. **Results:** The mean age of the FTC group was significantly lower than that of the OTC group. No significant differences were observed in sex, tumor size, multiplicity, T and N stages, or histological subtypes between the FTC and OTC groups. During the median follow-up duration, three patients with minimally invasive FTC (1.6%) had a locoregional recurrence, while there was no recurrence in OTC patients. Further, disease-free survival was not significantly different between the FTC and OTC groups. The disease-free survival in the FTC group were 98.9% and 98.4%, respectively. **Conclusion:** Although OTC has been reclassified as a separate subtype of differentiated thyroid cancer rather than a subtype of FTC, it has an excellent prognosis even with a relatively large tumor size. Lobectomy alone may be sufficient for the treatment of low-risk OTC.

THYROID CANCER CLINICAL

1114161 - COMPARING THE PERFORMANCE OF THREE THYROGLOBULIN ASSAYS IN PATIENTS WITH STRUCTURAL DISEASE AND POSITIVE THYROGLOBULIN ANTIBODIES

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Introduction: Thyroglobulin antibodies (TgAb) are present in approximately 25% of patients with differentiated thyroid cancer (DTC), posing a challenge for disease monitoring. Immunometric assays (IMA), commonly used to measure thyroglobulin (Tg), are susceptible to TgAb interference, often leading to falsely low or undetectable results. Liquid chromatography/tandem mass spectrometry (LC-MS/MS) shows promise for TgAb-positive patients, but its clinical utility is unclear. Studies find undetectable Tg values in up to 40% of DTC patients with structural disease. **Objective:** To evaluate the clinical performance of three different Tg assays in DTC patients with positive TgAb and structural disease. **Methods:** Samples from seventeen patients with structural disease and positive TgAb were analysed. All patients had Tg measurements by LC-MS/MS and at least by one IMA. The assays used for Tg dosage were Tg-Beckman (Chemiluminescent, FS 0.1 ng/mL), Tg-Roche (Electrochemiluminescent, FS 0.1 ng/mL), and an in-house LC-MS/MS assay (FS 0.7 ng/mL). TgAb measurements were performed using at least one of the 3 methods: Roche Elecsys anti-Thyroglobulin, ADVIA Centaur anti-Thyroglobulin and Atellica IM Anti-Thyroglobulin II. Positive results were defined as any value above FS. **Results:** Eleven out of 17 patients (64.7%) had distant metastasis and six (35.3%) presented disease confined to the neck. Tg-MS ranged from <0.7-5011 ng/mL, Tg-Beckman 0.1-5771 ng/mL and Tg-Roche <0.1-5445 ng/mL. Undetectable results were observed in 8/17 patients (47%) in IMAs and in 10/17 (58.8%) in the LC-MS/MS assay. One patient with negative Tg-MS and positive Tg-IMA had lung metastasis, while the other had cervical disease. The overall performance in detecting Tg was 53.3% in Tg-IMAs and 41.2% with Tg-MS. **Conclusion:** The sensitivity of detecting Tg in TgAb-positive patients with structural disease was higher with Tg-IMAs (53.3%) with FS of 0.1 ng/mL, as compared to Tg-MS (41.2%) with FS of 0.7 ng/dL, indicating no additional benefit in disease detection by measuring Tg-MS in these patients.

THYROID CANCER CLINICAL

1112433 - CONE-BEAM COMPUTED TOMOGRAPHY GUIDED PERCUTANEOUS CRYOABLATION OF BONE METASTASES DUE TO ENDOCRINE TUMORS: A PROSPECTIVE CLINICAL TRIAL

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Objective: To assess the feasibility, safety, efficacy, complications, local disease control, pain improvement, and the capacity to avoid subsequent major surgical interventions of CBCT-guided percutaneous cryoablation of bone metastases due to endocrine cancers. **Methods:** Seventeen patients were enrolled in a prospective, single arm, tertiary single-center, IRB approved study. The inclusion criteria were: adults (>18 years old); status performance (ECOG) 0-3; mean life expectancy over one month; biopsy-proven bone metastases under 7.0 cm diameter from endocrine tumors including thyroid and adrenocortical cancers, associated at least to one of the following: pain; risk of fracture; risk of compression of the spinal cord; hypercalcemia. CBCT-guided cryoablation was performed under general anesthesia or moderate sedation. Follow-up was carried out weekly for the first 8 weeks, 3, 6, 12 and 24 months with brief pain inventory and observation adverse events. **Results:** Patients were 58.3±17.3-years-old, 11 women. Primary cancers were: differentiated thyroid cancer - papillary (n=2; 11.8%) or follicular (n=6; 35.6%); medullary thyroid cancer (n=6; 35.6%), and adrenocortical cancer (n=3; 17.3%); Cementoplasty was provided to n=5 weight-bearing sites lesions. No severe adverse events (AE) were reported. One moderate (5.9%) and two (11.8%) mild AE were observed along an average 18.9±7.7 months of follow-up. An overall drop of >4 points (p<0.05) in the Visual Analogue Scale (VAS) as well as a MEDD overall intake reduction (p<0.05) was observed over time. None of the patients presented neurological impairment, spinal cord compression or required surgical approach due to disease progression in the treated sites. Additional external beam radiation therapy was required in n=3 (12.5%) of the treated lesions over time. **Conclusion:** Cryoablation was effective, safe and provided a rapid and durable pain palliation, local disease control, and improvement of quality of life of bone metastases due to endocrine cancers.

THYROID CANCER CLINICAL

1112213 - CORRELATION BETWEEN LOW-IODINE DIET ADHERENCE AND THE EFFECTIVENESS OF RADIOACTIVE IODINE THERAPY IN PAPILLARY THYROID CANCER USING SERUM THYROGLOBULIN CHANGES

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Introduction: A low iodine diet (LID) is essential for the effectiveness of radioactive iodine (RAI) therapy in patients with papillary thyroid cancer (PTC). However, evaluating LID adherence and its impact on therapeutic outcomes remains challenging. **Objective:** This study aims to assess LID adherence by measuring serum thyroglobulin (Tg) changes shortly after RAI therapy. **Methods:** A retrospective analysis was conducted on 895 PTC patients. LID adherence was assessed using the urine iodine-to-creatinine (I/Cr) ratio, with a cut-off value of 66.2 µg/g Cr. We investigated the relationship between LID adherence and the ratio of serum Tg levels before and after RAI therapy (ratioTg), which was used to evaluate the extent of cellular damage caused by the therapy. Additionally, we evaluated whether the factors predicting the effectiveness of RAI therapy varied based on LID adherence, after classifying the therapeutic response as either excellent response (ER) or non-excellent response (nER). **Results:** There was a significant difference in ratioTg between well-adherent (I/Cr ratio < 66.2 µg/g Cr) and poorly adherent (I/Cr ratio ≥ 66.2 µg/g Cr) LID patients (15.7 ± 2.2 vs. 8.9 ± 1.3, P = 0.007). Additionally, among patients who adhered well to the LID, the ratioTg in the ER group (18.7 ± 2.8) was significantly higher than in the nER group (5.8 ± 0.8) (P = 0.030). **Conclusions:** RatioTg allowed us to assess that LID adherence may influence thyroid cell damage following RAI therapy. Furthermore, ratioTg was identified as a predictive factor, particularly in patients with good LID adherence.

THYROID CANCER CLINICAL

1114079 - CUTANEOUS METASTASIS FROM PAPILLARY THYROID CARCINOMA: CASE REPORTS

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Case Presentation: Papillary thyroid carcinoma (PTC) is the most common malignant thyroid neoplasm. Cutaneous metastases occur in only 0.06%-0.82% of cases, typically presenting as slow-growing erythematous/violaceous nodular lesions on the head and neck. Spread mechanisms likely include hematogenous/lymphatic dissemination or tumor cell implantation during procedures. Case 1: A 64-year-old female underwent total thyroidectomy (TT) in 2011 for PTC (pT2NxMx; ATA: Intermediate Risk) with 150mCi radioiodine therapy (RIT). During 13 years of follow-up, thyroglobulin (Tg) levels progressively increased (3.99→22 ng/mL). Imaging revealed pulmonary micronodules and a cervical nodule. Fine-needle aspiration of the skin lesion confirmed thyroid neoplasia (aspirate Tg: 47,200 ng/mL). Resection confirmed PTC metastasis. Additional 200mCi RIT was administered due to elevated post-operative Tg (206 ng/mL), revealing pulmonary uptake. Follow-up continues. Case 2: A 76-year-old male underwent TT in 2002 for PTC. After 22 years of complete response, a cervical nodule resembling an epidermal cyst appeared. Excision confirmed PTC cutaneous. **Discussion:** These cases highlight PTC's potential for late cutaneous metastasis (>13 years post-treatment). Careful physical examination and biopsy of suspicious lesions are crucial for diagnosis, as they may mimic other dermatological conditions. Management should include surgical resection with pathological confirmation. **Final Comments:** Decisions regarding additional RIT depend on Tg values and coexisting structural disease. These cases emphasize the importance of long-term surveillance in PTC patients, as metastases can occur decades after initial treatment.

THYROID CANCER CLINICAL

1112630 - DEDIFFERENTIATION OF PAPILLARY THYROID CARCINOMA: A THERAPEUTIC CHALLENGE

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Case Presentation: An 18-year-old woman was diagnosed in 2020 with papillary thyroid carcinoma, classic variant, measuring 2.5 cm, and cervical lymph node metastases. She underwent total thyroidectomy with neck dissection and was treated with radioiodine therapy (150 mCi) and Sorafenib. A whole-body scan revealed iodine uptake in deep cervical lymph nodes (level III) and disseminated bilateral pulmonary micronodules. In 2023, she received additional radioiodine therapy (200 mCi), but the scan showed growth of pulmonary nodules (up to 0.7 cm) without significant radiotracer uptake. Elevated thyroglobulin levels (111 ng/mL) indicated TENIS syndrome (Thyroglobulin Elevated, Negative Iodine Scan). A PET/CT with 18F-FDG showed no increased glycolytic uptake in the pulmonary micronodules, suggesting low tumor activity or incomplete dedifferentiation. **Discussion:** TENIS syndrome poses a significant challenge in managing differentiated thyroid carcinoma. It is marked by elevated thyroglobulin levels and negative iodine scintigraphy, indicating impaired iodine uptake due to tumor dedifferentiation. This reduces the effectiveness of radioiodine therapy and necessitates alternative strategies. In this case, the absence of PET/CT uptake suggests low tumor activity or partial dedifferentiation, influencing treatment decisions. Tyrosine kinase inhibitors, such as Lenvatinib, have shown efficacy in advanced cases, while redifferentiation agents may restore iodine uptake. Emerging therapies, including immunotherapy, hold promise for future management. **Final Comments:** The progression to TENIS syndrome underscores the complexity of treating refractory papillary thyroid carcinoma. A multidisciplinary approach, integrating advanced imaging and targeted therapies, is essential to optimize outcomes. Rigorous follow-up and individualized management are crucial to preserving quality of life and improving prognosis.

THYROID CANCER CLINICAL

1112469 - DETECTION OF CENTRAL COMPARTMENT LYMPH NODE METASTASIS OF THYROID CANCER: USEFULNESS OF INTRAOPERATIVE THYROGLOBULIN MEASUREMENT IN FINE NEEDLE ASPIRATION WASHOUT WITH AND WITHOUT BLUE DYE INJECTION

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Introduction: The management of cervical lymph node metastasis of central neck compartment (CNC) in differentiated thyroid carcinoma is debated. Intraoperative measurement of thyroglobulin has gained attention to accurately detect metastases, reducing unnecessary CNC dissections. **Objective:** This prospective study explores the accuracy of intraoperative thyroglobulin measure in fine needle aspiration (Tg-FNA) of CNC lymph nodes to detect hidden metastases. **Methods:** A total of 37 patients underwent surgery. Intraoperative assay of thyroglobulin from fine needle aspiration (Tg-FNA) was performed on CNC lymph nodes, identified as sentinel lymph nodes by blue dye in 15 patients (23 nodes, group A) or clinically suspicious by inspection and palpation in 22 patients (35 nodes, group B). Tg-FNA values were compared with histology to calculate diagnostic accuracy. **Results:** In group A, the blue dye diffused widely, complicating lymph nodes identification: 2 were metastatic and 21 non-metastatic, with median Tg-FNA levels of 6,236 ng/mL and 99.20 ng/mL respectively. In group B, among 35 lymph nodes, 8 were metastatic and 27 benign, with median Tg-FNA levels of 4,063 ng/mL and 121 ng/mL ($p < 0.0001$), respectively. Tg-FNA values were higher in metastatic lymph nodes of both groups. ROC analysis identified the 500 ng/mL cutoff, achieving 100% sensitivity and 74% specificity in group B, and 90% sensitivity and 70% specificity overall. Finally, among all non-metastatic lymph nodes, group A exhibited some cases of very high Tg-FNA values compared to group B, with lower accuracy for the established cutoff, suggesting that blue dye injection might lead to increased Tg levels. **Conclusions:** Blue dye injection showed low accuracy. Intraoperative Tg-FNA was reliable for detecting CNC metastases, although a higher cutoff is needed in this compartment compared to what has been reported for lateral lymph nodes. Lymphatic drainage and surgical manipulation might explain these findings. Careful interpretation of Tg-FNA in CNC should be then adopted.

THYROID CANCER CLINICAL

1112381 - DIFFERENTIATED THYROID CANCER AND ITS RECURRENCE AFTER FIVE OR MORE YEARS OF DIAGNOSIS IN A COHORT OF MEXICAN PATIENTS

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Introduction: TC is the 7th most prevalent cancer worldwide, with a 98.1% 5-year survival rate. Its recurrence is variable (1-30%); numerous studies indicate that it occurs mainly in the first 5 years. **Objective:** Specify the recurrence of DTC after 5 years of diagnosis in adults and their risk factors. **Methods:** Longitudinal, ambispective, observational and descriptive study in which patients diagnosed with DTC and their records were reviewed. They had to be 18 years or older at diagnosis, followed for ≥ 5 years and have a complete histopathology report. **Results:** We followed 95 patients; 84 women (88.4%), 11 men (11.6%) with DTC (88% PTC, 11% FTC), for a median of 9.33 years (5.04-30.79 years) after total thyroidectomy (80%) or thyroidectomy in two surgical stages (15.8%). Patients were stratified according to the current AJCC and ATA risk system into: low 68 (71.6%) and intermediate risk 27 (28.4%), and treated with RAI at different doses. 6-18 months later, were reclassified into a dynamic response. All patients received suppressive therapy and clinical data obtained during follow up were used to identify recurrence. Throughout the follow-up, recurrence was observed in 11 patients (11.6%), of which recurrence after 5 years was found in 7 (7.4%). Our study showed a mean time from diagnosis of DTC to diagnosis of recurrence after 5 years of 8.5 years. And two significant risk factors to present recurrence after 5 years: Positive perithyroidal invasion (RR=9.4, 95% CI 2.6-34, p=.0077) and having a cumulative dose of RAI ≥ 200 mCi (RR=2.857, 95% CI 1.580-5.165, p=.0185). **Conclusion:** Recurrence of DTC during follow-up was observed in 11.6% of patients; 7.4% after 5 years, with a mean time from diagnosis of DTC to recurrence after 5 years of 8.5 years, besides two risk factors: positive perithyroidal invasion and a cumulative dose of RAI ≥ 200 mCi. Suggesting that follow-up for only 5 years may not be enough.

THYROID CANCER CLINICAL

1112291 - DIFFERENTIATED THYROID CANCER IN PREGNANCY. A RETROSPECTIVE ANALYSIS OF NEWLY DIAGNOSED PATIENTS

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Introduction: Watchful waiting is the preferred option in pregnant patients with differentiated thyroid cancer, and surgical intervention may be postponed to the postpartum period. **Objective:** The aim of this study is to analyze the dynamics of malignant thyroid nodules followed in pregnant women. **Methods:** A retrospective analysis of a group of 75 women at a mean age of 30.9 ± 4.8 with suspected thyroid nodules detected during pregnancy. All patients underwent fine-needle aspiration biopsy (FNAB). The FNAB result was classified according to the Bethesda System. Only patients with the Bethesda V category (suspicious for malignancy) or Bethesda VI category (malignancy) were considered. Patients were followed by neck sonography (US) every 2-3 months until surgery. The median follow-up from the diagnosis to surgery or the last follow-up was 10.0 months (range 1.0-39.0). **Results:** Papillary thyroid cancer (Bethesda VI) was diagnosed in 53 patients, whereas in the remaining 22 patients, the FNAB result was suspicious for papillary thyroid carcinoma (Bethesda V). The mean nodule diameter at the first US evaluation was 12 ± 7.7 mm. Thirty-nine nodules were ≤ 10 mm in diameter. In 29 nodules, the tumor diameter ranged between 11 and 20mm. Only 7 nodules (9.3%) were stable during the whole follow-up in 65 (86.6%) patients. The nodule diameter increased in 9 (12%), while in one patient, the nodule dynamics could not be evaluated. Lymph node metastases were diagnosed at initial evaluation in 2 patients. Although in 55 patients (73.3%) thyroid nodules were diagnosed before 24 weeks of gestation, the majority of them chose watchful waiting. Only 2 women were operated on during pregnancy. Sixty-five (86.7%) underwent surgery after delivery. **Conclusions:** Watchful waiting is a safe option for patients diagnosed with papillary thyroid carcinoma or suspicion of papillary thyroid carcinoma. However, careful monitoring should be considered to choose the most optimal time for surgery

THYROID CANCER CLINICAL

1112450 - DOES OBESITY IMPACT THE AGGRESSIVENESS, INITIAL TREATMENT RESPONSE, AND OUTCOMES OF DIFFERENTIATED THYROID CANCER? EXPERIENCE FROM TWO CENTERS IN ARGENTINA

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Introduction: Obesity is a risk factor for differentiated thyroid cancer (DTC) and may influence tumor aggressiveness, but evidence remains inconsistent. **Objective:** To assess the relationship between body mass index (BMI) and tumor aggressiveness at diagnosis, initial treatment response (IT), and clinical outcomes (Tf) in DTC patients. **Materials and Methods:** Medical records of 610 DTC patients (455 females, 155 males; median age 46, range 1884 years) were reviewed. According BMI (kg/m²) 12 patients (G1) had underweight (≤ 18.5), 256 (G2), normal weight (18.624.9), 202 (G3) overweight (2529.9), and 140 (G4), obesity (≥ 30). Tumor characteristics (TNM 8th ed.), ATA 2015 recurrence risk (RR), IT (excellent, biochemical incomplete, indeterminate, structural incomplete), and Tf after a 96-month median follow-up were assessed. For analysis, BMI groups were classified into three categories (G1+G2 or reference group, G3, and G4). Statistical tests included Chi-square, Kruskal-Wallis, and logistic regression to estimate crude and adjusted (for age and sex) odds ratios (ORs) with 95% confidence intervals (CIs). **Results:** BMI was associated with age (median: 42 years in G1/G2, 50.5 in G3, 51 in G4; $p=0.0001$) and sex (female: 86.57% in G1/G2, 64.63% in G3, 66.43% in G4; $p<0.001$). A 42.46% were T1a, 35.90% were N1, and 3.61% were M1, with no differences between BMI-based groups. Tumor size > 40 mm was associated with obesity ($p=0.015$), but the significance was lost after adjusting for age and sex. Multicentricity was significantly associated with obesity (G4 Crude OR 1.81, CI: 1.152.84; $p=0.010$; Adjusted OR 1.77, CI: 1.102.85; $p=0.018$). No associations were found between BMI-based groups and histological variants ($p=0.135$), mETE ($p=0.107$), ATA-RR ($p=0.965$), IT ($p=0.430$), or Tf ($p=0.715$). **Conclusions:** Obesity was associated with multicentric tumors, suggesting increased initial aggressiveness, but not with ATA recurrence risk, IT, or clinical outcomes. Obesity does not impact the long-term progression of DTC.

THYROID CANCER CLINICAL

1114176 - DUAL-TARGETING MICROPARTICLES WITH IMMUNE ESCAPE FOR SYNERGISTIC THERAPY OF RADIOIODINE-REFRACTORY THYROID CANCER

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Introduction: Radioiodine-refractory differentiated thyroid cancer (RAIR-DTC) poses significant clinical challenges due to loss of sodium-iodide symporter (NIS) function and tumor microenvironment resistance. Current strategies, including redifferentiation therapies and kinase inhibitors, are limited by transient efficacy, systemic toxicity, and acquired resistance. Emerging evidence suggests thyroid-specific biomarkers (thyroglobulin [Tg] and TSH receptor [TSHR]) could enable precision targeting, yet existing delivery systems fail to address both extracellular radioiodine (RAI) enrichment and intracellular retention in NIS-deficient tumors. **Objective:** We developed BiTT-131I@MP, a biomimetic microparticle system integrating three synergistic mechanisms: 1. Dual-antigen targeting: Tg-mediated RAI accumulation combined with TSHR-driven cellular internalization 2. Immune evasion: CD47 “don’t eat me” signaling to circumvent phagocytic clearance 3. Oncogenic pathway blockade: TSHR-PI3K/AKT signaling inhibition to enhance radiosensitivity. **Methods:** 1. Engineered human cell-derived microparticles co-expressing bispecific CAR (Tg/TSHR-scFv) and CD47 via lentiviral transduction 2. Ionophore-assisted ¹³¹I encapsulation for sustained radioablation 3. Longitudinal evaluation in orthotopic xenograft models using multimodal imaging (SPECT/CT) and histopathological analysis 4. Mechanistic validation through signal pathway profiling and immune cell interaction assays. **Results:** BiTT-131I@MP demonstrated superior therapeutic performance: 1. Enhanced tumor-selective RAI delivery with reduced off-target accumulation 2. Prolonged systemic circulation through effective evasion of mononuclear phagocyte system 3. Synergistic tumor suppression via concurrent radiation damage and PI3K/AKT pathway inactivation 4. Improved survival outcomes correlated with decreased serum Tg levels and delayed tumor progression. **Conclusion:** This triple-action platform addresses critical limitations in RAIR-DTC treatment: 1. Dual-targeting design overcomes NIS dependency for RAI delivery 2. Immune-evasive properties enhance tumor-specific drug retention 3. Signal pathway modulation creates radiosensitized tumor microenvironment 4. The integrated strategy provides a transformative approach for precision nuclear medicine, with potential applications in other therapy-resistant malignancies.

THYROID CANCER CLINICAL

1114246 - EFFICACY OF CHEMICAL ABLATION OF METASTATIC CERVICAL LYMPH NODES IN THE TREATMENT OF DIFFERENTIATED THYROID CANCER

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Introduction: Differentiated thyroid cancer has a very favorable prognosis; however, 5%-20% of cases may develop lymph node recurrence. Although surgical resection is the treatment of choice, each intervention carries a higher risk of complications. Therefore, chemical ablation has become a therapeutic option for patients with oligometastases and/or those who are not surgical candidates.

Objective: To evaluate the efficacy of chemical ablation of metastatic lymph nodes in recurrent differentiated thyroid cancer. **Methods:** This was an observational, descriptive, retrospective, and longitudinal study. Medical records of patients from the General Hospital of Mexico diagnosed with differentiated thyroid cancer and cervical metastases who underwent chemical ablation were evaluated. Data analysis was performed using descriptive statistics with measures of central tendency. Differences between qualitative variables were analyzed using the χ^2 test, and the Student's t-test was used for quantitative variables. A value of $p < 0.05$ was considered statistically significant. **Results:** A total of 57 lymph node lesions from 37 patients were studied: 33 women and 4 men. The most prevalent initial ATA risk classification was intermediate. The mode was 1 lymph node per patient (48.6%); 13 lymph nodes were located in the central compartment. The instilled volume of the chemical agent was 2.27 ± 1.73 ml. A statistically significant reduction in the short axis was identified at 9 and 12 months. During a follow-up period of 26.09 ± 10.8 months, lesion disappearance was documented in 10.8% patients, while 16.2% patients developed new lesions, with an average time of appearance of 9.2 ± 7.0 months. Patient outcomes were as follows: 7 opted for surgical, 8 were referred for dose of RAI, and the rest continue under strict surveillance. **Conclusion:** Lymph node chemical ablation could be considered an excellent alternative treatment, as it is a safe, effective, and quick procedure without significant complications, in patients who meet appropriate selection criteria.

THYROID CANCER CLINICAL

1112657 - EFFICACY OF DABRAFENIB AND TRAMETINIB COMBINATION THERAPY IN BRAF-V600E-MUTATED ANAPLASTIC THYROID CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Anaplastic thyroid cancer (ATC) is a rare and aggressive form of cancer, accounting for 1 to 2% of thyroid cancer cases, but its responsible for up to 50% of thyroid cancer-related deaths. The average survival of patients is less than 4 months, as ATC often presents with distant metastases and local invasion. Mutations in the BRAF-V600E, RAS, and p53 genes are common, along with other genetic alterations. Recent advances in molecular profiling have suggested that the combination of BRAF inhibition (dabrafenib) and MEK inhibition (trametinib) showed promising antitumor activity in BRAF-mutated ATC. **Objective:** Evaluate the effectiveness of the combined therapy of dabrafenib and trametinib in patients with anaplastic thyroid cancer with the BRAF V600E mutation. **Methods:** We conducted a systematic search of the EMBASE, PubMed, and Cochrane databases to identify clinical trials investigating the efficacy and safety of dabrafenib plus trametinib therapy in patients with BRAF-V600E-mutated anaplastic thyroid cancer. The primary outcome measures assessed included adverse events, rates of relapse, disease progression, stabilization, and complete response (cure).

Results: A total of 4 studies were included, with 100 patients undergoing the dual therapy. Regarding the presence of any type of toxicity, 98.63% (95% CI 90.91; 99.81) had a negative outcome. In relation to therapeutic response, 64% (95% CI 54.17; 72.78) had a partial response to treatment, while 8.71% (95% CI 4.02; 17.85) had a complete response. Concerning disease progression, 21.69% (95% CI 14.11; 31.82) of patients showed disease stability, while only 12% (95% CI 6.94; 19.95) experienced primary progression.

Conclusions: The results of this meta-analysis reaffirm the indication of dabrafenib and trametinib in ATC with the BRAF-V600E mutation as an effective treatment with a significant therapeutic response in a rare and aggressive cancer.

THYROID CANCER CLINICAL

1114133 - EMERGING RESEARCH TRENDS AND THEMATIC CLUSTERS IN OVERDIAGNOSIS OF THYROID CANCER: A TEXTUAL ANALYSIS OF SCIENTIFIC LITERATURE

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Introduction: Overdiagnosis has become a major issue given the increasing prevalence of thyroid cancer worldwide even with consistent death rates. Knowing how scientific output has handled this problem can help to direct future studies and health strategies.

Objectives: To find theme clusters and developing subjects in the literature connected to thyroid cancer overdiagnosis by text analysis of published research. **Methods:** A bibliometric and textual study of papers indexed in Scopus from inception to 2024 was conducted. Using co-occurrence mapping using the VOSviewer tool, titles, abstracts, and keywords were examined. Based on co-occurrence, terms were clustered, and overlay visualization was applied to show developing ideas related with thyroid cancer and overdiagnosis.

Results: Five main thematic clusters were found: (1) conservative management and patient-centered approaches, defined by terms like active surveillance, decision making, and benefit harm balance; (2) methodological comparisons with other cancer types, including breast and prostate cancer; (3) global epidemiology and public health policies, with emphasis on incidence trends and international recommendations; (4) diagnostic strategies and imaging tools such as cytology, ultrasound, and classification systems; and (5) social impact and communication, stressing patient awareness and the burden of unnecessary treatment. Emerging subjects included global burden, differentiated thyroid carcinoma, and socioeconomic disadvantages. **Conclusion:** This paper shows a definite change in thyroid cancer overdiagnosis studies. Patient-centered treatment, critical evaluation of diagnostic techniques, and increasing awareness of global inequalities and public health consequences are all trends. These results help to shape educated clinical and policy decisions and offer a platform for future research.

THYROID CANCER CLINICAL

1112586 - EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH MEDULLARY THYROID CARCINOMA IN A BRAZILIAN HOSPITAL

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Introduction: Thyroid cancer affects women more often than men and usually occurs between the ages of 25 to 65 years. Neoplasms of the thyroid gland are classified into four main types: papillary, follicular, medullary and anaplastic. Medullary thyroid carcinoma (MTC) accounts for 4% of all thyroid cancers. It presents as a palpable nodule in the neck and is typically associated with lymphadenopathy. The primary treatment with the highest likelihood of cure is total thyroidectomy with central compartment dissection. **Objective:** The study aims to analyze the epidemiological data of medullary thyroid carcinoma between 2000 and 2023 at a referral Brazilian institute.

Methods: This is a retrospective, descriptive and quantitative cohort study based on data extracted from patient records in a reference hospital. A total of 32 out of 140 patient records with Medullary Thyroid Carcinoma treated between 2000 and 2023 were randomly selected. Data were organized and systematized in Microsoft Excel spreadsheets and analyzed using descriptive statistics. **Results:** The most affected age group was adults aged 20 to 59 years (68.7%), followed by the elderly (21.9%) and children aged 0 to 19 years (9.4%). Regarding gender distribution, women were the most affected by the pathology, accounting for 71.9%. White individuals represented more than half of the patients (56.2%), followed by brown (28.1%) and black individuals (12.5%). The main complaint before diagnostic investigation was a neck nodule, reported by 71.9%, and 100% underwent total thyroidectomy at diagnosis or in a two-stage procedure. **Conclusion:** The analyzed data highlight that in recent decades, the profile of individuals with the highest incidence of medullary thyroid carcinoma has been women, adults, and white individuals. This epidemiological information emphasizes the importance of improving services aimed at the early diagnosis and efficient treatment of this pathology.

THYROID CANCER CLINICAL

1114314 - EVALUATION OF THE EFFICACY OF A SINGLE 0.9 MG INTRAMUSCULAR DOSE OF RECOMBINANT HUMAN TSH IN ACHIEVING TARGET SERUM TSH (>30 mIU/L) IN PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA UNDERGOING I-131 THERAPY

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Introduction: Recombinant human TSH (rhTSH) was approved as preparation for radioiodine therapy (RIT) in patients with differentiated thyroid carcinoma (DTC) by the EMA in 2005 and the FDA in 2007. The standard protocol involves two consecutive daily intramuscular injections of 0.9 mg rhTSH, followed by I-131 administration on the third day. Unlike thyroid hormone withdrawal, rhTSH allows continued LT4 therapy, sparing patients from hypothyroidism. **Objective:** To evaluate the proportion of DTC participants achieving serum TSH >30 mIU/L after a single 0.9 mg dose of rhTSH. **Methods:** In this prospective cross-sectional study, 128 thyroidectomized DTC participants received a single 0.9 mg intramuscular dose of rhTSH. Serum TSH was measured 24 hours post-injection. Six participants were excluded due to improper blood sampling timing. **Results:** Among the 122 evaluable participants, 82 were women, the mean age was 44.67 years (range: 13-77 years) and 70 were classified as an intermediate recurrence risk (RSS/ATA 2015). 100% reached serum TSH >30 mIU/L and the mean TSH level was 96.1 mIU/L (range: 31.67-150.0 mIU/L). **Conclusion:** A single 0.9 mg dose of rhTSH effectively achieved the target TSH threshold in all patients studied. These findings support the potential for simplified, cost-effective protocols and warrant further investigation for broader clinical application.

THYROID CANCER CLINICAL

1112468 - FAMILIAL PAPILLARY THYROID CARCINOMA: HISTOPATHOLOGICAL DIFFERENCES BETWEEN EARLY-ONSET, LATE-ONSET, AND SPORADIC FORMS

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Introduction: Familial papillary thyroid carcinoma (fPTC) demonstrates more aggressive behaviour compared to sporadic PTC (sPTC), but its etiology remains unclear. **Objective:** To compare the histological features of patients with fPTC to those of patients with sPTC. **Methods:** Thirty-one patients with fPTC and 31 patients with sPTC, matched by sex and age at diagnosis, were investigated in this retrospective study. Histological variant, multicentricity, tumor infiltration, angioinvasion, TNM stage, lymph node metastasis, BRAF and p53 expression, ATA risk and the presence of chronic lymphocytic thyroiditis were evaluated. Furthermore, patients were stratified by age of onset (≤ 35 or > 35 years) to assess potential behavioral differences. **Results:** Familial tumors were more aggressive, with medium-high TNM stage observed in 15/31 fPTC patients compared to 4/31 sPTC ($p < 0.01$). Early-onset fPTC (≤ 35 years) showed greater BRAF expression (7/16 vs 1/15, $p < 0.05$), as well as more frequent lymph node metastasis (8/14 vs 2/15, $p < 0.05$), medium-high TNM stage (11/16 vs 4/15, $p < 0.05$), and medium-high ATA-risk (9/16 vs 2/15, $p = 0.02$) than late-onset fPTC (> 35 years). Furthermore, medium-high TNM stage (11/15 vs 3/14, $p < 0.02$) and BRAF expression (7/16 vs 1/14, $p < 0.05$) were observed more frequently in early onset fPTC compared to early onset sPTC. Lastly, late-onset fPTC were more frequently associated with lymphocytic thyroiditis compared to early-onset fPTC patients (11/15 vs 6/16) and late-onset sPTC patients (11/15 vs 4/17, $p < 0.02$). **Conclusions:** Our preliminary data confirm a more advanced disease stage at diagnosis in fPTC compared to sPTC. Early-onset fPTC may be driven by direct genetic mechanisms, whereas autoimmune thyroiditis may contribute to carcinogenesis in late-onset fPTC. Further investigations are needed to explore whether different pathogenic mechanisms are involved in early-onset compared to late-onset fPTC.

THYROID CANCER CLINICAL

1112419 - FEASIBILITY AND RESULTS OF USING A REAL-WORLD EXTERNAL CONTROL ARM TO EVALUATE THE TREATMENT EFFECT OF SELPERCATINIB IN PATIENTS WITH RET MUTATION-POSITIVE MEDULLARY THYROID CANCER INCLUDED IN THE SINGLE-ARM LIBRETTO-001 TRIAL: THE RECALIB-RET STUDY

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Introduction: The efficacy of selpercatinib was evaluated in the single-arm Phase 1/2 LIBRETTO-001 trial (NCT03157128) for RET mutation-positive medullary thyroid cancer (RET-MTC), resulting in Global conditional approvals. The RECALIB-RET study assessed the feasibility and results of using a RWD ECA to generate comparative effectiveness data to support payor reimbursement decisions. **Methods:** The selpercatinib arm included the data of individual RET-MTC patients enrolled in the LIBRETTO-001 trial, treated in first or second-and-later (1L or ≥ 2 L) lines. ECA used pooled patient-level RWD of RET-MTC patients treated with standard of care (SoC) after June 2013, from: a chart review of European patient medical records (1L and ≥ 2 L), the French Refractory Thyroid Tumors (TUTHYREF) registry database (1L and ≥ 2 L) and a published retrospective US chart review (≥ 2 L). The primary outcome was progression-free survival (PFS). Baseline covariates were balanced using propensity score matching (PSM). Outcomes analysis used Cox proportional hazards model and Kaplan-Meier method. **Results:** The selpercatinib arm included 116 and 179 patients in the 1L and ≥ 2 L groups respectively. The ECA included 107 and 51 patients in the 1L and ≥ 2 L analyses, respectively. Before PSM adjustment, characteristics of the selpercatinib and SoC arms were largely comparable, with differences in time from advanced stage diagnosis (1L) and number of prior treatment lines (≥ 2 L). After adjustment, median PFS was significantly longer with selpercatinib compared to SoC in 1L (respectively NE (50.7NE) versus 26.1 (18.738.7), HR 0.34, CI95% = [0.200.58], $p < 0.0001$), with a non-significant trend toward benefit in ≥ 2 L (respectively 27.4 (18.344.3) versus 11.6 (5.480.8), HR 0.59, CI95% = [0.311.14], $p = 0.12$). **Conclusion:** Rare disease registry data can effectively form ECAs, enabling comparative analyses for payors. Selpercatinib demonstrated a PFS benefit over SoC in 1 L RET-MTC patients, and more than doubled PFS in ≥ 2 L.

THYROID CANCER CLINICAL

1112251 - FOLLICULAR CELL-DERIVED THYROID CANCER: IMPACT OF THE CHANGES OF THE RECURRENCE RISK LEVEL CLASSIFICATIONS ON POSTOPERATIVE RADIOACTIVE IODINE ADMINISTRATION

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Introduction: Postoperative management of follicular cell-derived thyroid cancer (TC) is based on the risk of recurrence. Compared with the 2006 ETA and the 2009 ATA classifications, there were more low-risk patients and fewer high-risk patients in the 2015 ATA classification, reducing the indications for postoperative radioactive iodine (RAI) administration. **Objective:** The aim was to evaluate the consequences of the changes in the risk level classification of the latest ATA classification on postoperative RAI indications. **Methods:** This is a single-centre retrospective study, including 474 consecutive patients operated for follicular cell-derived TC between January 2016 and December 2022. **Results:** The patients (76% women, mean age: 51 years), had papillary TC in 87% of the cases. According to AJCC 8th edition, TC were pT1, pT2, pT3 and pT4 in 61%, 25%, 13% and 1%, respectively. Tumours were pN0Nx in 73% of the cases and N1 in 27%. According to the 2006 ETA, 2009 and 2015 ATA classifications, patients were classified in the lowest-risk level in 22%, 37%, and 58% of the cases, as intermediate-risk level in 36%, 53%, and 31% of cases and as high risk in 42%, 10%, and 11 % of cases, respectively. Based on each guideline, RAI was considered or indicated in 70%, 56% and 46% of the cohort, respectively. Using the next ATA classification, 40% of the cases will be low risk, 24% low-intermediate risk 21% intermediate-high and 15% high risk. Compared to the 2015 classification, 25% of the patients will increase their risk level and 4% will decrease it. RAI will be considered or indicated in 60% of the patients, an increase of 30%. **Conclusions:** While the 2015 ATA guidelines led to a decrease in recurrence risk classification, the next ATA classification will have the opposite effect with a 30% increase in RAI indications.

THYROID CANCER CLINICAL

1112467 - FOLLICULAR THYROID CARCINOMA PRESENTING AS METASTASIS TO SKULL BASE WITH CRANIAL NERVE DYSFUNCTION - A CASE REPORT

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45-year-old female with known multinodular goiter followed in primary care for 20 years presented to the emergency department with diplopia and progressively reduced visual acuity. Cranial CT and, posteriorly, MRI showed large tumoral lesion spreading through the skull base with high signal in T2, centered in the sella turcica, measuring 43 × 42 mm. Mass extended into sphenoid sinus, clivus, and cavernous spaces, with complete involvement of left internal carotid, and was suggestive of meningioma. Physical examination revealed third cranial nerve palsy and large goiter. The patient reported compressive symptoms, therefore total thyroidectomy was performed, initially demonstrating a thyroid adenoma. Patient underwent just a transsphenoidal biopsy of the tumor, because it was considered to be irresectable during the procedure. Anatomopathology was diagnostic of bone metastasis of follicular carcinoma. Review of the thyroidectomy material confirmed the thyroid as the neoplasm's primary site. Currently, the patient is being monitored at our service and will undergo additional therapies, such as radioiodine therapy. Thyroid cancer accounts for 1.5% of all cancer in adults and follicular carcinoma (FTC) comprises 17%-20% of those. Overall, mean survival rate after 10 years is 85%, and metastasis has been reported in 6%-20% of patients. The most common metastatic sites are the lungs and bones. Skull base metastasis is rare, with less than 30 cases reported in literature. Most reports occurred in women, with symptoms related to cranial nerves involvement being common, like our patient. Surgical treatment of metastasis is the choice if possible and radioiodine therapy is an alternative. It was a rare case of widely invasive FTC with metastasis to the skull base that had been followed in primary care for over 15 years. Information about this entity is important for physicians to avoid delayed diagnosis of this rare disease.

THYROID CANCER CLINICAL

1112400 - FOLLOW-UP OF ANTITHYROGLOBULIN ANTIBODY-POSITIVE PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA: EXPERIENCE FROM A TERTIARY HOSPITAL

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Introduction: Thyroglobulin (Tg) measurement is crucial for follow-up on differentiated thyroid carcinoma (DTC) patients. Antithyroglobulin antibodies (TgAb) can compromise Tg levels, leading to false-negative results. **Objective:** Evaluate the clinical characteristics and follow-up of patients of DTC with positive TgAb. **Methods:** From 454 DTC patients, 26 patients (24 female) with positive TgAb (TgAb+) (5.7%) were selected. **Results:** The mean age was 46.8 years (13.581.2). Nineteen (73.1%) had preoperative TgAb+. All patients underwent total thyroidectomy and 10 (37%) neck dissection. Hashimoto's Thyroiditis (HT) was observed in 19 cases. According to ATA, 13 (50%), 4 (15.4%), and 9 (34.6%) were low, intermediate, and high risk for recurrence, respectively. The median follow-up was 6.9 years (4 months 12.4y), and TgAb levels became negative (TgAg-) in 13/19(68.4%) in median = 205 days: 11 remain with TgAb- and 2 with TgAb- by Immulite method developed TgAb+ by Atellica method without recurrence. Six patients maintain TgAb+: 4 without recurrence, and 2 patients with a follow-up < 1 year. Of 7 patients who did not have preoperative TgAb measurement, 6 had TgAb+ in the immediate postoperative period: 2 patients remained TgAb+, and 4 evolved with TgAb-; of these, 1 patient returned to have TgAb+ after 6 years of follow-up and lymph node metastasis was identified. One patient with TgAb- by Immulite developed TgAb+ by Atellica and is undergoing investigation for recurrence. No association was observed between the presence of HT at biopsy and the response to treatment (P=0.52). **Conclusions:** TgAB positivity varies according to ethnicity (15-30%). In our series, only 5.7% of patients had TgAb+. The period for TgAb to become negative was less than 7 months after surgery. In our series, there was no association between the presence of HT and a better response to treatment. We must emphasize the importance of maintaining the same TgAb dosage method during the follow-up of these patients.

THYROID CANCER CLINICAL

1112317 - FROM A LUMP IN THE NECK TO A THYROID LYMPHOMA: A CASE REPORT

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Primary thyroid lymphoma is a rare form of non-Hodgkin lymphoma that accounts for less than 5% of thyroid cancers and 2% of extranodal lymphomas. It predominates in older women and is associated with Hashimoto's thyroiditis. The most common subtype is diffuse large B cell lymphoma (DLBCL), although there are also T lymphomas and marginal zone lymphomas (MALT lymphomas). We present the case of a 24-year-old woman who attended an endocrinology consultation due to an increase in volume in the anterior aspect of the neck with a normal thyroid profile and elevated antithyroid antibodies. A thyroid sonography was performed, which reported a hypoechoic nodular lesion, without vascularity in the right thyroid lobe, and a fine needle aspiration (FNAC) was performed, which reported atypical lymphoid proliferation. An immunohistochemical study of the aspirate was performed, showing a CD45+, CD20+ and CD10+ population.; with a presumptive diagnosis of follicular lymphoma, so FISH was performed, which showed a 14:18 translocation. A PET/CT was performed that showed a hypermetabolic nodular formation in the right thyroid lobe measuring 3.8 of R-CHOP with an adequate response to treatment. This case highlights the importance of a comprehensive and multidisciplinary evaluation for the timely diagnosis and treatment of primary thyroid lymphoma, thus improving clinical outcomes. Furthermore, it highlights the need to consider thyroid lymphoma in the differential diagnosis of thyroid nodules, especially in patients with a history of autoimmune thyroiditis.

THYROID CANCER CLINICAL

1112397 - GENETIC PROFILE ASSOCIATED WITH RESPONSE TO THERAPY IN PEDIATRIC THYROID CANCER

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Introduction: We have demonstrated that, compared to adult papillary thyroid carcinoma (PTC), pediatric PTC is characterized by a higher prevalence of gene fusions and a lower frequency of point mutations. Furthermore, the AGK::BRAF fusion was significantly associated with younger age and the presence of lung metastases. It was reported that distant metastases and recurrences in children and adolescents occurred only in tumors with undetectable sodium/iodide symporter (NIS) expression and that the activity of 131I required to achieve remission was greater in these cases. **Objective:** To gain a deeper understanding of the role of AGK::BRAF in response to initial therapy and to identify potential markers that may cooperate with AGK::BRAF in disease progression. **Methods:** RNA sequencing was performed on samples from 5 patients with evidence of disease (structural and/or biochemical) and 5 patients without evidence of disease (n = 5), and normal thyroid tissue (n = 6) using the TruSeq Stranded RNA Library Prep Kit. Sequencing was carried out on the NextSeq 2000 platform. Single nucleotide variations were identified using the Genome Analysis Toolkit (GATK), and differential gene expression analysis was conducted using Noiseq. **Results:** We identify pathogenic variants in five genes that may aid in classifying patients into two groups: disease-free and evidence of disease. These variants also show a significant association with distant metastases (p < 0.05). The pathogenic variants were validated via Sanger sequencing. **Conclusion:** This study offers valuable insights into the molecular mechanisms driving the pathogenesis and progression of pediatric PTC, while also highlighting potential molecular markers that could improve patient stratification and prognostic assessment in this population.

THYROID CANCER CLINICAL

1112558 - GLOBAL TRENDS IN RET GENE MOLECULAR TESTING: A SCOPING REVIEW ANALYSIS OF TECHNOLOGICAL, ECONOMIC, AND CLINICAL PATTERNS

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Introduction: The implementation of RET gene molecular testing varies significantly across different contexts. Understanding temporal trends, economic factors, and testing criteria is crucial for developing effective diagnostic strategies. **Objective:** To analyze temporal patterns, socioeconomic factors, and implementation strategies in RET molecular testing across different contexts and populations, focusing on the relationship between testing technologies, economic characteristics, and sequencing criteria. **Methods:** A scoping review following JBI guidelines was conducted. Searches were performed in major databases without language or date restrictions. The analysis focused on temporal trends, economic characteristics, and testing criteria. **Results:** From 8734 references identified, 349 studies met inclusion criteria and were included. Significant technological evolution was observed during last decades ($p < 0.001$), with a marked reduction in probe genotyping (22.44% to 1.96%) and Restriction Fragment Length Polymorphism (RFLP) (21.9% to 1.9%), while Sanger sequencing remained predominant (63.18%). Next Generation Sequencing emerged after 2009 (7.36%). High-income countries showed diverse technological approaches, while upper-middle-income countries demonstrated higher NGS adoption (OR: 4.083; CI95%: 1.431-11.655; $p = 0.009$). Main testing indications were family screening (44.4%), clinical suspicion (36.4%), sporadic MTC (12.3%), and hereditary MTC confirmation (9.7%). Technology choice significantly correlated with testing indication ($p = 0.002$), with Sanger sequencing predominating in family screening (69.40%) and clinical MEN2 manifestations (66.10%), while probe techniques were more frequent in sporadic MTC cases (26.67%). **Conclusion:** RET molecular testing strategies show significant temporal evolution and vary based on economic context and testing indication. While high-income countries maintain established methods, emerging economies increasingly adopt advanced technologies. These findings highlight the need for context-specific implementation strategies considering technological capabilities and economic contexts while maintaining diagnostic quality.

THYROID CANCER CLINICAL

1114186 - HEMITHYROIDECTOMY WITH CENTRAL NECK DISSECTION IN PHENOTYPICALLY SPORADIC MEDULLARY THYROID CARCINOMA: IMPACT ON BIOCHEMICAL REMISSION AND EVENTLESS SURVIVAL

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Introduction: Medullary thyroid carcinoma (MTC) is a rare and aggressive form of thyroid cancer that can occur sporadically or in association with hereditary RET mutation. The standard treatment for MTC typically involves thyroidectomy with central neck dissection (CND); however, there remains ongoing debate about the necessity of such surgical approach. **Objective:** Does performing a hemithyroidectomy with CND in patients phenotypically and clinically classified as sporadic affect the likelihood of achieving biochemical remission? **Methods:** This retrospective study included 680 adult patients with histologically confirmed MTC who underwent initial surgery at SPbU Hospital between 2010 and 2023. Germline RET mutations were tested in 64.0% of cases, with 95.0% of these tests conducted postoperatively. Among those tested, 22.3% were found to have the RET mutation. According to national guidelines, the standard treatment for medullary thyroid cancer involves thyroidectomy with CND. However, to minimize potential complications, patients with phenotypically sporadic MTC were offered hemithyroidectomy with bilateral CND. "Phenotypically sporadic" was defined as unilateral thyroid nodules or all other nodules were negative cytologically. Patients with bilateral lesions, coexisting pheochromocytoma, or a family history of MTC were considered to have hereditary forms. Primary hyperparathyroidism without multiglandular disease was excluded, given its high prevalence in the general population. In 157 cases (23.1%), the final extent of thyroid resection was hemithyroidectomy. **Results:** Biochemical remission was achieved in 72.4% of patients available for follow-up. Among these, 2.5% were classified as pN1a and 0.6% as pN1b (OR = 13.5). The rate of biochemical remission following hemithyroidectomy with neck dissection was 72.86%, compared to 72.35% after thyroidectomy with neck dissection. No significant differences were observed in event-free survival between the groups. **Conclusion:** The decision regarding the extent of surgery can be made through consensus between the surgeon and the adult patient, based on the initial clinical presentation, prior to obtaining genetic test results.

THYROID CANCER CLINICAL

1114054 - HEMOSTATIC RADIATION FOR INTRACTABLE HEMORRHAGE AFTER THYROID LOBECTOMY FOR ANAPLASTIC THYROID CARCINOMA: A CASE REPORT

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Case Presentation: A 60-year-old man underwent right thyroid lobectomy for a toxic adenoma and was found to have a 4.5 cm anaplastic thyroid carcinoma with positive microscopic margins. Three weeks post-operatively, he developed a neck hematoma which re-accumulated despite two bedside aspirations. He subsequently underwent neck exploration and hematoma evacuation for persistent hemorrhage (>200 mL/day) three times over a one-week period; each time, there was diffuse ooze with no discrete bleeding source. Angiogram showed no active extravasation, and prophylactic embolization of the right superior and right inferior thyroid arteries was performed. Despite this, he had on-going hemorrhage requiring transfusion. Coagulopathy work-up was negative and he underwent a course of thromboxane per hematology recommendations without improvement in his bleeding. Wound bed biopsies ultimately showed residual anaplastic thyroid carcinoma involving skeletal muscle, making tumor bleeding the most likely source of his on-going hemorrhage. Radiation oncology was consulted and he underwent one dose of external beam radiation therapy (EBRT) in an effort to reduce bleeding. Bleeding initially increased after EBRT (>500 mL/day) but eventually stopped over the ensuing days and he was discharged home. He has since completed 5 weeks of chemoradiation without evidence of recurrent hemorrhage. **Discussion:** Intractable post-operative hemorrhage in the absence of coagulopathy is extraordinarily unusual after thyroidectomy, even for anaplastic thyroid cancer. If extensive attempts at surgical hemostasis fail, malignant hemorrhage must be considered even in the setting of isolated microscopic disease. A potential benefit of neoadjuvant treatment for initially-resectable anaplastic thyroid cancer may be a decrease in the likelihood of residual microscopic disease and therefore decreased morbidity from complications such as hemorrhage. **Final Comments:** Multidisciplinary collaboration was critical in this unusual case of intractable post-operative bleeding in a patient with anaplastic thyroid carcinoma. Hemostatic radiotherapy is an important option to consider in cases of malignant hemorrhage.

THYROID CANCER CLINICAL

1112578 - HIGH-GRADE DIFFERENTIATED THYROID CARCINOMA: CLINICAL PATHOLOGICAL ANALYSIS OF A NEW ENTITY

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Introduction: High-grade differentiated thyroid carcinoma (HG-DTC) is a rare cancer with intermediate behavior between well-differentiated and anaplastic DTC. WHO defined HG-DTC by ≥ 5 mitoses per 2 mm² and/or tumor necrosis in tumors retaining follicular thyroid cell features. **Objective:** Report clinicopathological characteristics and outcomes of HG-DTC patients treated at a national center. **Methods:** Retrospective study of 32 HG-DTC patients from 1103 DTC cases. Surgery extent based on fine-needle aspiration (FNA) and imaging. Follow-up every 6 months with ultrasound, thyroglobulin (Tg), and anti-Tg antibodies. **Results:** 27 (84.4%) were women, mean age 39.8 $\pm$ 15.6 years, median tumor size 2.0 cm. Ultrasound was ACR-TIRADS 3, 4, and 5 in 3 (9%), 8 (26%), and 20 (65%) patients. FNA resulted in Bethesda III-IV and V-VI in 8 (26%) and 23 (74%) cases. 11 (34.4%) had total thyroidectomy (TT), 11 (34.4%) TT with lymph node dissection, 10 (31.3%) lobectomy. 27 (84%) had papillary thyroid carcinoma (PTC), 5 (15.6%) follicular thyroid carcinomas. Among PTCs, 37% were tall cell, 18.5% solid, 14.8% classic, 11.2% follicular, 18.5% other subtypes. 23 (72%) had only ≥ 5 mitoses, 6 (18.6%) only necrosis, 3 (9.4%) both. Male sex, age, and tumor diameter associated with distant metastasis. 27 (84%) indicated for radioiodine. 28 (87.6%) stage I, 2 (6.2%) stage II, 2 (6.2%) stage IVb. 22 (69%) followed > 1 year (median 1.7 years). All alive at follow-up end: 14 (64%) excellent response, 4 (18%) indeterminate biochemical, 3 (14%) incomplete biochemical, 1 (4%) incomplete structural. **Conclusions:** HG-DTC is rare but may increase following WHO publication. Most cases were PTC with aggressive subtypes. Only 2 patients had distant metastases. After median 1.7 years, no deaths, one incomplete structural response. Larger studies and longer follow-ups needed.

THYROID CANCER CLINICAL

1112293 - HOW THERAPY RESPONSE EVOLVED AFTER SURGERY AND RADIOIODINE THERAPY IN A GERMAN COHORT OF DIFFERENTIATED THYROID CANCER PATIENTS OVER 5 YEARS OF FOLLOW-UP

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Introduction: The classification of the ATA is internationally accepted to categorize thyroid cancer risk groups. However, there are various basic conditions in the individual countries, e.g. in Germany, where thyroid carcinomas are often diagnosed incidentally due to endemic goiter caused by iodine deficiency and it is not yet investigated whether the ATA classification can be applied here.

Objective: The objective was to examine changes in response to therapy over a 5-year follow-up period in a cohort of German patients with differentiated thyroid cancer (DTC) following surgery and radioiodine therapy (RAIT). Additionally, we aimed to assess whether the initial ATA risk stratification can predict the 5-year therapeutic response in DTC patients within our population. **Methods:** We conducted a retrospective analysis of 69 patients referred to our University Hospital for initial RAIT, with a follow-up ranging from 4-7.1 years (median 5.35 years). Patients were categorized based on risk and therapy response was evaluated according to the ATA. We compared the 5-year response outcomes with those observed 1 year after treatment. **Results:** 39/49 (80%) low-risk patients showed an excellent response at 5 years, as did 6/10 (60%) intermediate-risk patients. 43/51 patients who exhibited an excellent response at 1 year maintained in an excellent response, 7 were reclassified as having an indeterminate response and 1 developed a structural incomplete response. None of the indeterminate or biochemical incomplete responses progressed to structural incomplete response. Among the 5 patients who had a structural incomplete response initially and received additional therapies, 2 progressed to a biochemical incomplete response. **Conclusion:** The clinical outcomes predicted by ATA risk stratification and response to therapy in this German cohort align closely with findings from other population groups in previous studies. The initial response to therapy appears to be a reliable predictor of the 5-year response.

THYROID CANCER CLINICAL

1112325 - IMMUNOLOGICAL CHARACTERIZATION IN MEDULLARY THYROID CARCINOMA: ASSOCIATION BETWEEN PATTERNS OF IMMUNE INFILTRATION, HISTOLOGICAL ARCHITECTURE AND CLINICAL OUTCOME

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Introduction: Medullary thyroid carcinoma (MTC) is a rare and aggressive form of thyroid cancer that presents a challenging prognosis. The role of the immune microenvironment in MTC remains poorly explored compared to more prevalent thyroid cancers. **Objective:** This study aims to explore the immune landscape of MTC by systematically assessing the infiltration of immune cells and the expression of immune markers in various tissue topographies. **Methods:** We employed immunohistochemical techniques to analyze tissue samples from 24 patients with MTC, focusing on the tumor core, the interface with healthy tissue, adjacent normal thyroid tissue and lymph node metastases. We also used Rapid Panotic as a method of visualizing mast cells and a descriptive analysis of the patients' clinical, relating it to the immunological analyses. **Results:** 58.3% of the patients were female, 75% were over 75 years old and 70.8% had sporadic MTC. Our results reveal a distinct immune profile characterized by increase in CD3+, CD4+, CD8+ and CD20+ lymphocytes in the normal tissues adjacent to the tumors and expressive infiltration of mast cells in the metastasis. We observed a notable presence of granzyme B+ cells at the tumor interface in patients who still had structural disease after thyroidectomy, representing 27.3% of patients. **Conclusion:** These results underscore the complex and spatially dependent immune landscape of MTC, suggesting potential implications for targeted immunotherapy. Furthermore, it suggests that the tumor presents some mechanism that bars the infiltration of lymphocytes into the tumoral center. This study offers novel insights into the immune microenvironment of MTC and highlights the need for further research to clarify its impact on disease progression and therapeutic responses.

THYROID CANCER CLINICAL

1112485 - IMPACT OF BRAF MUTATION STATUS ON CLINICOPATHOLOGICAL FEATURES IN PAPILLARY THYROID CARCINOMA

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Introduction: The prognostic role of BRAFV600E mutation in papillary thyroid carcinoma (PTC) is still controversial. Its prevalence is variable across studies, and it has been suggested that the frequency of this mutation is increasing. **Objective:** To investigate the prevalence of the BRAF V600E mutation and its correlation with clinical-pathologic characteristics and aggressiveness features of PTC samples from the South of Brazil. **Methods:** Forty consecutive PTC thyroid tissues from patients undergoing thyroidectomy at a university-based hospital in the South of Brazil were collected. BRAF V600E mutation was detected through DNA analysis using Sanger sequencing. **Results:** The mean age of patients at the time of diagnosis was 50.4 ± 15 years, and 62.5% were women. Of the 40 patients evaluated, 30 (75%) carried the BRAFV600E mutation. The tumor size was 2.3 ± 1.3 cm, 47.5% of patients had lymph nodes, and all patients were M0/Mx. According to the ATA risk stratification system, 19 (47.5%) patients were classified as low, 15 (37.5%) as intermediate, and 6 (15%) as high risk. The mutational status was not associated with clinical and pathological features, including microscopic extrathyroidal extension and lymph node metastasis. **Conclusion:** This study demonstrated a high prevalence of BRAFV600E mutation. However, it was not significantly associated with aggressiveness tumor characteristics. Longitudinal studies are necessary to evaluate the role of BRAFV600E in prognosis.

THYROID CANCER CLINICAL

1114144 - IMPACT OF PREOPERATIVE BETHESDA CLASSIFICATION (III/IV VS. V/VI) ON THE PROGNOSIS OF DIFFERENTIATED THYROID CARCINOMA

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Introduction: The Bethesda system classifies thyroid nodule fine-needle aspiration cytology into six categories. Bethesda III/IV (indeterminate) nodules are frequently subjected to diagnostic surgeries despite an estimated malignancy rate below 30%. We hypothesized that differentiated thyroid carcinomas (DTC) with preoperative Bethesda III/IV cytology exhibit less aggressive clinical behavior compared to Bethesda V/VI (suspicious/malignant), supporting the use of partial thyroidectomy for diagnosing and treating indeterminate nodules. **Objective:** To compare clinical outcomes of DTC based on preoperative cytological classification (Bethesda III/IV vs. V/VI). **Methods:** A retrospective analysis was conducted on patients with Bethesda III-VI nodules who had a final diagnosis of DTC and were evaluated and treated at an academic center. Clinical outcomes – including lymph node metastasis (LNM), distant metastasis (DM), recurrence/persistence, and survival – were compared between Bethesda III/IV and V/VI cytology. Multivariate logistic regression models assessed the independent risk associated with cytological classification. **Results:** A total of 525 DTC patients (75 Bethesda III, 47 IV, 113 V, 290 VI) were included. Bethesda III/IV nodules were associated with larger tumor size ($p = 0.019$) and higher frequencies of follicular and oncocytic carcinomas ($p < 0.001$). Bethesda V/VI DTC exhibited higher rates of extrathyroidal extension ($p = 0.004$). LNM was more frequent in Bethesda V/VI (37% vs. 20.5% in Bethesda III/IV, $p < 0.001$), while initial DM was more common in Bethesda III/IV (6.6% vs. 2.7%, $p = 0.047$). No significant differences were found in recurrence/persistence, disease-free survival, or cancer-related mortality. Bethesda V/VI cytology was an independent risk factor for LNM (odds ratio 2.12, $p = 0.008$). **Conclusion:** DTC with a preoperative Bethesda III/IV cytology classification exhibited distinct histopathological characteristics compared to those with Bethesda V/VI cytology. LNM was significantly more frequent in Bethesda V/VI cases, but DM rates during follow-up, recurrence/persistence, and survival outcomes were similar between groups.

THYROID CANCER CLINICAL

1112285 - IMPACT OF STARTING DOSE ON LENVATINIB TREATMENT IN ADVANCED, DIFFERENTIATED THYROID CANCER

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Introduction: The Summary of Product Characteristics recommends initiating lenvatinib (LEN) treatment for metastatic, radioactive iodine-refractory (RAIR) differentiated thyroid cancer (DTC) at the full dose of 24 mg. While a phase II trial confirmed that lower starting doses (18 mg) are less effective, real-life data suggest physicians often prescribe reduced starting doses to mitigate severe toxicities. The cost-effectiveness of this practice in clinical settings remains unclear. **Objective:** This study aimed to compare the efficacy and safety of LEN initiated at the full recommended dose compared to lower starting doses in patients with advanced RAIR-DTC. **Methods:** We retrospectively evaluated 34 patients treated with LEN. Efficacy was assessed by overall survival (OS) and treatment failure-free survival (TFFS, i.e. the time from LEN initiation to dose increase, progression, or death, whichever occurred first). Safety was evaluated by the incidence of severe adverse events (grade ≥ 3) and the need for LEN dose reductions, interruptions, and discontinuations. **Results:** The 16 patients starting on reduced doses (median 10 mg, range 4-18 mg) were older (median age: 77.1 vs 65.2 years, $p=0.0012$), had lower BMI (23.5 vs 27.2 kg/m², $p=0.025$), and a worse performance status (ECOG ≥ 1 : 50% vs 11.1%, $p=0.014$) compared to those on full dose. Tumour histotype and metastasis sites were similar between groups. Median OS (69 vs 78 months, Hazard Ratio (HR) 1.58, 95% Confidence Interval (C.I.) 0.416-12, $p=0.51$) and TFFS (36 vs 42 months, HR 1.35, 95% C.I. 0.55-3.28, $p=0.51$) were comparable. While no differences were found in the frequency of LEN dose reductions (88.9 vs 81.2%, $p=0.54$) and transient interruptions (72.2 vs 81.2%, $p=0.54$), grade ≥ 3 toxicities (77.8% vs 43.7%, $p=0.044$) and discontinuations (16.7% vs 0%, $p=0.073$) occurred more frequently in the full-dose group. **Conclusion:** Starting LEN treatment at a reduced dose is effective for frailer patients, improving tolerance without compromising disease control.

THYROID CANCER CLINICAL

1112555 - IMPACT OF TSH SUPPRESSION ON BONE MINERAL DENSITY IN THYROID CANCER PATIENTS

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Introduction: Thyroid cancer patients often undergo TSH suppression therapy as part of their treatment to reduce the risk of recurrence. However, prolonged suppression of TSH can have adverse effects on bone health, particularly in postmenopausal women. This study aims to evaluate the changes in bone mineral density (BMD) and identify correlations between TSH suppression degree, duration, and BMD decline in these patients. **Methods:** A cohort of 90 thyroid cancer patients (100% female, median age 55 years) was retrospectively analyzed. BMD measurements at the lumbar spine and hip were evaluated during a median follow-up of 8 years. Patients were stratified by TSH suppression levels (<0.1, 0.10-0.5, 0.52-0, and >2.0 mIU/L) and TSH suppression degrees (calculated by combining suppression level and duration). Changes in BMD and T-scores were statistically analyzed, with a focus on postmenopausal women ($n=50$). **Results:** Significant BMD and T-score of lumbar spine reductions were observed in patients with TSH <0.1 mIU/L compared to those with milder suppression ($p<0.05$). Higher suppression degrees correlated with more pronounced declines in lumbar spine BMD ($p=0.017$). Paradoxical increases in hip total BMD were noted, but T-scores consistently decreased across all suppression levels. No significant correlations with suppression degree were found. In postmenopausal Women, longer durations of severe TSH suppression were associated with greater reductions in lumbar spine BMD ($p<0.05$), highlighting their vulnerability to bone loss. **Conclusions:** Aggressive TSH suppression, particularly with prolonged durations, significantly affects lumbar spine BMD in thyroid cancer patients, while its impact on hip BMD remains minimal. These findings emphasize the importance of balancing TSH suppression goals with the risk of bone health deterioration, especially in postmenopausal women. Future guidelines should consider personalized TSH targets to minimize adverse skeletal outcomes.

THYROID CANCER CLINICAL

1112538 - IMPACT OF VASCULAR INVASION IN PAPILLARY THYROID CARCINOMA

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Introduction: According to the 2015 American Thyroid Association (ATA) guidelines, the presence of vascular invasion is a criterion for intermediate risk. However, the impact of vascular invasion in papillary thyroid carcinoma (PTC) is still not well understood, and the results in the literature are controversial. **Objective:** To assess the impact of histologic vascular invasion in papillary thyroid carcinoma. **Methods:** Our study included 93 patients treated for a PTC between 2010 and 2018. Only patients with a minimum of 5 years of follow-up were included. We used the Kaplan-Meier method to calculate the cumulative proportion of survival. Survival curves were compared using the log-rank test. **Results:** Vascular invasion was noted in 9.7% of cases. It had a significantly bad impact on global survival ($p = 0.02$): the 5-year global survival rate was 66.6 % in the case of vascular invasion versus 98% for the group without vascular invasion. The patients with vascular invasion had a high risk of lymph node metastasis ($p = 0.001$) without a statistically significant risk of distant metastasis. Vascular invasion in PTC was associated with higher local and lymph node recurrence rates ($p = 0.02$). **Conclusion:** Our study indicates that vascular invasion in PTC is associated with a poorer prognosis as well as increased recurrence and lymph node metastasis rates. For these reasons, vascular invasion should be considered as an important prognostic factor when stratifying the patients risk of relapse and determining the extent of treatment.

THYROID CANCER CLINICAL

1112568 - INCREASED RISK OF LDL-LOWERING AGENT INITIATION IN THYROID CANCER PATIENTS TREATED WITH TOTAL THYROIDECTOMY: IMPLICATIONS OF LEVOTHYROXINE DOSE

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Introduction: Supraphysiologic thyroid hormone supplementation to suppress thyroid-stimulating hormone (TSH) has been highlighted as the main cause of adverse metabolic outcomes in thyroid cancer patients. However, insufficient thyroid hormone supplementation may lead dyslipidemia. **Objective:** We investigated the risk of initiating Low-density lipoprotein cholesterol (LDL)-lowering agents among thyroid cancer patients after total thyroidectomy. **Methods:** From the Korean National Health Insurance data, 6,632 thyroid cancer patients (≥ 40 years of age) who underwent total thyroidectomy during 2011-2013 were selected. Non-cancer controls were selected using propensity score matching. Cox proportional hazards regression analysis was performed to estimate hazard ratio (HR) for starting LDL-lowering agents. Weight-adjusted levothyroxine doses grouped into quintiles (Q; 1[the lowest]-5[the highest]) were included as time-dependent covariates. **Results:** Overall, 1,727 of the patients (26.0%) and 1,416 (21.4%) of the matched controls started LDL-lowering agents during the follow-up period. The patients had increased risk of starting LDL-lowering agents (HR = 1.30, 95% confidence interval [CI] = 1.21-1.40). The size of the HR had a U-shape relationship between the levothyroxine dose (HR [CI] = 1.38 [1.24-1.54], 1.27 [1.13-1.42], 1.04 [0.92-1.18], 1.10 [0.97-1.26], and 1.32 [1.16-1.50] in Q1-5, respectively). When subjects who started or used statins were excluded from the analysis, the patients with high-dose levothyroxine showed a smaller increase in LDL-cholesterol compared to the control group (Q3-5, $P < 0.05$). In contrast, patients with lower doses of levothyroxine had changes in LDL-cholesterol levels similar to the control group (Q1-2, $P > 0.05$). **Conclusions:** This study highlighted an increased risk of initiating LDL-lowering agents in postoperative athyreotic thyroid cancer patients taking relatively low doses of levothyroxine. Further studies are needed to determine the optimal range of levothyroxine dose and TSH in these patients.

THYROID CANCER CLINICAL

1114310 - INDEPENDENT MULTICENTER VALIDATION OF THE MIR-THYpE® MOLECULAR TEST IN THE DIAGNOSIS OF THYROID NODULES WITH INDETERMINATE CYTOLOGY

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Introduction: Fine-needle aspiration (FNA) of thyroid nodules often yields indeterminate cytology (Bethesda III/IV) in up to 30% of cases, posing challenges for clinical management. The mir-THYpE test, a microRNA-based expression classifier, can enhance diagnostic accuracy and possibly decrease the number of unnecessary surgeries. The original version of the test was released in 2018, and it was updated to its current version in 2020. This study presents the first independent, real-world validation of the mir-THYpE test, comparing its two versions. **Objective:** To independently validate and compare the performance of the initial and updated versions of the mir-THYpE test in FNA samples from patients with indeterminate thyroid nodules. **Methods:** This retrospective, multicenter study was conducted in four Brazilian states (Santa Catarina, São Paulo, Minas Gerais and Rio de Janeiro), including adult patients with Bethesda III/IV thyroid nodules tested with mir-THYpE between February 2018 and January 2023. FNA samples were analyzed using the test version available at the time. For patients who underwent surgery, test results were compared to final histopathology. A subset of samples was reanalyzed with the updated algorithm. **Results:** A total of 430 patients were included. Of these, 157 tested with the initial version underwent surgery, showing the following performance: 97.50% sensitivity, 20.78% specificity, 56.12% PPV, 88.89% NPV, and 59.87% accuracy, with a malignancy prevalence of 49.68%. The updated version, tested in 156 patients who also underwent surgery, showed: 97.14% sensitivity, 67.44% specificity, 70.83% PPV, 96.67% NPV, and 80.77% accuracy, with a malignancy prevalence of 43.59%. **Conclusion:** The initial mir-THYpE version provided good sensitivity but had lower specificity and accuracy compared to previous studies. The updated test significantly improved specificity and accuracy without compromising sensitivity. This study represents the first independent validation of the mir-THYpE test comparing its two versions and confirms its utility in stratifying the risk of indeterminate thyroid nodules, enhancing clinical decision-making.

THYROID CANCER CLINICAL

1114088 - INFLUENCE OF CALCITONIN MEASUREMENT ON SURGICAL APPROACH AND PROGNOSIS OF MTC PATIENTS IN A REFERRAL INSTITUTION IN BRAZIL

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Introduction: Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor derived from thyroid C cells, which produce calcitonin. Serum calcitonin measurement is a key diagnostic tool, alongside imaging studies and fine-needle aspiration (FNA) biopsy. Together, these assessments improve preoperative evaluation and prognosis. It is recommended to investigate regional or distant metastases when serum calcitonin levels exceed 150 pg/mL and 400 pg/mL, respectively. Calcitonin also guides surgical planning and serves as a biochemical marker for disease monitoring. **Objective:** To analyze the proportion of MTC patients who had pre and postoperative calcitonin measurements and their biochemical behavior in a sample of 31 individuals treated at a referral institution between 2000 and 2023. **Methods:** This retrospective, descriptive cohort study analyzed patient records from a referral hospital in Brazil. Thirty-one cases were randomly selected from 140 MTC patients treated between 2000 and 2023. Data were organized in Excel and analyzed using descriptive statistics. **Results:** Among 31 patients, 97% had postoperative calcitonin measurements, 48% had preoperative measurements, and 15% had data from both periods. In total, 42% had regional or distant metastases. Among 14 patients with both pre and postoperative calcitonin data, 57% had histopathological confirmation of lymph node involvement, all with preoperative calcitonin levels above 300 pg/mL. After thyroidectomy, 29% maintained calcitonin levels above 800 pg/mL, while distant metastases were found in 9%. Additionally, 29% achieved an excellent biochemical response with postoperative calcitonin ≤ 2 pg/mL. **Conclusion:** Preoperative calcitonin measurement is a valuable tool for detecting metastases, guiding surgical decisions, and monitoring remission. However, over half of the patients in this study lacked preoperative data. Early calcitonin assessment, timely diagnosis, and effective treatment are essential to optimizing patient outcomes.

THYROID CANCER CLINICAL

1113648 - INTERMEDIATE-RISK PAPILLARY THYROID CANCER: NOT EVERYONE NEEDS RADIOACTIVE IODINE

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Introduction: Intermediate-risk papillary thyroid cancer (IRPTC) is a heterogeneous entity. Traditionally, its treatment has included total thyroidectomy (TT), radioactive iodine (RAI) therapy and TSH suppression. With the adoption of risk-adapted management, the intensity of treatment for IRPTC is a matter of controversy. **Objective:** To report the clinicopathological characteristics and outcomes of patients with IRPTC treated without RAI in a national center. **Methods:** Ninety-six patients with IRPTC as defined by the 2015 ATA guidelines were treated with TT or thyroid lobectomy (TL) and followed for at least one year. The indication for RAI was determined based on histology, cervical ultrasound, thyroglobulin (Tg), and anti-Tg antibodies (TgAb) measured up to six months post-surgery. Follow-up was conducted every six months using the same parameters for the first two years, then at variable intervals depending on treatment response. **Results:** Of 96 patients followed for a median of 4.44 years, 85.4% were female, with a median age of 41 years. Median tumor size was 1.0 cm. Surgical management included TT (49%), TT with lymph node dissection (30.2%), and TL (20.8%). Intermediate-risk features included multifocality (42.5%), bilaterality (23.9%), aggressive histology (26%), microscopic extrathyroidal extension (52.1%), lymphatic invasion (19.8%), and lymph node involvement (34.4%, median size 2.5 mm, 10% with microscopic extranodal extension). Among 76 patients undergoing TT ± lymph node dissection, 92.1% had postoperative TgAb measured; 64.2% were TgAb negative with a median Tg of 0.1 ng/dL. Most cases (97.9%) were AJCC 8 stage I. No significant clinicopathological differences were observed between TT and TL. No mortality or further interventions were required. **Conclusion:** In IRPTC patients, selective use of RAI is a safe alternative after an appropriate initial evaluation, even in cases with microscopic extrathyroidal extension, limited lymph node involvement, or aggressive histological subtypes without other risk factors. Prolonged follow-up will confirm these findings and may support changes in the definition and therapy of IRPTC.

THYROID CANCER CLINICAL

1112324 - INTERNATIONAL REGISTRY OF THYROID CANCER IN LATIN AMERICAN COUNTRIES (CATALINA) FOR THE VALIDATION OF STATISTICAL AND MACHINE LEARNING PREDICTION MODELS

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Introduction: Despite advances in the diagnosis and treatment of Differentiated thyroid cancer (DTC), up to 20% of patients experience recurrence. Both statistical and machine learning predictive models have been developed to assess the risk of recurrence and guide clinical decision-making. These models often face limitations such as retrospective design, lack of diversity in study populations, and absence of external validation Latin American (LA) population. **Objective:** To externally validate and adapt existing machine learning predictive models for DTC recurrence using prospective data from a diverse LA hospital. **Methods:** The CaTaLiNA study is a multicenter prospective study conducted across hospitals in Latin American countries (Ecuador, Peru, Uruguay, and Mexico). Data collection includes baseline clinical, surgical, and histological characteristics, treatment details, and follow-up outcomes. Statistical predictive models include risk calculators or nomograms generated with logistic regression or survival models. Machine learning models include K-nearest neighbors, support vector machines (SVM), tree-based models, XGBoost, and artificial neural networks (ANN). **Results:** The study aims to recruit 1,667 patients, accounting for a 20% dropout rate, to ensure at least 200 events and 200 non-events for robust external validation. Statistical analysis will follow the TRIPOD and TRIPOD+AI guidelines, using imputation strategies for missing data and evaluating the calibration and discrimination of the prediction models. Calibration measures include the ratio of expected and observed events, calibration slope, and calibration plot, while discrimination will be assessed using the C-index and AUROC. Performance metrics for machine learning models will include accuracy, precision, recall, and F1 measures. **Conclusion:** This study will be the largest prospective validation of DTC recurrence risk models in LA. By addressing current methodological limitations and incorporating diverse patient data, the study aims to enhance existing statistical and machine learning models' predictive accuracy and clinical utility, thereby improving personalized treatment strategies and patient outcomes in DTC management.

THYROID CANCER CLINICAL

1112539 - INTRATHYROID METASTASIS: REPORT OF 3 CASES

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Introduction: Despite its rich vasculature, metastases to the thyroid gland are uncommon: 1.5 - 3% of all thyroid malignancies. The clinical manifestations are not specific. Most reported primary tumors are the kidney, colorectum, lung, and breast. Surgery is still the main treatment. **Objective:** To describe the clinical and histological features of intrathyroid metastases as well as their management. **Methods:** We report 3 cases of thyroid metastasis treated in our department between 2011 and 2024. **Results:** Two men and one woman, with no medical history, were included. The mean age was 67 years. The clinical manifestations were anterior neck swelling in all cases, associated with cervical lymph nodes in 2 cases. No extracervical symptoms were noted. Cervical ultrasound showed thyroid nodules with suspicion of malignancy (EUTIRADS 5) in all cases. Fine needle aspiration (performed in 2 cases) suggested papillary carcinoma. All patients underwent total thyroidectomy with lymph node dissection (central neck dissection in all cases and lateral neck dissection in 2 cases). Histological examination with immunohistochemistry confirmed the diagnosis of a thyroid metastasis of lung cancer in 2 cases and pancreatic cancer in 1 case. Two patients had favorable evolution after treatment of the primary. One patient (lung primary) presented a locoregional recurrence. **Conclusion:** The thyroid gland is a rare site of tumor metastasis. They are most often related to renal cell carcinoma. Lung and pancreatic primaries are very uncommon.

THYROID CANCER CLINICAL

1112199 - INVESTIGATION OF SALIVARY GLAND FUNCTION 72 HOURS AFTER RADIOIODINE THERAPY IN PATIENTS WITH PAPILLARY THYROID CANCER

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Introduction: After radioiodine therapy (RAIT) in patients with papillary thyroid cancer (PTC), one of the most common side effects is xerostomia. The accumulation of sodium iodide in the salivary gland acinuses can lead to damage to the intracellular epithelium, periacinoductal inflammation, narrowing of the duct lumen, mucus retention and duct blockage, fibrosis, leads to loss of the ability to secrete saliva. **Objective:** Assessment of the secretory activity of the salivary glands after RAIT in the early post-radiation period. **Methods:** The outcome of the treatment were analyzed in 12 patients with PTC 72 hours after RAIT at a dosage of 3.0-4.5GBq. Complaints, anamnesis, clinical manifestations, results of mixed saliva sialometry, post-therapeutic scintigrams were evaluated. Using a shielded spectrometer and a Marinelli vessel, the radioactivity of saliva was determined. **Results:** Patients complained of a feeling of dryness in the oral cavity, the appearance of viscous thick saliva, swelling and pain in the neck area. During sialometry of mixed saliva, a decrease in secretion is noted: without stimulation (≤ 0.18 mL/min), the norm is 0.25 mL/min, with stimulation (≤ 0.45 mL/min), the norm is 0.75 mL/min. According to the results of diagnostic scintigraphy in the "whole body" mode 72 hours after RAIT, the size of the glands is normal, despite a decrease in functional activity, which indicates incomplete selective damage to cellular structures. The proportion of excreted activity in the collected saliva with and without stimulation was 0.48% and 0.55% of the activity in the whole body. **Conclusion:** An increase in the percentage of accumulation of salivary radioactivity indicates the functional activity of the salivary glands, a lower salivary radioactivity index indicates a decrease in the function of the salivary glands and a slowdown in the excretion of radiopharmaceuticals. Therefore, radiometric examination is of great diagnostic importance and suggests a violation of salivation.

THYROID CANCER CLINICAL

1112500 - LIMITED DIAGNOSTIC ROLE OF 18F FDG PET/CT IN PEDIATRIC THYROID CARCINOMA: A RETROSPECTIVE ANALYSIS

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Objective: To evaluate the usefulness for disease detection of 18-FDG PET/CT in differentiated thyroid carcinoma (DTC) of pediatric and adolescent populations treated with radioactive iodine (RAI). **Methods:** A retrospective analysis was conducted on 264 patients (median age 11 years; range 6-18) who underwent total thyroidectomy for DTC and received RAI therapy (1 MCi/kg with systematic whole body scan/SPECT-CT) at Gustave Roussy (1991-2019). A total of 17 patients performed 18 FDG PET and were considered for this analysis. **Results:** 13/17 patients presented with Papillary DTC. The TNM stage was respectively: 35% T2, 29% T3a, 17% T3b, 11% T4a and 5% T1b), 82% N1b, 11% Nx 5% N1a) and 14 patients presented M1 at diagnosis. Median Tg at the moment of RAI treatment was 414 ng/mL (range: 29-4200 ng/mL). A median number of 3 (range: 2-10) 131I treatment were administered. The initial 131I WBS revealed thyroid remnant in 15 patients, cervical lymphnodes metastases in 9, and distant metastases in 14 patients (lung =13, mediastinal lymph nodes 1). In 16/17 patients 18 FDG PET was negative without any significant uptake despite 131I WBS uptake or abnormal Tg levels. The only case of positive 18-FDG PET/CT examination revealed cervical lymph nodes and bilateral pulmonary micro nodular lesions uptake in a 13 years old female patient, WBS was also positive at the same sites. After a median follow up of 90 months 12/17 patient were in remission and 5/17 presented persistent elevated Tg or structural disease. The patient with positive 18-FDG PET/CT received a total of 7 RAI treatment showing stable disease at last follow up. **Conclusion:** FDG PET is rarely positive in pediatric thyroid cancer and might have limited utility in disease detection or outcome prediction, despite it is proposed in guidelines. Further studies are need to confirm these data.

THYROID CANCER CLINICAL

1112498 - LOW-RISK DIFFERENTIATED THYROID CARCINOMA WITH EXCELLENT RESPONSE TO INITIAL TREATMENT: OVER 5-YEAR OUTCOMES IN A MULTICENTER COHORT

Carlos Garcia Regal¹; Jhonatan Boris Quiñones Silva¹; Noemi Brox Torrecilla¹; Cristina Familiar Casado²; Alberto Martínez Lorca¹; Héctor Gerardo Pian Arias¹; Ignacio Ruz Caracuel¹; Ana Maria Garcia Cano¹; Marta Rosillo Coronado¹; Aurelio López Guerra³; Elisa Fernández Fernández²; María Josefa Pamplona Civera⁴; Victoria Alcázar Lázaro⁵; María Guadalupe Guijarro de Armas⁶; Paloma Iglesias Bolaños⁶; Miguel Paja Fano⁷; Pablo Valderrábano Herrero¹

1 - Hospital Universitario Ramon y Cajal; 2 - Hospital Clínico San Carlos; 3 - Hospital Universitario Gregorio Marañón; 4 - Hospital Royo Villanova; 5 - Hospital Severo Ochoa; 6 - Hospital Universitario de Getafe; 7 - Hospital Universitario de Basurto

Introduction: Patients with low-risk differentiated thyroid carcinoma (DTC) who achieve an excellent response to initial treatment have an estimated recurrence risk of less than 1%. Despite this, indefinite follow-up is standard practice. **Objective:** This study aimed to evaluate treatment response rates and recurrence rates at the end of follow-up in low-risk DTC patients with an excellent initial treatment response. **Methods:** This retrospective, multicenter study included low-risk DTC patients treated between 2015 and 2018. Eligible patients had an excellent initial response, thyroglobulin (TG) levels measured using ultrasensitive assays (< 0.1 ng/mL) from diagnosis, and at least 5 years of follow-up. The study analyzed predictors of indeterminate response, calculating incidence per 1,000 person-years (Poisson distribution) and cumulative incidence. Predictive variables were compared using the log-rank test, and Cox regression was used to estimate hazard ratios. **Results:** Among 378 patients, 88% had papillary thyroid cancer, 8% follicular, and 4% oncocytic. Tumor staging included 58% T1a, 27% T1b, 11% T2, and 4% T3a; 94% were N0/Nx, and 6% N1a/b. The median follow-up was 83 months [60111]. At follow-up, 92% maintained an excellent response, 7% had indeterminate response, and 1% had a biochemical incomplete response. The incidence of indeterminate response was 11.2 per 1,000 person-years (95% CI: 7.516.2), with a median onset of 3 years. Radioactive iodine therapy (NaI[131]) was significantly associated with reduced risk of indeterminate response (p=0.02; HR 0.4 [0.20.9]). However, under Roger Chous newer criteria for indeterminate response, no significant difference was observed between patients treated with or without NaI[131] (p=0.6; HR 0.8 [0.31.9]). No structural recurrences occurred. **Conclusion:** Low-risk DTC patients with an excellent initial response have an insignificant recurrence rate, suggesting follow-up could be safely discontinued after 5 years.

THYROID CANCER CLINICAL

1113632 - LOW-RISK DIFFERENTIATED THYROID CARCINOMA WITH EXCELLENT RESPONSE TO INITIAL TREATMENT: OVER 5-YEAR OUTCOMES IN A MULTICENTER COHORT

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Introduction: Patients with low-risk differentiated thyroid carcinoma (DTC) who achieve an excellent response to initial treatment have an estimated recurrence risk of less than 1%. Despite this, indefinite follow-up is standard practice. **Objective:** This study aimed to evaluate treatment response rates and recurrence rates at the end of follow-up in low-risk DTC patients with an excellent initial treatment response. **Methods:** This retrospective, multicenter study included low-risk DTC patients treated between 2015 and 2018. Eligible patients had an excellent initial response, thyroglobulin (TG) levels measured using ultrasensitive assays (<0.1 ng/mL) from diagnosis, and at least 5 years of follow-up. The study analyzed predictors of indeterminate response, calculating incidence per 1,000 person-years (Poisson distribution) and cumulative incidence. Predictive variables were compared using the log-rank test, and Cox regression was used to estimate hazard ratios. **Results:** Among 378 patients, 88% had papillary thyroid cancer, 8% follicular, and 4% oncocytic. Tumor staging included 58% T1a, 27% T1b, 11% T2, and 4% T3a; 94% were N0/Nx, and 6% N1a/b. The median follow-up was 83 months [60-111]. At follow-up, 92% maintained an excellent response, 7% had indeterminate response, and 1% had a biochemical incomplete response. The incidence of indeterminate response was 11.2 per 1,000 person-years (95% CI: 7.5-16.2), with a median onset of 3 years. Radioactive iodine therapy (NaI[131]) was significantly associated with reduced risk of indeterminate response ($p=0.02$; HR 0.4 [0.2-0.9]). However, under Roger Chou's newer criteria for indeterminate response, no significant difference was observed between patients treated with or without NaI[131] ($p=0.6$; HR 0.8 [0.3-1.9]). No structural recurrences occurred. **Conclusion:** Low-risk DTC patients with an excellent initial response have an insignificant recurrence rate, suggesting follow-up could be safely discontinued after 5 years.

THYROID CANCER CLINICAL

1114162 - LYMPH NODE AND DISTANT METASTASIS IN PAPILLARY THYROID MICROCARCINOMA: 20-YEAR EXPERIENCE IN THE SUPPLEMENTARY HEALTH SYSTEM IN CEARÁ - BRAZIL

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Introduction: Papillary thyroid microcarcinoma (PTMC) accounts for about 35% of papillary thyroid cancer worldwide. Despite its generally indolent nature, lymph nodes (LNM) and distant metastasis (DM) have been described and specially central LNM is considered to be one of the most important risk factors associated with recurrence. There is no published data on LNM and DM in PTMC in Northeast Brazil, especially with regard to the more than 50 million supplementary health users in the country. **Objective:** To evaluate the incidence and clinicopathological features of LNM and DM in PTMC. **Methods:** Medical records of 75 patients diagnosed with PTMC, followed in the supplementary health system in Ceará-Brazil, between 2005 and 2025, were reviewed. All ethical principles were followed. **Results:** LNM were found in 13.3% of patients and in 20% of them more than 1 lymph node was affected. DM was found in 1.3% of patients. The mean age was 32.6 years and women were 80% of patients. Classic, follicular and tall cell variants occurred in 60%, 20% and 10%, respectively. Tumor's multifocality, two tumor foci and lymphocytic thyroiditis occurred in 10%, 30% and 30%, respectively. The tumor was 0.5 cm or larger in 80% of patients. Only the patient with DM had tumor extension into the capsule. **Conclusion:** Our data revealed that the most frequent features in patients with metastatic PTMC were age below 45 years old and tumor size larger than 0.5 cm. PTMC is an indolent disease, but does pose a risk for metastasis. More aggressive treatment or more frequent follow-up should be considered for patients with unfavorable features. Further research on thyroid cancer should be encouraged, especially in regions where data are not available.

THYROID CANCER CLINICAL

1112438 - LYMPH NODE METASTASIS AS THE INITIAL PRESENTATION OF OCCULT THYROID CANCER: A CASE REPORT

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Papillary thyroid carcinoma (PTC) is the most common type of thyroid malignancy, often presenting as a thyroid nodule, but in some cases, it may manifest initially as metastatic cervical lymphadenopathy, representing an occult primary tumor. We present the case of a 34-year-old woman with a history of hypothyroidism with positive antithyroglobulin antibodies and Addisons disease. During a routine endocrinology follow-up, a cervical mass was identified. Cervical ultrasonography revealed a suspicious lymph node at level VA, confirmed by computed tomography. Fine needle aspiration (FNA) of the lymph node suggested follicular thyroid disease, but due to diagnostic discrepancies, an excisional biopsy was performed, which revealed findings consistent with Papillary Thyroid Cancer. The patient underwent total thyroidectomy with lymph node dissection, followed by postoperative radioactive iodine therapy. This case highlights the importance of considering occult thyroid carcinoma in the differential diagnosis of isolated cervical lymphadenopathy, particularly in patients with underlying thyroid disease. Early recognition and comprehensive evaluation are essential for accurate diagnosis and timely management, improving patient outcomes.

THYROID CANCER CLINICAL

1112336 - LYMPHOCYTES IN THYROID FINE NEEDLE BIOPSY CORRELATE WITH THE TALL CELL SUBTYPE OF PAPILLARY THYROID CARCINOMA

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Introduction: Context: An intense lymphocytic infiltrate characterizes the histological specimens of tall cell carcinoma, the most frequent aggressive subtype of papillary thyroid carcinoma (TC-PTC). It is not known whether cytological specimens of fine-needle aspiration biopsy (FNAB) of TC-PTC display lymphocytic infiltration as well. **Objective:** Correlate the presence of lymphocytes in FNAB with the TC-PTC. Design: The finding of lymphocytes, described with a semi-quantitative assessment, in FNAB smears of thyroid nodules was related to the TC-PTC and the other histological subtypes of papillary thyroid carcinoma (PTC). Coexistent thyroid autoimmunity, i.e., serum thyroid autoantibodies was taken into account. Patients: Patients who underwent thyroidectomy because of high-risk indeterminate, suspicious of malignancy or malignant thyroid nodules (n. 583). **Results:** In patients without serum thyroid autoantibodies (n. 389), the finding of lymphocytes in FNAB specimens was more common in TC-PTC compared to the other subtypes (11/22 vs 44/231, $p < 0.001$). In contrast, in patients with serum thyroid autoantibodies (n.167) no difference was observed comparing TC-PTC to the other subtypes of PTC. At the blinded revision of FNAB smears, the number of lymphocytes/20 high-power field (HPF) was 107 ± 59 for specimens previously reported as with lymphocytes and 44 ± 38 for those classified as without lymphocytes, with the cut-off of 61 best discriminating nodules with lymphocytes in FNAB samples ($AUC = 0.89$, $p < 0.001$). Evaluating the PTC subtypes, the number of lymphocytes/20HPF was 82 ± 58 in TC-PTC and 56 ± 50 in the other subtypes, with the cut-off of 59 best discriminating TC-PTC from the other subtypes ($AUC = 0.67$, $p = 0.03$). **Conclusions:** In patients without serum thyroid autoantibodies, lymphocytes in FNAB specimens of high-risk indeterminate, suspicious of malignancy or malignant thyroid nodules correlate with TC-PTC.

THYROID CANCER CLINICAL

1112504 - MALIGNANT PLEURAL EFFUSION FROM THYROID CANCER: SINGLE-CENTER EXPERIENCE

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Introduction: Malignant pleural effusion from thyroid cancer is rare and often indicates poor prognosis. Detailed outcomes and prognostic factors remain underreported. **Objective:** This study aimed to evaluate clinical outcomes and identify factors influencing prognosis in patients with malignant pleural effusion from thyroid cancer. **Methods:** We retrospectively analyzed 36 patients diagnosed with pleural metastasis or malignant pleural effusion from thyroid cancer at a single center. After excluding 2 patients with bilateral pleural effusion caused by multi-organ failure and 4 patients with dry pleural metastasis, 30 patients were included in the final analysis. **Results:** The median age at initial thyroid cancer diagnosis was 60.3 years (interquartile range [IQR] 50.966.4), and 63% (19/30) of the patients were male. Most had papillary thyroid cancer, with one-third showing synchronous metastases. Pleural metastases were typically diagnosed during follow-up for lung metastases, with a median interval of 9.3 years from initial thyroid cancer diagnosis, except for 3 patients who had pleural involvement at diagnosis. Symptomatic pleural effusion requiring drainage was observed in 23 patients, whereas 7 patients exhibited asymptomatic effusion. Targeted therapy with sorafenib or lenvatinib was administered to 19 patients (63%). The median survival time following the development of pleural effusion was 13.4 months (IQR 7.221.4). Patients with asymptomatic pleural effusion had significantly better survival compared to those with symptomatic effusion (23.2 vs. 10.8 months, respectively, $p=0.03$). However, targeted therapy did not significantly improve overall survival ($p=0.31$). **Conclusion:** Malignant pleural effusion from thyroid cancer is associated with poor clinical outcomes, particularly in symptomatic cases. Despite the use of targeted therapies, their efficacy in improving survival remains limited for patients with symptomatic pleural effusion. These findings underscore the importance of earlier and more aggressive interventions, even for asymptomatic patients, as supported by recent guidelines.

THYROID CANCER CLINICAL

1112447 - MALIGNANT STRUMA OVARII (MSO) CLINICAL CHARACTERISTICS AND OUTCOMES: A RETROSPECTIVE TERTIARY CANCER CENTER EXPERIENCE

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Introduction: MSO is a rare malignancy arising from thyroid components of an ovarian teratoma. Literature is limited, with no established guidelines. Further characterization would allow more accurate prognostication and individualized care. **Methods:** Retrospective review of patients with MSO at a tertiary cancer center. Patients were sub-divided by presence of metastases at diagnosis. Primary objective was to characterize clinical presentation and outcomes. **Results:** Twenty-three patients were identified from 3/2001-3/2024 with median follow-up of 53months(range:12-291). Median age at diagnosis was 43years(range:25-66); 68% were premenopausal. Fifteen patients without metastases at diagnosis had: papillary thyroid cancer (PTC; $n=12$), follicular thyroid cancer (FTC; $n=1$) and poorly differentiated thyroid cancer (PDTC; $n=2$). Thyroidectomy (TT) was performed in 5/15 patients. 3/5 (2 PTC, 1PDTC) received radioiodine(RAI) with median cumulative activity of 32.2 mCi (range: 32.1-403). One patient with PDTC later developed metastases. There were no other cases of recurrence and no known deaths. Eight patients with metastases at diagnosis had: FTC ($n=3$), FVPTC ($n=4$) and PDTC ($n=1$). Metastases were located: fallopian tube ($n=1$), uterus ($n=1$) and abdomen/pelvis ($n=5$). 6 patients had NGS: PTEN ($n=1$), BRAFK601E ($n=2$), KRASG12V+ERBB2 ($n=1$), MET ($n=1$), NRASQ61R ($n=1$). All underwent TT and RAI. 6/8 patients posttreatment scan had uptake outside of the neck. 5/8 had multiple RAI due to persistence/recurrence with median total cumulative activity of 394mCi (range:348.6-729. 5). 2 patients had progressive disease despite RAI+/-surgical interventions. One patient with NRASQ61R FVPTC was started on trial with RAF+MEK inhibitor. One patient with KRASG12V+ERBB2 FTC was initiated on sorafenib and succumbed despite multiple TKIs and immunotherapy. Patients with MSO of unknown malignant potential and those with benign SO who subsequently developed metastases, will be reported separately. **Conclusion:** Patients without metastases at diagnosis and low risk thyroid cancer did well without TT or RAI; whereas patients with metastases tend to have persistent/recurrent disease. Limited molecular analysis showed RAS-like mutations. Molecular testing of MSO may help facilitate individualized therapeutic decision making.

THYROID CANCER CLINICAL

1112567 - MALIGNANT *STRUMA OVARII*: PAPILLARY THYROID CARCINOMA ARISING IN AN ADNEXAL MASS. A TWO YEAR FOLLOW UP OF A RARE CASE

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The *struma ovarii* represents 2%-3% of all ovarian teratomas, with 5% of them corresponding to malignant *struma ovarii* (MSO). Case: A 59-year-old postmenopausal woman, not on hormone replacement therapy, with a history of hypertension and dyslipidemia, presented in May 2022 with metrorrhagia. A transvaginal ultrasound (TVUS) revealed uterine myomas. Four months later, she presented with abdominal distension, without other symptoms. A repeat TVUS showed a 10 cm left adnexal mass. Tumor marker studies revealed elevated CA-125 (175 U/mL; normal range 0-35) and CA 19-9 (101 U/mL; normal range 0-39). In June 2022, she underwent a hysterectomy with bilateral salpingo-oophorectomy, and left internal and external iliac lymphadenectomy. Pathological examination revealed an 11*5 cm left adnexal tumor. Immunohistochemistry showed Ki67 (+): 25%, PS3, WT1, and Alpha-Inhibin negative; estrogen receptor (++); progesterone receptor (++); TTF-1 (++), and Thyroglobulin (+); consistent with *struma ovarii*, with a 20 mm intraovarian papillary thyroid carcinoma, without lymphovascular invasion. The patient presented to the endocrinology evaluation with no symptoms suggestive of thyrotoxicosis, signs of thyroid eye disease, pretibial myxedema, or goiter. A thyroid ultrasound showed findings suggestive of chronic thyroiditis and a 3 mm right colloid cyst. CA-125 and CA 19-9 levels have remained within normal limits. Anti-TPO antibodies were 9 IU/mL (normal range < 34) and TRAB 1.0 IU/mL (normal range < 1.75). She was evaluated at the Thyroid Cancer Committee, indicating to maintain follow-up. To date, after two years of initial surgery, she remains euthyroid, with no signs of local nor distant dissemination and thyroglobulin levels below the reference range with negative anti thyroglobulin antibodies. There have been attempts to stratify risk in MSO, in a similar fashion to the differentiated thyroid carcinoma. This case could be classified as a low risk of recurrence, allowing to maintain surveillance with thyroglobulin and no need of thyroidectomy nor radioactive iodine.

THYROID CANCER CLINICAL

1114007 - MANAGEMENT OF METASTATIC DIFFERENTIATED THYROID CANCER WITH LENVATINIB IN TWO INSTITUTIONS IN MEDELLÍN BETWEEN 2022 AND 2025

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Introduction: Patients with metastatic differentiated thyroid cancer (m-DTC) and radioiodine refractory differentiated cancer (RR-DTC) represent a population with a worse survival prognosis. Systemic therapy with tyrosine kinase inhibitors is a management option to reduce tumor volume, comorbidity, and progression-free survival. **Objective:** To describe our experience with lenvatinib for m-DTC. **Methods:** Retrospective cohort study of patients with m-DTC in clear progression and/or RR-DTC treated with lenvatinib in 2022 and 2025. **Results:** 14 patients with metastatic papillary thyroid cancer were included, 11 with neck metastases (78.6%), 10 lung metastases (71.4%), 3 bone metastases (21.4%), and 2 brain metastases (14.3%); 10 of them met the criteria for RR-DTC (71.4%). 50% were women, with an average age of 65 years (SD 11.2); 13 patients had been treated with total thyroidectomy and 13 with I-131 therapy, with a median of 315 mCi (IQR 200-550). The most frequent adverse effects of lenvatinib were hypertension (78.6%) and hand-foot-mouth syndrome (29%). One patient presented PRESS (7%). Four patients died after a median of 315 days (IQR 204-539). The median overall follow-up was 332 days (IQR 149-530). Among the four patients with follow-up images, the response by RECIST 1.1 showed three partial and one complete response for a median reduction of 82%. **Conclusion:** Management with lenvatinib in patients with progressive metastatic cancer resistant to iodine can reduce tumor burden, mortality and improve progression-free survival

THYROID CANCER CLINICAL

1112337 - METATHYRAF PROSPECTIVE STUDY RESULTS FOR RADIOFREQUENCY IN DIFFERENTIATED THYROID CANCER METASTATIC LYMPH NODE: SAFETY AND EFFICACY

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Introduction: Radiofrequency ablation (RFA) could be technically feasible and effective in the treatment of lymph node metastases of differentiated thyroid cancer. It could constitute a minimally invasive and feasible therapeutic alternative in ambulatory, allowing a reduction of the tumoral volume sufficient to limit the symptoms even to induce a tumor remission, a normalization of the tumoral markers and a better quality of life. **Objective:** The aim of METATHYRAF study was to evaluate the anti-tumor echographic efficacy radiofrequency on iodo-resistant lymph node (LN) metastasis of thyroid cancer and clinical tolerance. **Methods:** Inclusion criteria: patients who have previously undergone thyroid surgery and radioiodine treatment, with cytologically confirmed persistent cervical lymph node (LN) metastasis of differentiated thyroid cancer (DTC). Radiofrequency ablation (RFA) was performed under ultrasound guidance following local anaesthesia, conducted by a trained operator who identified the target lesion during a prior whole lymph-nodes staging. Clinical, biological, and ultrasound follow-up evaluations were carried out over a period of two years. **Results:** 14 patients were treated by RFA: 10 females and 4 males. The mean age at the time of RF was 51 yo (40-75 yo). After local anaesthesia, duration of the radiofrequency procedure was less than two minutes. The follow up after RF were > 2 years, > 1 year and > 6 months for 10, 2 and 2 patients respectively. All the patients showed tumor response at 3 and 6 months. None patient need supplementary treatment during follow up. 1 patient experimented grade 2 immediate complication (pain) due to spinal accessory nerve proximity. Other patients had good immediate and long term tolerance. **Conclusion:** The study confirms the efficacy and good tolerance of radiofrequency ablation for persistent lymph node metastases. Local anaesthesia is effective even for patients with contraindications to general anaesthesia. Additional data collection is ongoing

THYROID CANCER CLINICAL

1112473 - MOLECULAR ALTERATIONS IN PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA WHO UNDERWENT CERVICAL EXTERNAL BEAM RADIOTHERAPY

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Introduction: A small percentage of patients with differentiated thyroid carcinoma (DTC) present with advanced locoregional (LR) disease, but its presence is associated with increased morbidity and mortality. **Objective:** Evaluate which molecular alterations are found in patients with DTC with LR disease requiring cervical radiotherapy (EBRT). **Methods:** Retrospective analysis of 80 patients with DTC who underwent cervical EBRT between 1995 - 2022, and molecular analysis of the primary tumor material in 21 patients. Molecular analysis was performed using next-generation sequencing and we used a custom hybrid capture approach for the enrichment of 24 genes for DNA sequencing and 9 genes for RNA sequencing. **Results:** 80 adults, a median age of 61 years, 21.2% T3 tumors, 43.7% T4 tumors, and 47.5% having distant metastases and 77.5% of patients died during follow-up (cancer-related death). Among those who underwent molecular analysis, 12 (57.2%) had classic/follicular papillary thyroid carcinoma (PTC), 6 (28.5%) had aggressive variants of papillary carcinoma, 1 (4.8%) had follicular carcinoma, and 2 (9.5%) had oncocyctic carcinoma. BRAF was the most common genetic variant, in 12 patients (57%, n=21). Of these, 11 were classic and follicular PTC (91%, n=12). TERT occurred in 4 patients (19%, n=21), 2 with classic/follicular papillary histology (16%, n=12) and 2 patients with aggressive PTC variants (33%, n=6). Other variants found (n=33): Tp53 6%, FAT1 6%, RET 6%, KRAS 3%, ROS1 3%, DIRCER1 3%, NTRK1 3%, NTRK2 3%, NF1 3%, ERBB2 3%, NRAS 3%, ALK 3%, and CCDC6/RET fusion 3 %. No association was found between the presence of pathogenic variants and the progression of cervical disease after cervical EBRT. **Conclusion:** We observed a high prevalence of pathogenic variants in the BRAF gene, particularly in patients with PTC and further studies are needed to clarify the best responders to cervical EBRT regarding molecular profile

THYROID CANCER CLINICAL

1114140 - NEOADJUVANT TREATMENT FOR LOCALLY ADVANCED WELL-DIFFERENTIATED THYROID CANCER

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Case Presentation: We report two patients with papillary thyroid carcinoma submitted to neoadjuvant therapy with Lenvatinib due to local advanced extension of the tumor. The first patient is a 55-years old male who presented persistent hoarseness. He received a diagnosis of thyroid nodule five years ago with benign cytology at fine needle aspiration. Laryngeal examination disclosed vocal fold paralysis without mucosal lesion. A new FNA revealed papillary carcinoma. The patient was staged using neck and chest CT and PET-CT scans that showed multiple metastatic lymph nodes in the neck and mediastinum and a primary tumor with extensive laryngeal invasion. After an institutional multidisciplinary tumor board discussion, neoadjuvant treatment with Lenvatinib was indicated. The neoadjuvant treatment lasted for 12 months with significant radiological (both tumor reduction and SUV reduction) and clinical (restoration of vocal fold mobility) response. The patient was then treated with total thyroidectomy and adjuvant iodine therapy, with larynx preservation. The second patient was a female patient with an occasional finding thyroid nodule. Although the ultrasonography did not show extrathyroidal extension, a direct tracheal and esophageal invasion were observed during the surgical procedure. The surgery was aborted, and the patient received six months of neoadjuvant Lenvatinib after a multidisciplinary tumor board discussion. Radiological maximum diameter reduction was 60% in the magnetic resonance images. The patient was treated by total thyroidectomy with adjuvant radioiodine without the need of tracheal and esophageal resection. **Discussion:** Although papillary thyroid cancer presents excellent cure rates, its removal may lead to significant morbidity. In our series, extensive resection including the larynx, tracheal rings or the esophagus would be necessary. The neoadjuvant treatment allowed for a significant tumor reduction and improvement of functional outcomes. **Final Comments:** The use of neoadjuvant Lenvatinib therapy for selected patients with advanced papillary thyroid cancer may improve functional and quality of life outcomes.

THYROID CANCER CLINICAL

1112338 - NON-CLINICAL FACTORS IN SURGICAL DECISION MAKING FOR LOW-RISK THYROID CANCER: WHAT'S CHANGED?

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Introduction: The 2015 American Thyroid Association (ATA) Guidelines recommended thyroid lobectomy as an appropriate alternative to total thyroidectomy for low-risk thyroid cancer. Yet in response, surgical decision-making between these procedures remained variable over the last decade, suggesting unexplored non-clinical factors may impact these decisions. **Objective:** To identify non-clinical, surgeon- and practice-level factors affecting surgical decision-making for low-risk thyroid cancers. **Methods:** In this ethnographic study, semi-structured interviews were conducted with 17 surgeons (general, endocrine, and otolaryngology) recruited from community and academic centers. Additionally, field-observations were performed at five surgical practices statewide with varying rates of total thyroidectomy use. Interviews were audio-recorded, transcribed verbatim, and analyzed using qualitative content analysis. **Results:** Participating surgeons were a mean of 46.5 years-old, 70.6% male, and 76.5% white. Several non-clinical, surgeon- and practice-level factors influenced surgical decision-making including practice culture, surgeon preferences, and practice resources. Surgeons described a spectrum of practice culture ranging from a collective preference towards lobectomy to a majority doing total thyroidectomies. Surgeons discussed differing personal preferences and almost exclusively performed total thyroidectomies or defaulted to lobectomy. Although referring physicians generally deferred to the surgeons decision on extent of thyroid surgery, some surgeons considered the referring physicians preference due to their long-term role in patient care. Practice resources, such as availability of ultrasonography, fine needle aspiration, and accuracy of cytology influenced one surgeon to perform total thyroidectomies because pathology was not stellar. Previously explored non-clinical, patient-level factors were redemonstrated to influence surgical decision-making such as patient preference, anxiety, access to healthcare, and insurance status. **Conclusion:** Nearly a decade after the ATA guidelines, significant variability in surgical decision-making for low-risk thyroid cancer persists. This study identified novel non-clinical, surgeon- and practice-level factors that may be driving these decisions. Interventions targeted at these factors may be necessary to decrease overtreatment of low-risk thyroid cancer.

THYROID CANCER CLINICAL

1112335 - NON-INVASIVE FOLLICULAR THYROID NEOPLASIA WITH PAPILLARY-LIKE NUCLEAR CHARACTERISTICS (NIFTP): CLINICO-PATHOLOGICAL ANALYSIS IN A CHILEAN CENTER

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Introduction: Non-invasive follicular thyroid neoplasia with papillary-like nuclear characteristics (NIFTP) is characterized by an indolent behavior and was defined to avoid overtreatment. **Objective:** To report the clinicopathological characteristics and outcomes of patients with NIFTP treated at a Chilean center between 2016 and 2023. Design: Observational retrospective study. **Methods:** Of 1103 patients with thyroid neoplasia, 104 (9.42%) had NIFTP. Clinicopathological variables and follow-up results were recorded. **Results:** Of 104 patients, 85 (81.7%) were female, 44±14.2 years and a median tumor size of 1.7 cm (range 0.1-7.1). Eighty-six (82.7%) had preoperative staging ultrasound: 1 (1.2%), 39 (45.3%), 38 (44.2%), and 8 (9.3%) were ACR-TIRADS 2, 3, 4, and 5, respectively. Sixteen (15%) were incidental, which were smaller than non-incidental NIFTP (median 0.4 cm (0.1-2.2) vs. 1.9 cm (0.6-7.1), p<0.001). Of the 86 FNAB available, 2 (2.3%), 10 (11.6%), 20 (23.3%), 24 (27.9%), and 30 (34.9%) were Bethesda I, II, III, IV, and V, respectively. Forty-three patients (41.3%) were treated with lobectomy, 58 (55.8%) with total thyroidectomy (TT), and only 3 (2.9%) with TT and lymph node dissection. In Bethesda II patients, surgery was indicated for nodular growth, showing a larger tumor size (3.0±1.4 vs. 1.8±1.02 cm, p=0.015). There were no differences between TP and TT regarding sex, ACR-TIRADS or tumor size. Fifty-two patients (54%) were followed for ≥1 year: thirty-four (65%) had excellent, 15 (28.8%) indeterminate, 3 (5.7%) incomplete biochemical, and no incomplete structural response. TP and TT had similar types of response. There were no deaths, and no new interventions requirement. **Conclusions:** In this series, NIFTP showed indolent behavior and excellent prognosis. Ultrasound findings indicated that 90% presented as ACR-TIRADS 3 or 4, with less than 10% as ACR-TIRADS 5. Regarding FNAB, nearly half were indeterminate, and one-third were Bethesda V. No significant differences in clinical outcomes were found between TP and total thyroidectomy.

THYROID CANCER CLINICAL

1112546 - OCCULT METASTATIC PAPILLARY THYROID CARCINOMA IN A YOUNG WOMAN: A RARE CASE REPORT

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Case Presentation: We present the case of a 22-year-old woman with occult papillary thyroid carcinoma, who initially consulted for a painless cervical mass located in levels IV to VI on the left side. The diagnosis was a central metastatic lymphadenopathy, positive for papillary thyroid cancer. However, the preoperative ultrasound did not reveal any nodules or suspicious features of carcinoma. After performing a total thyroidectomy with central cervical lymph node dissection, the pathological examination was negative, showing no evidence of neoplastic cells. **Discussion:** We describe a rare case of occult papillary thyroid carcinoma, which presented exclusively as metastasis in a lymph node in the central compartment. Occult papillary thyroid carcinoma (PTC) is characterized by the presence of metastasis without the identification of a primary thyroid tumor on preoperative imaging. Boucek et al. classified occult PTC into four groups, while Liu et al. proposed a fifth group, which corresponds to this case. In this group, the thyroid gland shows benign disease on pathological examination, while locoregional lymph nodes or distant organs show confirmed metastases of thyroid carcinoma. This subtype of primary carcinoma is uncommon in clinical practice, and very few cases meet the established diagnostic criteria. **Final Comment:** In some cases, the primary focus of thyroid carcinoma may be small and go unnoticed during pathological examination, making its diagnosis challenging. Therefore, it is crucial to reduce the rate of false negatives in the diagnosis of occult papillary thyroid carcinoma by improving diagnostic and pathological methods. Total thyroidectomy with cervical dissection, followed by TSH suppression and radioactive iodine therapy, remains the most appropriate diagnostic and therapeutic approach in these cases.

THYROID CANCER CLINICAL

1113635 - OVERCOMING RESISTANCE IN ATC: A CASE REPORT ON COMBINING IMMUNOTHERAPY AND TARGETED THERAPY TO ACHIEVE DISEASE REMISSION

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Case Presentation: Anaplastic thyroid carcinoma (ATC) is an aggressive malignancy with a median survival of less than six months. BRAF mutations provide a therapeutic target and dabrafenib and trametinib demonstrate efficacy in disease control. However, resistance often develops and new therapeutic approaches are needed. Recent studies suggest that adding immune checkpoint inhibitors, such as pembrolizumab, may enhance clinical outcomes. Case presentation A 44-year-old male presented with a rapidly enlarging cervical mass, dysphagia, and hoarseness. Fine-needle aspiration cytology and subsequent histopathological examination confirmed the diagnosis of ATC. Imaging showed extensive local disease with lymph node involvement, but no distant metastases. The patient was treated with total thyroidectomy, radiotherapy, and cytotoxic chemotherapy. Six months later pulmonary metastases occurred. Genetic analysis of the primary tumor revealed a somatic BRAFV600E mutation and the patient was started on dabrafenib (150 mg twice daily) and trametinib (2 mg once daily), achieving complete response for three years when a new pulmonary lesion was detected. The patient underwent surgery for metastasis resection; genetic and immunohistochemical analyses showed BRAFV600E mutation and 90% PD-L1 expression. After 3 months, a new pulmonary lesion was detected, prompting the administration of pembrolizumab (200 mg every three weeks). Three months later, PET-CT showed no active disease, and the response has persisted until now (16 months). The patient tolerated the therapy well, experiencing manageable fatigue and intermittent pyrexia while maintaining a ECOG performance status of 0 throughout the treatment. **Discussion:** This case highlights the synergistic potential of combining targeted therapy with immunotherapy for BRAF-mutant ATC. BRAF/MEK inhibitors suppress tumor growth, but the immunosuppressive tumor microenvironment may reduce their efficacy. Pembrolizumab, an anti-PD-1 antibody, enhances the immune response, likely contributing to the complete response observed. **Final Comments:** This report highlights the potential of combined targeted and immunotherapy for ATC, providing insights into overcoming resistance and improving outcomes in a real-life scenario.

THYROID CANCER CLINICAL

1114309 - PAPILLARY THYROID CANCER IN A HYPERFUNCTIONING AUTONOMOUS NODULE

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Case Presentation: A 63-year-old woman with hyperthyroidism, prediabetes, and osteoporosis was referred to our center. Examination revealed a Grade IB goiter with irregular consistency, predominantly nodular on the right. Laboratory findings showed suppressed TSH (<0.005 μ IU/mL), elevated Free T4 (25.55 pmol/L) and Free T3 (7.69 pmol/L), with negative thyroid antibodies. Ultrasound detected a solid, hypoechoic, subcapsular nodule with microcalcifications and poorly defined borders (ACR-TIRADS 5). Color Doppler showed mixed vascularization, and SWE indicated high stiffness (140.2 kPa). Tc-99m scintigraphy revealed a hot nodule in the right thyroid lobe (RTL), partially suppressing the surrounding parenchyma. FNAC confirmed papillary thyroid carcinoma (PTC, Bethesda VI). The patient underwent total thyroidectomy, revealing a 2x2 cm firm nodule in the upper RTL. Histopathology confirmed PTC, subtype: classic (40%) and oncocytic (60%), measuring 13 mm without capsule or extrathyroidal extension, the remaining thyroid showed macrofollicular hyperplasia. The patient had a favorable outcome, did not receive radioactive iodine, and remains on thyroid hormone replacement. Genetic testing for TSH receptor mutations and PTC-related oncogenes is unavailable in our setting. **Discussion:** Hyperthyroidism, autonomous nodule, and PTC coexistence is rare. There are discrepancies in thyroid nodule management guidelines. While ATA and ETA advise against FNAC for suppressed TSH or autonomous nodules on scintigraphy, the Japanese Thyroid Association recommends FNAC based on ultrasound findings. This may be due to higher malignancy rates in hyperfunctioning nodules in Japan (5-12%) compared to Western populations, likely influenced by iodine intake differences. Some studies suggest BRAF V600E and TSHR D727E mutations may contribute to hyperfunctioning thyroid carcinoma as part of a multi-hit process. **Final Comments:** Although the incidence of hyperfunctioning thyroid carcinoma is low in Western populations; FNAC may play a crucial role in diagnosing clinical thyrotoxicosis. The classic malignancy described in such cases is follicular thyroid carcinoma; but reports also include PTC and Hürthle cell carcinoma.

THYROID CANCER CLINICAL

1114073 - PAPILLARY THYROID CARCINOMA COEXISTING WITH PRIMARY HYPERPARATHYROIDISM: A CASE REPORT

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Case Presentation: A 54-year-old female patient with a 3-year history of thyroid nodular disease was currently under follow-up. At the last follow-up, glandular asymmetry and changes in the morphology of one of the thyroid lesions were observed, leading to a request for fine-needle aspiration. The report confirmed a lesion suspicious for malignancy (Thyroid Nodule Suspected of Papillary Carcinoma, Bethesda V). The patient was evaluated for thyroidectomy. The requested tests revealed an elevated intact PTH level of 312 pmol/L. A Tc-sestamibi scan revealed an area of increased uptake at the level of the left thyroid lobe, suggestive of a left parathyroid adenoma.

Discussion: The incidence of thyroid cancer appears to increase by 4% each year; it is currently the 8th most common cancer in women. Most are diagnosed between the ages of 30 and 50. Only 1% to 7% of patients have distant metastases at the time of diagnosis, and 15% experience disease recurrence. Primary hyperparathyroidism is a common cause of endocrine disease; its clinical presentation is characterized by minimal symptoms or signs of hypercalcemia or parathyroid hormone excess. It is a medically treatable disease, but cure can only be achieved through surgery, due to the repercussions of the disease, with a return of serum calcium levels to normal.

Final Comments: The coexistence of thyroid carcinoma (Ca) with previously undiagnosed primary hyperparathyroidism has been reported in 2.3% to 4.3% of patients undergoing surgery for hyperparathyroidism. The etiological association between both entities is unknown, but it generally occurs in patients with a history of head and neck radiation.

THYROID CANCER CLINICAL

1112370 - PAPILLARY THYROID CARCINOMA IN STRUMA OVARII: CASE REPORT

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Introduction: *Struma ovarii* (SO) is a germ cell neoplasm in which there is a predominant presence of thyroid tissue. It is mostly a benign tumor, but about 5% of cases can undergo malignant transformation, mainly to papillary thyroid carcinoma. In this study, we present a rare case of papillary thyroid carcinoma found in a *Struma ovarii*, in a young female patient, already with the presence of metastasis in the peritoneum, treated with left salpingoophorectomy with excision of peritoneal lesions, in addition to thyroidectomy and iodine therapy. Therefore, although rare, the differential diagnosis of *Struma ovarii* in ovarian tumors and its possible malignancy should be considered.

THYROID CANCER CLINICAL

1112625 - PAPILLARY THYROID CARCINOMA WITH CYSTIC PATTERN: CASE REPORT OF LOCAL RECURRENCE, PULMONARY METASTASES, AND METABOLIC PROGRESSION

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Case Presentation: A 76-year-old male underwent partial thyroidectomy in 2009 due to a large nodule in the right thyroid lobe (10 cm), with cricoid muscle invasion. Pathological analysis revealed nodular adenomatous goiter with no signs of malignancy. After more than 10 years without follow-up, the patient noted the appearance of a supraclavicular nodule, which further examinations showed to be associated with tracheal infiltration and bilateral pulmonary metastases. In 2023, biopsy confirmed papillary carcinoma with a cystic pattern. Due to refusal of surgery, the patient underwent radioiodine therapy (30 mCi), but the disease progressed, as evidenced by FDG-PET, showing high metabolic uptake in both the cervical lesion and the lungs.

Discussion: Papillary carcinoma is the most common subtype of thyroid cancer, typically associated with a good prognosis. However, more aggressive variants, such as the cystic pattern, are rare and pose a higher risk of local invasion and metastasis. The lack of follow-up after the initial thyroidectomy delayed the early diagnosis of recurrence, worsening disease progression. FDG-PET was critical for evaluating disease progression and guiding therapeutic planning, especially given the patients refusal of surgery. The standard management of papillary carcinoma includes total thyroidectomy and radioiodine therapy, but refractory or advanced cases may require targeted therapies. These approaches, although effective, require careful evaluation due to potential side effects and costs. **Final Comments:** This case underscores the importance of regular follow-up in patients diagnosed with papillary carcinoma, particularly in high-risk situations. It also highlights the need for individualized strategies to manage aggressive presentations or patients who decline conventional treatments. FDG-PET proved essential in disease management, aiding in prognosis assessment and therapeutic decision-making, contributing to more assertive approaches in complex cases.

THYROID CANCER CLINICAL

1114148 - PAPILLARY THYROID CARCINOMA WITH UNCOMMON THYMIC METASTASIS: A CASE REPORT

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Case Presentation: A 65-year-old female patient was initially diagnosed with classical variant Papillary Thyroid Carcinoma (PTC), measuring 3.5 × 2.5 cm, based on the histopathological analysis of a right hemithyroidectomy performed in 2011, followed by total thyroidectomy. Initially staged as T2N0M0 and classified as low risk, she received radioiodine therapy (RAI) at a dose of 100 mCi in 2012, achieving an excellent response. In 2014, cervical metastasis was detected, leading to bilateral neck dissection and a second RAI treatment (150 mCi). After years of follow-up with satisfactory response, in 2022, a progressive increase in thyroglobulin (Tg) levels was observed, ranging from 0.95 to 35.05 ng/mL, without structural evidence of cervical recurrence. A chest CT scan revealed a solid lesion in the left anterosuperior mediastinum. The patient underwent thymectomy, and Histopathological analysis of a lesion measuring 2.3 × 1.2 cm confirmed thymic metastasis, with immunohistochemical positivity for CK7, TTF-1, Thyroglobulin, Galectin-3, and PAX8. Following surgery, Tg levels significantly decreased (0.95 ng/mL), and the patient experienced clinical improvement in chest pain. **Discussion:** We present a case of thymic metastasis from PTC diagnosed after a long disease course. Metastatic spread to the thymus is rare and may be underdiagnosed. Late detection can occur due to the absence of specific symptoms and the diagnostic challenges of conventional imaging studies. A multidisciplinary approach involving endocrinology, thoracic surgery, nuclear medicine, and oncology teams was essential for patient management. The post-resection drop in Tg (0.35 ng/mL) supports the hypothesis that the thymic lesion was the primary source of Tg production. **Final Comments:** This case highlights the importance of long-term follow-up in PTC patients, even after an initially favorable response to treatment. Rising Tg levels should prompt an extensive investigation to identify potential metastatic sites.

THYROID CANCER CLINICAL

1112194 - PAPILLARY THYROID MICROCARCINOMA: CLINICALLY RELEVANT PROGNOSTIC PARAMETERS FOR OUTCOME

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Introduction: A significant increase in the incidence of papillary thyroid microcarcinoma (mPTC) has been reported. Due to its indolent nature, active surveillance has been recommended. **Objective:** To evaluate the clinical characteristics and follow up with patients with mPTC treated at a University Hospital for over 42 years. **Methods:** 220 with mPTC were selected between 1978 and 2020. The V600EBRAF mutation analysis in cytological samples was evaluated in 80 patients. **Results:** 220 patients were selected (Female = 85.4%; Male = 14.6%) with a median age of 48 (15-81). At presentation, 41.8%-N=92 had an initial diagnosis of multinodular goiter, 43.2%-N=95 of uninodular goiter, and 2.3%-N=5 came due to cervical adenomegaly. 36 were V600EBRAF positive and 44 V600EBRAF negative. 87.3%-N=192 were submitted to total thyroidectomy, 11.4%-N=25 to total thyroidectomy with neck dissection, and three patients to hemithyroidectomy. 33.6%-N=74 had multifocal disease; subtypes identified were 49.1% classical, 38.6% follicular, 2.7% oncocytic, 1.8% sclerosing, 0.5% trabecular, and 7.2% mixed; 3.2%-N=7 with vascular invasion; 15.5%-N=34 with lymph node metastasis at biopsy. 51.4% were treated with 131I. The median follow-up was 8.9 years (1-41.4 years). Lymph node metastasis was observed in 7/36 V600EBRAF positive tumors, 7/44 V600EBRAF negative tumors, and 23/140 without BRAF analysis. The presence of nodal metastasis had a relevant impact on prognosis (OR=5.2, 95%IC 1.1-24.9). Recurrence was observed in 10 patients [lung (N=2), cervical nodal (N=8) and thyroid bed (N=1)]. 22 patients died, all from unrelated causes. **Conclusions:** In most cases, mPTC is a frequent finding in goiter surgery and has an excellent prognosis. In our series, only 10 recurred, 4 presenting nodal metastasis at initial diagnosis. Recurrence occurred despite total thyroidectomy and radioiodine therapy. Active surveillance is a good option for managing mPTC. However, careful case selection is essential. Molecular studies may help in this selection. In this series, isolated V600EBRAF analysis was not associated with a worse prognosis.

THYROID CANCER CLINICAL

1112198 - PHARMACOSAFETY TECHNOLOGIES IN RADIOIODINE THERAPY

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Introduction: During radioiodine therapy (RAIT) of differentiated thyroid cancer (DTC), the development of radiation-induced sialadenitis and obliteration of nasolacrimal ducts occur often. Less frequently, there are changes in liver function, reproductive system and hematopoiesis. **Objective:** Development of technologies for risk assessment, monitoring of adverse reactions and prevention methodology. **Methods:** The study enrolled 200 patients with DTC. The preparation of 100 DTC patients included the withdrawal of thyroid hormones for 4 weeks, and recombinant human thyroid-stimulating hormone was administered in other 100 cases. Scintigraphic studies were performed with GE Discovery NM/CT 670, GE Discovery NM 630, Xeleris 4 DR Workstation. Fifteen patients underwent dosimetry of a blood sample. In order to assess the ovarian reserve, AMH was measured before the RAIT, 3 and 6 months after it in 39 cases. **Results:** A method was developed to assess the risk of SALDO based on the patient's age, the presence of menopause and current lacrimation, total activities, the fact of administration of recombinant human thyroid-stimulating hormone, accumulation index I-131 in the lacrimal duct. The limits of low, medium, high intensity accumulation by salivary glands of less than 0.041%, 0.041%-0.070%, 0.71% and higher were established. The frequency of fixation of I-131 in the liver was estimated at 26% cases of DTC. A method for calculating the absorbed dose in the salivary glands has been developed. The limits of low, medium, high intensity accumulation by salivary glands of less than 0.18%, 0.18%-0.30%, 0.30% and higher were established. The absorbed dose in 1 mL of blood is $(7.4 \pm 2.8) \cdot 10^{-5}$ Gy with the administration of 1 MBq. AMH was significantly lower after the treatment compared to the baseline ($P < 0.001$). **Conclusion:** The presented technologies and results will allow us to develop a set of measures to prevent adverse effects and develop a system for monitoring them.

THYROID CANCER CLINICAL

1112459 - PREDICTORS OF LENVATINIB EFFICACY AND SAFETY IN SOUTH ASIAN PATIENTS WITH RADIOIODINE-REFRACTORY THYROID CANCER

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Introduction: Advanced well-differentiated thyroid cancer (DTC) is a significant challenge in south Asia. While radioiodine therapy is the mainstay of treatment, resistance to this therapy frequently develops. Lenvatinib is a Tyrosine Kinase inhibitor and has shown to be effective in iodine-refractory thyroid cancer. However, identifying patients who will benefit from Lenvatinib and understanding its safety in the south Asian context remain unclear. **Objective:** To determine factors predicting treatment response and evaluate Lenvatinib's safety to optimize patient care. **Methods:** This study included 34 patients with advanced thyroid cancer resistant to radioiodine therapy, treated with Lenvatinib at a North-Indian tertiary care hospital from February 2021 to July 2023. Patients received Lenvatinib at gradually increasing doses up to 24 mg daily. Comprehensive baseline assessments were conducted, encompassing clinical, laboratory evaluations. Treatment response, side effects, and supportive care were recorded throughout the study period. Progression-free survival was analyzed using standard statistical methods, and correlations between side effects and patient characteristics were explored. **Results:** Patients achieved a median progression-free survival (PFS) of 10.64 months (95% CI: 9.68-11.59). Factors associated with longer PFS included female sex, well-differentiated tumor type, specific tumor subtypes (PCT and FCT), lung-only metastases, better baseline health status (lower ECOG score), and achieving a significant tumor response. Women experienced a longer PFS compared to men (11.04 vs. 9.81 months, $p = 0.04$), and well-differentiated tumors demonstrated a longer PFS than poorly differentiated ones (11.17 vs. 6.75 months, $p = 0.007$). Higher Lenvatinib doses correlated with increased incidence of mouth sores (stomatitis) and diarrhea, while other side effects were less consistent. **Conclusion:** This study identified that female sex, tumor histology, and better baseline health status predict a favorable treatment response to Lenvatinib in patients with advanced thyroid cancer. Larger studies with longer follow-up periods are needed to further validate these results and refine treatment strategies.

THYROID CANCER CLINICAL

1112622 - PREDICTORS OF OUTCOMES IN PATIENTS UNDERGOING CRICOTRACHEAL RESECTION FOR THYROID CARCINOMA: A RETROSPECTIVE ANALYSIS

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Introduction: Patients with thyroid carcinoma with laryngotracheal involvement tend to have reduced local control and decreased survival when compared to tumors limited to the thyroid gland. Varying methods of the surgical management of laryngotracheal invasion have been described, ranging in extent from tangential shave resection, window resection, cricotracheal resection to total laryngectomy and/or adjuvant radiation therapy. This is an analysis of outcomes of patients treated with cricotracheal resection. **Objective:** This study aimed to assess the factors predictive of outcomes in patients undergoing cricotracheal resection for thyroid carcinoma at our institution. **Methods:** A retrospective chart review of patients who underwent cricotracheal resection for thyroid carcinoma at a single institution from 2009 to 2024. Data was collected including patient demographics, operative details, tumor histology, tumor size, tumor mutations, margin status, metastatic disease, locoregional recurrence and adjuvant treatment strategies. Disease-specific survival and locoregional recurrence was analyzed using the Kaplan-Meier method. **Results:** 29 patients were included for analysis. Mean age was 64 years and the male to female ratio was 1:1.42. The majority 21/29 (72%) had papillary thyroid carcinoma. 3/29 (10%) were diagnosed with anaplastic thyroid carcinoma on final pathology. The 5-year overall survival was 95.8%. The 1- and 5-year recurrence free survival was 95.8% and 79.1%, respectively. In the 16 patients with genetic testing, 16/29 (55%) and 10/16 (63%) BRAF p. V600 or TERT promoter region mutations, respectively. There was one mortality from post-surgical complications. **Conclusion:** Cricotracheal resection is a safe and effective surgical treatment strategy for thyroid carcinoma with laryngotracheal involvement. Patients with anaplastic thyroid carcinoma or distant metastatic disease at the time of surgery had worse outcomes in regards to locoregional recurrence and mortality.

THYROID CANCER CLINICAL

1112320 - PREOPERATIVE DIAGNOSIS OF CERVICAL LYMPH NODE METASTASIS IN PATIENTS WITH THYROID CANCER: PROPOSAL OF NEW COMBINED INTERPRETATION OF US AND CT BASED ON INTEGRATIVE ANALYSIS OF THE IMAGING FEATURES

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Introduction: For the diagnosis of lymph node (LN) metastasis in thyroid cancer, current consensus consider any suspicious feature from either US or CT as indicative of malignancy. However, the optimal method for combining US and CT remains underexplored. We analyzed the malignancy risks of LNs according to the concordance of US/CT imaging features, and proposed a new integrative algorithm to improve the diagnosis of LN metastasis. **Methods:** 277 cytopathologically proven cervical LNs (53.1%, malignant) of 228 thyroid cancer patients who underwent US-guided biopsy and preoperative US and CT were retrospectively analyzed. Malignancy risks of LNs were calculated according to the concordance of US and CT imaging features, by matching cortical hyperechogenicity or abnormal vascularity on US (US-echo-vascularity) with strong or heterogeneous enhancement on CT (CT-enhancement), cystic changes on US (US-cystic) with those on CT (CT-cystic), and echogenic foci (EF) on US (US-EF) with calcifications on CT (CT-calcification). Diagnostic accuracies were compared between the US, CT, the current US/CT interpretation algorithm, and the new interpretation algorithm based on the calculated malignancy risks. **Results:** Malignancy risks of positively concordant cases were higher than those of negatively concordant cases in all imaging features (US-echo-vascularity/CT-enhancement (93.5% (101/108) vs. 8.1% (9/111), $p=0.0001$), US-cystic/CT-cystic (94.4% (34/36) vs. 40.7% (87/214), $p=0.0001$), US-EF/CT-calcification (84.6% (22/26) vs. 33.5% (58/173), $p=0.0001$)). Those were not significantly different from those of the discordant cases of US-cystic/CT-cystic (96.3% (26/27), $p=1.000$), US-EF/CT-calcification (85.9% (67/78), $p=1.000$) but larger than those of the discordant cases of US-echo-vascularity/CT-enhancement (63.8% (37/58), $p=0.0001$). In the discordant cases of US-echo-vascularity/CT-enhancement, CT presented higher diagnostic odds ratio (3.896[95% CI, 0.078-0.842] vs. 0.257[95% CI, 1.188-12.775], $p=0.002$) and sensitivity (81.1% vs. 18.9%, $p<0.001$) than US. Accordingly, the new algorithm adopted CT results and modified decisions in 7 cases, correctly diagnosing 6 benign cases but missing only 1 malignant case. **Conclusion:** For discordant cases in US-echo-vascularity and CT-enhancement, prioritizing CT result can enhance diagnostic accuracy for LN metastasis.

THYROID CANCER CLINICAL

1112477 - PRIMARY THYROID LYMPHOMA: A CASE REPORT

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Case Presentation: A 61-year-old female presented with cervicgia for 2 weeks radiating to the left auricular pavilion, anterior cervical swelling over the past 3 months, dysphagia, and dyspnea when lying down. Medical history includes hypothyroidism, pre-diabetes and anxiety disorder. Physical exam revealed a diffuse, asymmetrical goiter on the left lobe with cervical lymphadenopathy. Thyroid ultrasound showed a volume of 94.3 cm³ with abnormal cervical lymph nodes up to 2.1 cm. Cytology of TI-RADS 4 nodules was Bethesda II (with increased lymphocytic count), yet due to the goiter's rapid progression, partial thyroidectomy and tracheostomy were performed. Histopathology confirmed diffuse large B-cell non-Hodgkin lymphoma (CD10+/CD20+/BCL2+/Ki67:60%) with angiolymphatic invasion. Ann Arbor staging II E. Following initiation of Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone (R-CHOP) chemotherapy, the patient retained lymphadenopathy with a residual 6.1 cm mass, under clinical control despite side effects (asthenia and nausea). **Discussion:** Primary thyroid lymphoma, a rare entity (0.6 to 5% of thyroid neoplasms), predominantly affects women between ages 50-70. Five-year survival is 75%-85% for disease confined to the gland, with poorer prognosis seen in patients over 60, elevated LDH, and advanced staging. Hashimotos thyroiditis is a known risk factor due to chronic lymphocytic inflammation. Typical symptoms include a rapidly growing cervical mass, tracheoesophageal compression, and dysphagia. Fine-needle aspiration (FNA), the initial examination for nodules, has limitations, with high false-negative rates, so core needle or excisional biopsy and PET/CT with 18-FDG are recommended for staging high-grade lymphomas. **Final Comments:** Primary thyroid non-Hodgkin lymphoma should be considered in rapidly growing cervical masses. FNA is useful but has pitfalls, requiring additional surgical biopsy and immunohistochemistry for definitive diagnosis.

THYROID CANCER CLINICAL

1112540 - PROGNOSTIC FACTORS IN NON-METASTATIC DIFFERENTIATED THYROID CANCERS

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Introduction: Although differentiated thyroid cancer (DTC) is associated with a good prognosis, a certain group of patients may experience bad outcomes. The study of the prognostic factors helps to select patients with poor prognostic factors in order to benefit from an optimized therapeutic protocol. **Objective:** To study the prognostic factors of non-metastatic DTC. **Methods:** Our study included patients treated for a non-metastatic DTC between 2010 and 2018. Only patients with a minimum of 5 years of follow-up were included. We used the Kaplan-Meier method to calculate the cumulative proportion of survival. Survival curves were compared using the log-rank test. We used the Cox regression model for multivariate analysis. **Results:** One hundred patients were included. The overall survival at 5 years of DTC, papillary thyroid carcinoma, and follicular thyroid carcinoma was 97%, 97.8%, and 85.7% respectively. The negative prognostic factors found in the univariate analysis were: age $\geq$ 55 years, male gender, cervical lymph nodes on ultrasound, tumor size $\geq$ 4 cm, invasion of the tumor capsule, vascular invasion, extrathyroidal extension, presence of tumor necrosis, lymph node extracapsular extension, vesicular carcinoma with a massive invasion variant, tall-cell variant of papillary thyroid carcinoma, positive surgical margins, initial postoperative thyroglobulin level greater than 10 ng/mL, tumors classified pT3 and pT4, stages III and IV. In multivariate analysis, only an initial postoperative thyroglobulin level greater than 10 ng/mL, as well as stages III and IV had influenced the overall survival. Local progression was noted in 2 cases. Local and/or lymph node recurrence was noted in 8 cases. **Conclusion:** An initial postoperative thyroglobulin level greater than 10 ng/mL, as well as stages III and IV, are independent negative prognostic factors in DTC.

THYROID CANCER CLINICAL

1112362 - PROGNOSTIC ROLE OF ANGIOINVASION IN PAPILLARY THYROID CARCINOMA

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Introduction: While the impact of angioinvasion on the prognosis of follicular thyroid cancer is well-established, its role in papillary thyroid carcinoma (PTC) remains controversial. **Objectives:** This study aimed to define the impact of angioinvasion on the outcome of PTC patients. **Methods:** We retrospectively analysed 719 PTC patients with available outcome data and detailed information on angioinvasion at histology. Angioinvasion was defined as the presence of tumour cells within the vascular wall or lumen, according to ATA guidelines. **Results:** Angioinvasion was found in 101/719 (14%) subjects. These patients were younger (40 vs 47 years, $p=0.033$), had larger tumours (22 vs 11 mm, $p<0.0001$), more often displayed a more aggressive PTC subtype (16.8 vs 6.5%, $p=0.0004$), extrathyroidal extension (36.7 vs 14.9%, $p<0.0001$), lymph-nodal and/or distant metastases (57.5 vs 31.9%, $p<0.0001$), and were more frequently treated with lymphadenectomy (62.4 vs 39.6%, $p<0.0001$) and radiometabolic therapy (87.5 vs 47.5%, $p=0.0017$). After a median follow-up of 4 years, angioinvasion patients had more frequent incomplete biochemical or structural responses (36.6 vs 14.4%, $p<0.0001$). Multivariable analysis showed that angioinvasion was an independent predictor of disease persistence (OR 2.03, $p=0.012$). With propensity score matching, we identified a 1:1 control group with comparable clinical-pathological characteristics and treatment modalities. After matching, patients with angioinvasion more frequently showed evidence of disease (36.6 vs 21.8%, $p=0.023$), with an OR of 2.71 ($p=0.03$). A sub-analysis of 33 patients showed that those with at least four invaded vessels ($n=12$) more frequently had biochemical/structural persistence of disease (41.6 vs 9.5%, $p=0.03$), with a higher frequency of distant metastases (25 vs 0%, $p=0.018$). **Conclusion:** This study, based on a large PTC cohort with data on angioinvasion, demonstrates the negative prognostic impact of vascular invasion, independent of other clinical-pathological factors. The outcome is further worsened if the angioinvasion has a large extension, i.e. ≥ 4 vascular sections invaded.

THYROID CANCER CLINICAL

1112236 - PROGNOSTIC SIGNIFICANCE OF BRAFV600E STATUS IN PATIENTS DIAGNOSED WITH PAPILLARY THYROID CANCER (PTC)

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Introduction: BRAFV600E mutation is the most common oncogenic driver in PTC. **Objective:** Assess the prognostic significance of BRAFV600E by evaluating its association with disease extent and progression-free survival (PFS). **Methods:** Patients with PTC and BRAFV600E mutation testing undergoing primary thyroid cancer surgery between 2000-2023 at a quaternary cancer center were included. Multivariate Cox-regression survival analyses were adjusted for age, sex, stage, radioactive iodine (RAI) treatment, and pathologic variant. PFS was defined as time from surgery to structural disease progression and/or recurrence. **Results:** 365 patients were included, with median age of 50 years (range 18-86), and median tumor size of 2.5 cm (range 0.1-9.5). 202 (54%) were female. 272 (75%) tumors were BRAFV600E-mutated, 300 (82%) had positive nodal disease, including 57% with N1b disease, and 78 (21%) had distant metastases at presentation. Between BRAFV600E-negative and positive cohorts, secondary mutations such as TP53, TERT and PIK3CA were equally distributed. RAS mutations were only detected in BRAFV600E-negative specimens. BRAFV600E status was not associated with multifocal disease, lymphovascular invasion, perineural invasion, gross extrathyroidal extension, extranodal extension, primary tumor size, nodal, or distant metastases ($p=0.050-0.575$). BRAFV600E-positivity was only associated with a median older age (53 vs 41 years; $p=0.001$), and PTC conventional variant (84% vs 49%; $p<0.001$). RAI was given in 61% (57/93) of BRAFV600E-negative and 59% (159/272) of BRAFV600E-positive patients ($p=0.631$). Median follow-up was 5.2 years (range 0.3-23.9). In BRAFV600E-negative vs positive PTCs, respectively: locoregional failure rates were 15% vs. 27% ($p=0.076$), distant failure rates were 24% vs. 29% ($p=0.079$), median locoregional PFS was not reached vs. 17 years (HR=0.91 95%CI 0.44-1.90) and median distant PFS was not reached vs. 18 years (HR=0.77 95%CI 0.35-1.67). **Conclusion:** In this large cohort of 365 patients with PTC, BRAFV600E-positivity was not associated with any aggressive pathological risk factors. Furthermore, BRAFV600E-mutated tumors were not associated with a higher rate of locoregional and/or distant failure.

THYROID CANCER CLINICAL

1114131 - PROGNOSTIC SIGNIFICANCE OF MORPHOLOGICAL SUBTYPES IN MEDULLARY THYROID CARCINOMA: A RETROSPECTIVE ANALYSIS

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Introduction: The prognostic significance of medullary thyroid cancer (MTC) subtypes remains unclear, unlike follicular-derived thyroid carcinomas. Notably, the 2022 WHO classification does not distinguish prognostic differences among MTC subtypes. **Objective:** To assess the correlation between the morphological characteristics of MTC and its clinical presentation as well as long-term outcomes. **Methods:** A continuous group of 57 patients primarily treated in 2016-2017 in SPBU Hospital with MTC was studied. A revision of histological conclusions was conducted to quantitatively assess the proportion of morphological patterns of the primary tumor (lobular, trabecular, papillary, pseudopapillary, follicular, and spindle cell), evaluate the condition of the capsule, identify signs of invasive tumor growth, necrosis, mitotic activity, and other relevant parameters. **Results:** The trabecular type was found to be characteristic of hereditary forms (gamma correlation = 0.66). The papillary type was associated with a poor prognosis (correlation coefficient = 0.81), while multifocality (1.0) likely indicated intrathyroidal metastasis. The spindle cell type showed a weak correlation with male sex and younger age (0.42 and 0.47, respectively). The follicular type correlated with older age (correlation coefficient = 0.74). The presence of calcifications in tumor tissue demonstrated a moderate correlation with poor prognosis and male sex, as well as a strong correlation with familial forms of MTC, but no correlation with age. In our study, the desmoplastic stromal reaction was not associated with an unfavorable prognosis. **Conclusion:** Our study identifies key correlations between tumor morphology and tumor behaviour. The trabecular type is linked to hereditary forms, the papillary type to poor prognosis, and multifocality to intrathyroidal metastasis. While the spindle cell type shows weak associations with male sex and younger age, the follicular type correlates with older age. Calcifications strongly associate with familial medullary thyroid carcinoma but not with age. Notably, the desmoplastic stromal reaction was not linked to poor prognosis.

THYROID CANCER CLINICAL

1112190 - PROPOSAL OF SUBCLASSIFICATION OF EXTRATHYROIDAL EXTENSION CORRESPONDING TO T4a FOR MORE APPROPRIATE RISK CLASSIFICATION OF PAPILLARY THYROID CARCINOMA

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Introduction: Extrathyroidal extension (Ex) is one of the important prognostic factors for papillary thyroid carcinoma (PTC). In the risk classification conducted by the Japan Association of Endocrine Surgery, Ex corresponding to T4a was classified as a high-risk feature, together with tumor size >4 cm, node metastasis ≥3 cm, extra-nodal extension, and distant metastasis at diagnosis. However, T4a includes PTCs with wide range of biological aggressiveness, and we investigated the difference in prognosis according to extended organs. **Methods:** Between 2011 and 2022 at Kuma Hospital, 9,247 PTC patients underwent locally curative surgery. We classified T4a into two categories based on intraoperative findings: T4a1, extending to the tracheal adventitia and/or cartilage, esophageal muscle layer, recurrent laryngeal nerve, or cricothyroid and inferior pharyngeal constrictor muscles, and T4a2, extending to the subcutaneous soft tissues, larynx, tracheal mucosa, esophageal mucosa, jugular vein, brachiocephalic vein, or sternocleidomastoid muscle. The median postoperative follow-up period was 7.3 years. **Results:** Of the 2,239 high-risk patients, 1,213 (54.1%) were classified as high-risk only for T4a1 (T4a1-high), and the remaining 1,026 (45.9%) were classified as high-risk because of other reasons (other-high). The cause-specific survival (CSS) (10-year, 99.6% vs. 97.7%), distant recurrence-free survival (DR-FS) (97.1% vs. 92.2%), and local recurrence-free survival (LR-FS) rates (92.9% vs. 87.5%) of T4a1-high-risk patients were significantly better than those of other-high-risk patients ($p < 0.001$). The CSS of T4a1-high-risk patients did not differ from intermediate-risk patients (2,902 patients) (10-year, 99.6% vs. 99.7%, $p = 0.607$). Although DR-FS and LR-FS of intermediate-risk patients were better ($p = 0.008$ and $p = 0.001$) than those of T4a1-high-risk patients, the difference in survival rates was small between the two groups (10-year, 98.7% vs. 97.1%, and 95.6% vs. 92.9%). **Conclusion:** Our findings suggest that T4a1-high-risk patients are better to be downgraded to intermediate-risk, which should be applied for other staging systems, including TNM staging.

THYROID CANCER CLINICAL

1112288 - RADIOACTIVE IODINE THYROID ABLATION AFTER PARTIAL THYROIDECTOMY IN INTERMEDIATE TO HIGH-RISK DIFFERENTIATED THYROID CANCER

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Introduction: Radioactive iodine (RAI) thyroid lobar ablation is not a common practice in management of differentiated thyroid cancer (DTC), but in selected cases where a completion thyroidectomy is contraindicated after complications during the initial surgery with risk of bilateral recurrent laryngeal nerve paralysis as the most common cause, it can be an alternative. **Objective:** Evaluate the efficacy of seriate administrations of RAI in ablating the remnant thyroid lobe after partial surgery (lobectomy or isthmectomy) in patients with intermediate to high-risk DTC. **Methods:** Single center retrospective study. 13 consecutive patients treated between 2010 and 2023 by partial thyroidectomy for intermediate to high-risk DTC, without known persistent disease, who received at least two RAI administrations, were included. Thyroid ablation and patients response were defined according to the 2015 ATA Guidelines as excellent, indeterminate, biochemical incomplete or structural incomplete. **Results:** Patients received small ablative activities of 0.74 -1.1 GBq followed in 12/13 cases by adjuvant activity of at least 3.7 GBq in order to avoid post RAI thyroiditis. The median accumulated activity that resulted in excellent response was 4.4 GBq (120 mCi, range: 60 130 mCi). For the eight remaining patients, the median accumulated activity was 4.9 GBq (135 mCi, range: 110 195 mCi). After a mean follow up of 20 months since last RAI treatment, 9 patients (69%) had satisfactory response with 5 (38%) excellent and 4 (31%) indeterminate response and stable thyroglobulin level. 3 patients (23%) had an incomplete biochemical response and 1 (8%) had an incomplete morphologic response with stable RAI refractory disease. **Conclusion:** RAI thyroid lobar ablation can be a safe, non-invasive and effective alternative to completion thyroidectomy for patients who have contraindications to reoperation.

THYROID CANCER CLINICAL

1112421 - RADIOFREQUENCY ABLATION FOR LOCALLY RECURRENT PAPILLARY THYROID CANCER

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Introduction: Although papillary thyroid cancer (PTC) typically has a favorable prognosis, a significant challenge exists for 20%50% of patients presenting with cervical lymph node metastases at diagnosis. For patients with recurrent PTC who are either unsuitable for surgery or decline it, radiofrequency ablation (RFA) is a potential treatment alternative. **Case Description** A 71-year-old woman with a history of acute myocardial infarction underwent a right lobectomy due to a goiter (2002). Subsequently, totalization was done by diagnosing PTC (2017), followed by radiotherapy I-131 200 mCi. The initial TNM stadification was pTxN1bMx. After the fifth year of follow-up, the ultrasound (US) revealed a lymph node at level III (14x10x8 mm). Recurrence was confirmed by US-guided fine needle aspiration cytology and serum thyroglobulin (Tg) washout. The pretreatment Tg level was 4.91 mg/dL. The patient refused surgery and elected to have RFA for treatment. Technique A head and neck surgeon performed RFA by placing lidocaine local anesthesia and using the RFA system (STARmed Co Ltd) with an 18G needle, 7 mm tip, and 30 W of power. Hydrodissection was carried out to protect adjacent normal tissues. The ablated area demonstrated hyperechogenicity indicative of effective thermal ablation. **Results:** At the 1-year follow-up, the US revealed that the target node had reduced in size (11x9x6 mm) and 2-year follow-up it was undetectable. Post-treatment Tg levels were remarkably low, measuring <0.1 ng/dL. Six months after RFA, the lymph node showed a 73% volume reduction on the follow-up US (Fig. 2). The Tg level was 0.04 ng/mL. **Conclusion:** RFA achieves significant nodule reduction, as evidenced by imaging and biochemical markers, with favorable safety outcomes. These results highlight RFA as a viable alternative for patients unable or unwilling to undergo surgery, offering promising potential in the management of recurrent PTC.

THYROID CANCER CLINICAL

1114066 - RADIOIODINE TREATMENT IN METASTATIC DIFFERENTIATED THYROID CANCER: HOW MANY AND WHICH PATIENTS ARE REALLY CURED?

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Introduction: Radioiodine (¹³¹I) treatment is a cornerstone of differentiated thyroid carcinoma (DTC) treatment. **Objective:** To determine how many and which patients with radioavid metastases were cured only with repeated ¹³¹I treatments. **Methods:** Between 2009 and 2012, 1457 consecutive DTC patients received ¹³¹I treatment after total thyroidectomy±lymph node dissection. Response to the therapy was classified according to 2015ATA-guidelines (ER: excellent, BiR/InR: biochemical incomplete/indeterminate, SiR: structural incomplete response). **Results:** 1,271 (87.2%) patients received 30 mCi and 186 (12.8%) 100 mCi of ¹³¹I. Post-¹³¹I whole body scan (pt-WBS) showed metastatic uptake in 51 (3.5%) cases [23 (45.1%) treated with 30 mCi, 28 (54.9%) with 100 mCi]. Radioavid metastases were lymph nodes [29 (56.8%)], lungs [21 (41.2%)] and bone [1(2%)]. Five (9.8%) patients received treatments other than ¹³¹I and therefore were excluded by the following analysis. The remaining 46 (90.2%) patients received only ¹³¹I treatments [1 treatment in 17 (37%), 2 in 12 (26.1%), and ≥3 in 17 (37%)]. At the last evaluation (median time: 8.3 years), 23 (50%) showed ER, 11 (23.9%) had BiR/InR and the remaining 12 (26.1%) had SiR. Comparing patients without SiR (ER and BiR/InR) and patients with SiR, the former were more frequently <55 years (79.4% vs 41.7%; p=0.015). None patients without SiR were high risk of recurrence, whereas 33% of patients with SiR were high risk (p= 0.003). The size of radioavid metastases at the first pt-WBS were more frequently sub-centimetric in patients without SiR than in SiR patients (67.6% vs 33.3%, p=0.038). Moreover, stimulated thyroglobulin (s-Tg) values at the time of the first ¹³¹I treatment were lower in patients without SiR (4.3 vs 24.9 µg/L; p=0.025). **Conclusion:** ¹³¹I treatments allow to cure half of patients with radioavid metastases at the first pt-WBS. Younger age, low/intermediate risk of recurrence, sub-centimetric metastatic lesions and low s-Tg values at the time of the first ¹³¹I treatment are the features identifying patients who can be cured by ¹³¹I repeated treatments.

THYROID CANCER CLINICAL

1112259 - RECURRENCE RATE IN 260 PATIENTS WITH ONCOCYTIC THYROID CANCER AND RISK FACTORS FOR RECURRENCE - A SINGLE-INSTITUTION EXPERIENCE

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Introduction: Oncocytic thyroid carcinoma (OTC) is a rare disease. There is little information about risk factors for recurrence. **Objective:** The aim of our retrospective, single-institution study was to determine the frequency and risk factors for recurrence in patients with OTC. **Methods:** Altogether 260 patients with OTC (57 men, 203 women; mean age 60.35 years; range 16-90 years) treated from 1972 to 2024 were included. Initially, regional and distal metastases were diagnosed in 15 (6%) and 25 (10%), respectively. Data on age, clinical and histopathological factors and stage of disease were collected. Cox's multivariate regression model was used to identify risk factors for recurrence. **Results:** The follow-up period ranged from 1 to 543 (mean 118) months. Recurrence was diagnosed in 39 (16%) of the 235 patients without disease after initial treatment. Locoregional, distant, and locoregional and distant were diagnosed in 18, 14, and 7 cases, respectively. The 5-year, 10-year, and 20-year disease-specific survival rates were 98%, 92%, and 81%, respectively. The 5-year, 10-year, and 20-year disease-free survival rates were 87%, 79%, and 74%, respectively. Among the 154 patients with an excellent response, recurrence occurred in 6.5%, and among the 81 patients without an excellent response, it occurred in 36% (p<0.001). Independent risk factors for recurrence were: gender, age, N stage, and residual tumor after surgery. **Conclusion:** The recurrence rate in patients with and without excellent response was 6.5% and 35%, respectively. Recurrence was more common in men, older patients, those with regional metastases, and those with residual tumor after surgery.

THYROID CANCER CLINICAL

1112525 - REFINING RISK STRATIFICATION IN INTERMEDIATE-RISK THYROID CANCER USING BRAF AND TERT AS A SIMPLE MOLECULAR APPROACH

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Introduction: Intermediate-risk thyroid cancer encompasses a heterogeneous and challenging group of patients, with a risk of recurrence of 5%-20%, and with a gap of clear guidance regarding treatment and follow-up. **Objective:** To evaluate if a simple molecular approach using BRAF mutations (BRAF mut) and TERT promoter mutations (TERTp mut) could refine risk stratification in intermediate-risk thyroid cancer. **Methods:** We retrospectively analysed a cohort of patients with papillary thyroid carcinoma (PTC) followed in a single institution. Patients with intermediate-risk were included, clinico-pathological data was collected and BRAF and TERTp mutational status was determined. Rate of recurrence and disease-free survival (DFS) was compared between the groups with or without a single mutation, and between the 4 groups (double wt for BRAF and TERTp, BRAF mutated, TERT mutated, and BRAF and TERT mutated), evaluating if any of these groups could be upstaged to high-risk or downstaged to low risk. **Results:** From a total of 241 patients with PTC (mean follow-up of 7.0±2.9 years), we identified 121 intermediate risk tumours, with an overall recurrence rate of 15.7%. When comparing the rate of recurrence and DFS, we found: BRAF mut=14.6% vs BRAF wt=18.8%, HR=0.78 (0.29-2.04), p=0.61; TERT mut=50.0% vs TERT wt=11.8%; HR=7.5 (2.24-25.11), p<0.001. Considering both BRAF and TERTp for risk of recurrence and DFS and using double wt as reference, we found: BRAF wt/TERT wt=11.1%; HR=1.0 (ref); BRAF mut=11.4%, HR=1.18 (0.32-4.36), p=0.80; TERT mut=75.0%, HR=8.38 (1.69-41.67), p=0.009; BRAF mut & TERT mut=40.0%, HR=5.67 (1.26-25.4), p=0.023. **Conclusion:** Risk stratification can be refined using a simple and feasible molecular approach in PTC. The presence of TERT mutations, with or without concomitant BRAF mutations, should upstage patients to the high-risk category. Single BRAF mutations seem not to be useful in this setting.

THYROID CANCER CLINICAL

1112430 - ROBOT-ASSISTED MODIFIED RADICAL NECK DISSECTION THROUGH BILATERAL AXILLARY BREAST APPROACH(BABA) IN PATIENTS WITH N1B PAPILLARY THYROID CARCINOMA: A COMPARATIVE STUDY WITH INITIAL EXPERIENCE AT SINGLE INSTITUTION

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Objective: The purpose of this study was to verify the safety and feasibility of robotic modified radical neck dissection (MRND) compared to open procedure. **Methods:** We retrospectively reviewed 76 patients with N1b papillary thyroid carcinoma (PTC) who underwent total thyroidectomy, bilateral central neck dissection, and unilateral MRND between September 2021 and August 2024. Of these patients, 58 underwent an open procedure, while 18 underwent a robotic procedure using the bilateral axillary breast approach (BABA). **Results:** The mean age, body mass index, and tumor size were not significantly different between the groups. Proportion of female patients was 63.8% in the open group, while no male patient was included in the robotic group. Operation time was significantly shorter in the open group than in the robotic group (242.7±40.4 vs 384.7±46.3 min, p<0.001). The number of retrieved lymph nodes was significantly larger in the open group compared to the robotic group in terms of both central and lateral lymph nodes (46.4±14.1 vs 32.2±11.9, p<0.001; 11.3±6.2 vs 7.6±6.0, p=0.025; 35.0±11.3 vs 24.6±8.9, p<0.001). The number of metastatic lymph nodes between the groups showed no significant difference. Stimulated thyroglobulin (sTg) level at first radioactive ablation was 1.75±2.37 ng/mL in the open group, 2.20±4.47 in the robotic group (p=0.586). The proportion of sTg level was 56.9% in the open group, and 55.6% in the robotic group (p=0.920). There was no statistical difference in postoperative complications between the groups. **Conclusion:** MRND through robotic BABA approach is technically feasible and safe in terms of completeness of LN dissection and postoperative complications.

THYROID CANCER CLINICAL

1113931 - ROLE OF VOLUMETRIC MODULATED ARC RADIOTHERAPY (VMAT) IN THE ADJUVANT TREATMENT OF LOCALLY ADVANCED DIFFERENTIATED THYROID CANCER: SINGLE INSTITUTION EXPERIENCE

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Introduction: A small percentage of patients with differentiated thyroid carcinoma present at diagnosis with locally advanced disease, which has higher risk of recurrence and mortality, and requires multidisciplinary therapeutic evaluation. The use of adjuvant external beam radiotherapy (EBRT) after surgery and radioiodine therapy (RAI) is a topic of debate. **Objective:** This study aimed to evaluate the efficacy of EBRT with volumetric modulated arc radiotherapy (VMAT) in improving locoregional relapse-free survival (LRFS) in addition to surgery and RAI. Secondary objective was to assess the tolerability of EBRT with VMAT. **Methods:** This monocentric, retrospective study included patients with locally advanced DTC, positive resection margins (R1) or lymph node metastases with extra-nodal extension who underwent total thyroidectomy and RAI. Patients were grouped based on whether they received adjuvant EBRT after surgery and RAI, and outcomes were compared. **Results:** Overall, 25 patients were included. EBRT group comprised 10 patients and non-EBRT group 15 patients. In the EBRT group, none experienced locoregional recurrence, compared to 60% in the non-EBRT group. Comparison of the survival curves showed a statistically significant difference ($p=0.043$). Despite the differences in observation time between the groups, at 36 months 26.6% of non-irradiated patients had already developed locoregional recurrence. Additionally, no severe treatment-related adverse effects were reported in the EBRT group, indicating good tolerability. Distant Disease-Free Survival (DDFS) was similar between the two groups, suggesting that the addition of EBRT did not impact the control of distant disease. **Conclusion:** Adjuvant EBRT using VMAT improves LRFS in patients with locally advanced DTC, without adding significant toxicity. Locoregional control potentially avoid repeated neck surgeries and their associated side effects. Despite some limitations, our findings support the integration of EBRT into treatment protocols for selected high-risk patients. Further studies are needed to confirm these results and to evaluate the long-term impact of EBRT on survival and quality of life.

THYROID CANCER CLINICAL

1112588 - SCREENING OF THE RET PROTO-ONCOGENE AND MEN2 SYNDROME SYMPTOMS AMONG MTC PATIENTS IN A BRAZILIAN HOSPITAL

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Introduction: Medullary Thyroid Carcinoma (MTC) occurs in two forms: sporadic or hereditary. The hereditary form, caused by an activating mutation in the RET proto-oncogene, may be associated with Multiple Endocrine Neoplasia type 2 (MEN2), divided into types A and B (MEN2A and MEN2B). This syndrome is linked to various clinical manifestations due to tumors in other endocrine organs (adrenal gland and parathyroid), such as pheochromocytoma, mucosal neuromas, Marfanoid features, and hyperparathyroidism. **Objective:** This study aims to analyze the proportion of patients with the RET germline mutation and those who developed MEN2 among MTC cases diagnosed in a reference Brazilian institution from 2000 to 2023. **Methods:** A retrospective, descriptive, and quantitative cohort study was conducted using data extracted from patient records. Of 140 MTC cases treated from 2000 to 2023, 32 records were randomly selected. Data were organized into Excel spreadsheets and analyzed using descriptive statistics. **Results:** Among the analyzed sample, 12 patients (37.5%) had the RET mutation, 43.7% tested negative, and 12.5% were not genetically tested. A family history of thyroid malignancy was present in 21.9% of cases, but only 15.6% had both a positive RET mutation and a family history. MEN2 symptoms were observed in 9.4% of individuals. **Conclusion:** Genetic evaluation of the RET proto-oncogene is crucial at MTC diagnosis and for family members of positive cases. The United States National Cancer Institute estimates that 25% of MTC cases are hereditary. Additionally, serum calcitonin, metanephrine, and calcium testing are vital for investigating metastases, pheochromocytoma, and hyperparathyroidism. The best prognosis can be achieved with early diagnosis and total thyroidectomy, highlighting the importance of improving public health policies in Brazil to provide more effective care for users of the Unified Health System (SUS).

THYROID CANCER CLINICAL

1112608 - SELPERCATINIB TREATMENT DOES NOT IMPAIR LEAN SOFT TISSUE AND ENERGY EXPENDITURE IN ADVANCED MTC PATIENTS: A PILOT STUDY

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Introduction: In cancer patients, weight loss is a progressive wasting condition primarily marked by the depletion of adipose tissue and skeletal muscle. Notably, substantial weight loss has been observed following the initiation of treatment with tyrosine kinase inhibitors. In contrast, weight gain has been reported during treatment with selpercatinib. **Objective:** Our study aimed to evaluate changes in body weight, BMI, and body composition including fat mass (FM) and lean soft tissue (LST) using dual-energy X-ray absorptiometry (DEXA) in patients with advanced or metastatic medullary thyroid carcinoma (MTC) undergoing treatment with selpercatinib. Additionally, we assessed sleeping metabolic rate (SMR) through whole-room indirect calorimetry (metabolic chamber). **Methods:** We evaluated 8 patients with advanced/metastatic MTC, six of whom initiated selpercatinib as a second- or third-line therapy. All patients underwent clinical evaluation, DEXA and SMR before and after 3 and 6 months of treatment with selpercatinib. Twenty-four-hour energy expenditure and thermic effect of food were not analyzed due to variability in individual food intake during the 24-hour session in the metabolic chamber. **Results:** Baseline and 6-month values were as follows: 75.8 ± 12.1 vs 76.2 ± 12.6 kg, BMI 25.3 ± 3.5 vs 25.4 ± 2.9 kg/m², FM 24.0 ± 6.6 vs 24.4 ± 7.7 kg, LST 48.4 ± 11.2 vs 48.0 ± 12.2 kg. SMR was 1258 ± 264 vs 1378.5 ± 258 kcal/d. No statistically significant differences were observed in any of the evaluated parameters at any time point compared to baseline. **Conclusion:** The findings of this pilot study suggest that selpercatinib treatment in patients with advanced MTC does not significantly impact body weight, body composition, or energy expenditure. The preservation of LST may play an important role in supporting the long-term therapeutic benefits of selpercatinib.

THYROID CANCER CLINICAL

1114287 - SHOULD THE PRESENCE OF BRAF V600E AND TERT MUTATIONS AND HIGH MIR-146B EXPRESSION CHANGE THE MANAGEMENT OF PAPILLARY THYROID MICROCARCINOMA?

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Introduction: Papillary thyroid microcarcinoma (PTMC) is often managed through active surveillance, currently categorized as ideal, appropriate, or inappropriate based on patient, nodule, and care team characteristics. Mutations in BRAF V600E, TERT promoter, and overexpression of microRNAs such as miR-146b have been associated with aggressive behavior and increased recurrence risk in papillary thyroid carcinomas. However, their predictive value in PTMC remains uncertain. **Objective:** To evaluate BRAF V600E, TERT promoter mutations, and miR-146b expression in PTMC and correlate them with clinical and pathological features to assess their prognostic relevance and influence on management. **Methods:** Retrospective study including 40 PTMC cases from multiple centers, with 27 patients undergoing surgery and 13 under active surveillance. Clinical, ultrasonographic, cytological, pathological, and treatment data were collected. FNA samples were analyzed using the mir-THYpe[®] pre op test to assess molecular markers. **Results:** No statistically significant correlation was found between molecular markers and clinicopathological features. BRAF V600E mutation and high miR-146b expression were not associated with aggressive features such as extrathyroidal extension ($p = 1.000$ and $p = 1.000$), vascular invasion ($p = 0.296$ and $p = 1.000$), or recurrence risk ($p = 0.658$ and $p = 1.000$). The TERT promoter mutation was identified in only one case, which showed no signs of aggressive behavior during follow-up. **Conclusion:** BRAF V600E mutation and miR-146b overexpression were not associated with poor prognostic features in PTMC. The TERT mutation, although linked to worse outcomes in conventional PTC, was rare and not related to aggressive behavior. These findings suggest limited prognostic value of these markers in PTMC and indicate they should not be decisive in choosing between surgery and active surveillance.

THYROID CANCER CLINICAL

1114110 - STUDY ON PYROPTOSIS OF ANAPLASTIC THYROID CANCER INDUCED BY BETULINALDEHYDE BASED ON SCD-GSDME AXIS AND ITS MECHANISM

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Introduction: Anaplastic thyroid cancer (ATC), a rare (1-2%) but lethal subtype (50% of deaths), has a median survival of 4-10 months and <7% 5-year survival. Current therapies fail due to resistance and heterogeneity. Betulinaldehyde (BA), a Betula triterpenoid with multi-target potential, remains unexplored in ATC despite analogs' anti-cancer efficacy, positioning it as a novel candidate. **Objective:** This study aimed to investigate the anti-tumor effects of betulinaldehyde (BA) on anaplastic thyroid cancer (ATC) and elucidate its underlying molecular mechanisms. Specifically, we sought to determine whether BA inhibits ATC progression by inducing pyroptosis – a lytic, inflammatory form of programmed cell death – and to identify key regulatory targets involved. We hypothesized that BA's multi-target activity, derived from its triterpenoid structure, might overcome the therapeutic limitations of conventional ATC treatments. **Methods:** Five ATC cell lines (KHM-5M, C643, 8505C, CAL62, HTH-7) were treated with BA. In vitro assays assessed cytotoxicity (CCK-8), proliferation (colony formation), migration/invasion (scratch/Transwell), apoptosis (flow cytometry), and pyroptosis markers (LDH, IL-1 β , GSDME cleavage via WB). RNA sequencing identified SCD as a target. In vivo, subcutaneous ATC xenografts in nude mice and thyroid cancer organoids evaluated BA's efficacy and safety via tumor growth inhibition, organ toxicity (serum biochemistry, HE staining), and Ki67 expression (IHC). **Results:** BA induced dose-dependent ATC cell death, with "balloon-like" swelling and elevated LDH/IL-1 β indicating pyroptosis. Proliferation, migration, and invasion were suppressed. Flow cytometry revealed concurrent apoptosis ($\uparrow$ cleaved caspase-3, $\downarrow$ PARP) and pyroptosis (GSDME activation). RNA sequencing and WB confirmed SCD downregulation. In vivo, BA inhibited tumor growth without organ toxicity. Organoid models mirrored these effects, confirming BA's anti-ATC activity. **Conclusion:** BA inhibits ATC progression by downregulating SCD and activating GSDME-dependent pyroptosis, demonstrating efficacy and safety in preclinical models. This highlights BA's potential as a novel ATC therapeutic and identifies SCD as a promising target.

THYROID CANCER CLINICAL

1114279 - SUCCESSFUL TARGETED THERAPY WITH SELPERCATINIB IN A PEDIATRIC PATIENT WITH METASTATIC RET-FUSION PAPILLARY THYROID CARCINOMA

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Case Presentation: A previously healthy 13-year-old male developed progressive cervical lymphadenopathy. In January 2023, ultrasonography identified an infiltrative left thyroid lesion with bilateral lymphadenopathy. Fine-needle aspiration classified it as Bethesda V. Staging CT revealed diffuse pulmonary micronodules. In February 2023, he underwent total thyroidectomy with bilateral lymph node dissection. Histopathology confirmed classic papillary thyroid carcinoma (PTC) with lymphovascular invasion and metastases in 46 of 58 lymph nodes. TNM staging was pT3bN1bM1, with a 3.5 cm primary tumor. In April 2023, he received 100 mCi of radioactive iodine (RAI), and a whole-body scan confirmed metastases to the cervical nodes, lungs, and skull base. Despite RAI, six-month follow-up imaging showed disease progression, including a new 1.2 cm retropharyngeal lymph node. Molecular analysis of the primary tumor identified an NCOA4-RET fusion, leading to the initiation of selpercatinib (160 mg BID) through a compassionate use program by Lilly Pharmaceuticals in April 2024. CT scans at 12, 24, and 36 weeks post-treatment showed progressive regression of cervical lymphadenopathy and pulmonary metastases. Biochemically, anti-thyroglobulin antibodies decreased, whereas thyroglobulin levels remained undetectable. The treatment was well-tolerated, with only transient grade 1 xerostomia. Routine laboratory tests, electrocardiographic monitoring, and assessments of bone age and pubertal development remained normal. **Discussion:** Pediatric PTC often presents with extensive lymphatic and distant metastases. While thyroidectomy and RAI are standard treatments, targeted therapy is crucial for progressive or RAI-refractory disease. RET fusions are key oncogenic drivers in pediatric PTC, with a reported prevalence of 15%-77%. Selective RET inhibitors, such as selpercatinib, offer a promising therapeutic approach. **Final Comments:** This case highlights the importance of molecular profiling PTC and demonstrates the safety and efficacy of selpercatinib in RET fusion-positive in pediatric patients.

THYROID CANCER CLINICAL

1112564 - SURGEON PERFORMED RAPID ON-SITE EVALUATION OF FINE NEEDLE ASPIRATION CYTOLOGY IN THYROID DISEASE

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Introduction: Fine Needle Aspiration Cytology (FNAC) is established standard diagnostic procedure for thyroid nodules. Despite its proven utility, the average non diagnostic rate (NDR) for thyroid FNAC is 5%-20%. The implementation of Rapid On-Site Evaluation (ROSE) utilizing rapid staining methods, such as toluidine blue, has demonstrated a significant reduction in the NDR. Furthermore, when FNAC is conducted by surgeons, it leads to improved cost-effectiveness and enhanced patient convenience, particularly within the framework of a one-stop clinic model. **Objective:** To estimate NDR and diagnostic accuracy in surgeon-performed ROSE-FNAC using toluidine blue dye. **Methods:** Patients with thyroid swelling were recruited prospectively. USG characterisation of thyroid nodule was done and FNAC was performed by surgeon either palpation guided or USG guided when required and was evaluated on site using toluidine blue dye for specimen adequacy. Samples were sent to Pathology department for reporting. **Results:** Interim analysis of 126 patients was done. Out of 126 cases, 24(19%) cases were deemed unsatisfactory as assessed by rapid staining. A repeat FNAC in the same sitting on these 24 cases showed adequate material in 22 cases (17.4%). The NDR for FNAs with on-site evaluation is 3.96% on final reporting by pathologist. The average time of the procedure was 4.5 minutes. We achieved a sensitivity of 91.3%, specificity of 95.5%, positive predictive value of 84%, negative predictive value of 97.7%, and accuracy of 94.6%. **Conclusion:** Implementation of ROSE on thyroid nodules improves NDR of FNAC with a good diagnostic accuracy. The technique is easy enough for surgeons to incorporate into their routine practice.

THYROID CANCER CLINICAL

1112309 - SURGICAL TREATMENT, MORBIDITY AND MORTALITY IN PATIENTS WITH T1 AND T2 THYROID CANCER

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Introduction: The main treatment of thyroid cancer is surgery. The current Danish guidelines recommend de-escalation of treatment for selected patients with differentiated cancers <4 cm. **Objective:** Our objective was to evaluate surgically treated cancer patients from 2017 to 2021 with attention on outcome after total thyroidectomy (TT) versus hemithyroidectomy (HT). **Methods:** All thyroid operations were prospectively entered in an online database from January 2017. We evaluated pathology and clinical outcomes retrospectively on patients with final diagnosis of thyroid cancer. **Results:** In a five-year period, we performed 2804 thyroid operations. This study included 614 patients (916 operations) with a final diagnosis of thyroid cancer. For patients with cancer <4 cm (N=484, 79%), T-stages were T1a (27%), T1b (30%), and T2 (43%). Lymph node and distant metastases were found in 11% and 0.6%, respectively. The thyroid resection was HT in 165 patients (34%), and TT in one (66 (14%)) or two steps (253 (52%)). Within a mean follow-up time of 56 months the overall mortality was 6%. One patient died from pneumonia 2 months after surgery, but no other patients had disease specific or treatment related mortality. In 137 patients (54% of patients with T1 or T2 cancers treated with TT in two stages) we would now recommend HT according to the current guidelines. In these 137 patients we saw 7% permanent hypoparathyroidism, 100% hypothyroidism, and 1.5% permanent recurrent laryngeal nerve palsy. Further, 59 (43%) had cancer in the contralateral lobe. **Conclusion:** The disease-specific mortality was extremely low in this group of patients, but there are high risks of hypothyroidism and hypoparathyroidism when undergoing surgery for thyroid cancer. Following the introduction of recent guidelines, number of TT is reduced and both number of operations, short-term morbidity and permanent complications will be reduced as well, but small cancers may remain in the contralateral lobe.

THYROID CANCER CLINICAL

1112196 - SYNCHRONOUS FOLLICULAR AND PAPILLARY THYROID CANCERS: RETROSPECTIVE OUTCOME ANALYSIS

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Introduction: Synchronous follicular thyroid carcinoma (FTC) and papillary thyroid carcinoma (PTC) within the same thyroid lobe is rare, complicating diagnostic and therapeutic strategies. This study aims to enhance understanding of the clinical management and outcomes of these synchronous thyroid malignancies. **Methods:** A retrospective study was performed to analyze the medical records of patients who underwent thyroidectomy for thyroid cancer at Gangnam Severance Hospital between March 2003 and December 2021. Of these, 258 cases were reviewed, including 44 patients with synchronous FTC and PTC (Group1) and 214 patients with FTC only (Group2). Clinical and pathological characteristics were analyzed. **Results:** Group1 had a higher female proportion (84.1% vs. 74.6% in Group2) and a greater rate of total thyroidectomy (77.3% vs. 40.4%, $p<0.001$) and lateral neck dissection (9.1% vs. 0.9%, $p=0.008$). The extrathyroidal extension was more prevalent in Group1 (43.2% vs. 22.1%, $p=0.006$). Group2 had eight cases of recurrence, while Group1 showed superior disease-free survival. **Conclusion:** The synchronous occurrence of FTC and PTC is rare but increasingly recognized. While patients with synchronous FTC and PTC had lower recurrence and metastasis rates, their long-term prognosis was similar to those with FTC only, as reflected by comparable disease-free survival curves.

THYROID CANCER CLINICAL

1112629 - TENIS SYNDROME IN PAPILLARY THYROID CARCINOMA: DIAGNOSTIC CHALLENGE AND LATE PROGRESSION IN AN INITIALLY LOW-RISK CASE

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Case Presentation: A 50-year-old woman underwent total thyroidectomy in September 2017 for papillary carcinoma measuring 1.0 x 0.7 cm, with no invasion or extrathyroidal extension and negative surgical margins. In June 2024, she presented with metastatic lymph nodes in levels VI and VII, confirmed by biopsy, with infiltration into striated skeletal muscle. PET-SCAN with FDG revealed metastases in the cervical and pulmonary regions. The patient received radioiodine therapy (200 mCi) with recombinant TSH stimulation; however, post-treatment scintigraphy showed no abnormal radiopharmaceutical uptake, despite elevated serum thyroglobulin levels (26 ng/mL). No iodine-avid tissues suggesting residual thyroid or secondary lesions were identified. **Discussion:** This case highlights the diagnostic challenges in patients with papillary carcinoma initially classified as low risk. Despite the favorable features of the primary tumor, the patient experienced late progression with lymph node and pulmonary metastases. The absence of iodine uptake, combined with elevated thyroglobulin levels, characterizes TENIS syndrome, a condition often associated with tumor dedifferentiation, in which sodium-iodide symporter (NIS) expression is reduced. Diagnosing this syndrome requires careful correlation of clinical, laboratory, and imaging findings. PET/CT with FDG proved essential in identifying the extent of metastases and guiding management. This case underscores the importance of rigorous follow-up and a high degree of clinical suspicion in patients initially considered low risk. **Final Comments:** The unpredictable biological behavior of papillary carcinoma can pose significant diagnostic and management challenges. Integrating biomarkers such as thyroglobulin and advanced imaging technologies is crucial to overcoming these difficulties and directing more effective therapeutic strategies. This case demonstrates the need for individualized follow-up and interventions, even in patients initially considered to have a favorable prognosis.

THYROID CANCER CLINICAL

1112429 - THE INTEREST OF THYROGLOBULINE MEASUREMENT IN FNA EXAMINATION OF THE CERVICAL LYMPHATIC NODES

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Introduction: Approximately half of patients with thyroid carcinoma present with pathological lymph nodes at the time of diagnosis, and the appearance of secondary adenopathy is a common progression of the disease. The diagnosis of lymph node invasion can be achieved using fine needle aspiration (FNA) combined with thyroglobulin (Tg) measurement. The objective of this study is to evaluate the diagnostic improvement when using FNA cytology alone versus FNA combined with Tg measurement. **Materials and Methods:** In this single-center study, all adult patients who underwent ultrasound-guided FNA for suspicious lymph nodes (either at initial diagnosis or during ultrasound monitoring) between January 2019 and May 2023 were included. Cytological examination and Tg measurement were performed on all FNA samples. The gold standard was definitive histology or patient follow-up. Sensitivity, specificity, and positive and negative predictive values (PPV and NPV) were determined for cytology alone (Cyto), Tg alone, and the combination of cytology and Tg (Cyto/Tg). **Results:** A total of 249 patients with 307 FNA procedures were included. Sensitivity was 85%, 77%, and 98% for Cyto, Tg, and Cyto/Tg, respectively. Specificity was 88%, 88%, and 87% for Cyto, Tg, and Cyto/Tg, respectively. PPV was 93%, 90%, and 91% for Cyto, Tg, and Cyto/Tg, respectively, while NPV was 75%, 73%, and 98% for Cyto, Tg, and Cyto/Tg, respectively. **Conclusion:** This study confirms a significant improvement in the diagnostic performance for pathological lymph nodes when cytology is combined with Tg measurement in FNA examinations. Tg measurement increased the sensitivity of cytology by 23% while maintaining specificity.

THYROID CANCER CLINICAL

1114297 - THYROID CANCER IN PATIENTS WITH HYPERTHYROIDISM: A RARE BUT CRITICAL RELATIONSHIP

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Introduction: Although hyperthyroidism (due to Graves' disease, toxic multinodular goitre or autonomous adenoma) is rarely associated with thyroid cancer, recent studies highlight that its coexistence, although rare, requires meticulous clinical attention. **Objective:** To analyse the relationship between hyperthyroidism and thyroid cancer. To present clinical data and recommendations for early diagnosis. Prevalence of malignancy: Only 1.4% of autonomous nodules are malignant (example: classical papillary carcinoma). In patients with Graves' disease, the incidence of cancer is low but not zero. Demographic characteristics Mean age: 50 ± 19 years. Female/male ratio: 2.31 (30 females vs. 13 males). Tumour size: ≤1 cm: 4.7% | >1-2 cm: 11.6% | >2-4 cm: 39.5% | >4 cm: 44.2%. Risk factors: "Hot" nodules with atypical ultrasound features. Family history, radiation exposure or rapid growth. **Methods:** We analysed the data of 3 patients who underwent total thyroidectomy for hyperthyroidism, the ages were 51, 56, 61 years with an average of 56 years, the patients debuted with hyperthyroidism, 2 of the patients presented autonomous nodules by scintigraphy, in which they had suppression of TSH, and elevation of free T4, the average size was 1 cm (0.8-1.2 cm) **Results:** These findings suggest that, although malignancy in patients with severe disease, hyperthyroidism and autonomous thyroid nodules is rare, it cannot be completely ruled out. Hyperfunctioning ("hot") nodules: Traditionally considered benign, but recent reviews suggest that 0.5-1.5% may be malignant. Example: Patient P2 (0.8 cm papillary carcinoma in autonomous nodule). Graves' disease: Theoretical increased risk due to chronic TSH receptor stimulation (TSI antibodies). Patient P1 had incidental carcinoma post-surgery. **Conclusion:** The coexistence of cancer and hyperthyroidism is rare, but not non-existent. The key is a high clinical suspicion and the use of diagnostic tools (ultrasound + FNAB). Do not rule out malignancy in hyperfunctioning nodules with risk factors.

THYROID CANCER CLINICAL

1114134 - THYROID CANCER SURGERY OUTCOMES ACCORDING TO REIMBURSEMENT MODALITY

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Introduction: Well-differentiated thyroid cancer is one of the most common solid neoplasms with rising incidence. Its treatment is surgical and may be followed by adjuvant iodine therapy. The extension of the surgery may range from partial thyroidectomy to an extended multiorgan resection, and a neck dissection may be necessary. Although safe, thyroid surgery may cause morbidity and sequelae, including hypoparathyroidism, vocal fold palsy, and post-operative hemorrhage. **Objective:** To evaluate the extension of the surgery, the need for adjuvant therapy and, the risk of post-operative complications and sequelae in patients treated for well-differentiated thyroid carcinoma in a single, tertiary cancer center. **Methods:** A series of 1,070 patients treated for well-differentiated thyroid cancer were included in this study. Patients were divided according to reimbursement modality in public versus private cohorts. The outcomes of interest were time from diagnosis to treatment, hospital length of stay, post-operative hypoparathyroidism, post-operative dysphonia, infection, reoperation, indication of neck dissection, need of multiorgan resection and indication of adjuvant radioiodine. **Results:** The median time lapse from diagnosis to treatment was 41 days in private patients and 243 days in public patients ($p < 0.001$). Patients from the public cohort had higher rates of extended resection ($p < 0.001$), neck dissection ($p = 0.032$) while indication of radioiodine trended towards a higher rate ($p = 0.081$). The incidence of vocal fold palsy ($p < 0.007$) and definitive hypoparathyroidism ($p = 0.050$) was higher in public patients. The need for reoperation was also higher in public patients ($p = 0.041$). **Conclusion:** The short time of follow-up does not allow for survival analysis, but public patients experience longer waiting times for treatment. This is reflected in higher rates of extended resections, and neck dissection with a substantial increase in post-treatment complications and sequelae. Treatment delay impacts extent of resection and the need for adjuvant therapy causing significant morbidity and higher costs.

THYROID CANCER CLINICAL

1112279 - THYROID INCIDENTALOMAS IN LYMPHOMA PATIENTS UNDERGOING FDG-PET/CT: PREVALENCE, CHARACTERISTICS, AND RISK FACTORS

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Objective: To analyze the prevalence, characteristics, and risk factors of thyroid incidentalomas detected on FDG-PET/CT in lymphoma patients, and to assess the relationship between uptake patterns and thyroid malignancy. **Methods:** We conducted a retrospective study of 815 lymphoma patients who underwent FDG-PET/CT for staging between January 2018 and October 2023. Thyroid uptake was categorized as focal, diffuse, or absent. Demographic, clinical, and imaging data were analyzed, and thyroid ultrasound, biopsy, and autoantibody results were included when available. Logistic regression and ROC curve analysis were used to identify predictors of thyroid uptake and malignancy. **Results:** Thyroid abnormalities were observed in 16.9% of patients (138/815). Among these, 52 exhibited FDG uptake (32 focal and 20 diffuse), and 86 had CT abnormalities only. Focal uptake was associated with a 12.5% malignancy rate, while diffuse uptake correlated with thyroid autoantibodies ($p = 0.004$). Age and female gender were independent predictors of thyroid uptake ($OR = 1.04$, $p < 0.001$; $OR = 2.16$, $p = 0.011$, respectively). ROC analysis revealed age thresholds of 68.6 years for females and 59.8 years for males ($AUC = 0.72$). After adjusting for age, lymphoma type (Hodgkin vs. non-Hodgkin) did not significantly predict thyroid uptake patterns, and SUV values did not distinguish benign from malignant lesions. **Conclusions:** Thyroid incidentalomas on FDG-PET/CT are common in lymphoma patients, with focal uptake posing a higher malignancy risk and diffuse uptake linked to autoimmunity. Older age and female gender increase the likelihood of thyroid uptake. These findings underscore the importance of evaluating incidental thyroid findings to optimize patient management.

THYROID CANCER CLINICAL

1114257 - THYROID PARAGANGLIOMA: CHALLENGES AND PITFALLS IN CYTOLOGICAL EVALUATION

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Case Presentation: A 52-year-old woman with a one-year history of progressive increase in right anterior cervical mass. Physical examination revealed a palpable thyroid nodule on the right side measuring 2 cm. Cervical ultrasound revealed a solid, iso-echoic, well-defined, vascularized nodule with lobulated contours in the right thyroid lobe, measuring 24 x 18 x 18 mm. Fine needle aspiration (FNA) revealed the absence of colloid and findings of thyroid follicular neoplasm compatible with Bethesda IV. Total thyroidectomy was performed. The biopsy showed a well-defined nodular lesion of moderate cellularity in the right thyroid lobe. The cells are arranged in small nests (Zellballen) of low risk according to the Grading System for Adrenal Pheochromocytoma and Paraganglioma (GAPP), compatible with paraganglioma. The diagnosis was confirmed with immunohistochemical study: positive for synaptophysin, chromogranin, S-100, GATA3 and SDHB; negative for TTF-1, thyroglobulin, calcitonin, CEA and PTH; Ki67 <1%. **Discussion:** Thyroid paraganglioma is extremely rare and represents a significant diagnostic challenge. Ultrasound typically shows well-circumscribed hypoechoic and highly vascular nodules. Histologically, the tumor is composed of cells arranged in well-defined rings surrounded by a fibrovascular stroma. It is occasionally misdiagnosed as follicular neoplasm, medullary thyroid carcinoma, intrathyroid parathyroid proliferation, and especially secondary neuroendocrine tumors. Immunohistochemical staining is essential to establish the diagnosis. Loss of the succinate dehydrogenase subunit B (SDHB) complex can be evaluated to determine the need for genetic study. Positive immunohistochemical results rule out the presence of a mutation in the succinate dehydrogenase complex. Total thyroidectomy is the preferred treatment option. **Final Comments:** Thyroid paragangliomas are erroneously diagnosed by FNA due to the rarity of the location and overlapping morphology with neoplasms. Given the low clinical suspicion, routine methods used in the study of cervical masses are ineffective in diagnosis, making immunohistochemistry indispensable in all cases.

THYROID CANCER CLINICAL

1112494 - TRANSITIONING CARE FOR DIFFERENTIATED THYROID CARCINOMA: PRELIMINARY RESULTS FROM A TELEMEDICINE-SUPPORTED RANDOMIZED CLINICAL TRIAL

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Introduction: Differentiated thyroid cancer (DTC) has low recurrence rates (2%-5%). Despite this, the CDT consensus recommends long-term follow-up. Telemedicine is a strategy that allows a soft transition of care for patients from tertiary care to primary health care (PHC). **Objective:** To evaluate the impact of the transition of care between specialized care and PHC for patients with DTC supported by telemedicine. **Methods:** Patients with DTC and excellent response to initial treatment were randomized to follow-up in-person consultations in a tertiary service or transfer for PHC with telemedicine navigation. This support was provided through telephone calls to patients and health units to ensure linkage in PHC and to provide support through telephone consultations. The primary outcome was DTC recurrence, assessed in a face-to-face consultation through thyroglobulin measurement and neck ultrasound. **Results:** Out of the 869 patients evaluated, 206 were included, the majority of whom were female (n=175; 85.0%) and had papillary thyroid carcinoma (n=176; 85.4%). Concerning the ATA risk classification, 110 patients were low (54.2%), 91 were intermediate (44.8%), and 2 were high risk (1.0%). All patients were treated with total thyroidectomy, 133 (64.6%) received radioactive iodine. One hundred and forty-five (70.4%) patients were reevaluated in face-to-face consultations, 80 from the intervention group and 65 from the control group. In the intervention group, one patient presented DTC recurrence, and one presented indeterminate response. In the control group, one patient presented DTC recurrence, and five presented indeterminate response. The rates of euthyroidism were the same in both groups (53.7%, P=0.81). **Conclusion:** The provision of care for patients with DTC and excellent response after initial treatment to PHC appears to be safe, without an associated increase in relapse rates or inadequate management of hypothyroidism. **Funding:** Departamento de Tireoide da SBEM/Conselho Nacional de Desenvolvimento Científico e Tecnológico.

THYROID CANCER CLINICAL

1112506 - ULTRASONOGRAPHIC APPEARANCE OF INTRATHYROIDAL THYMIC CARCINOMA: A CASE REPORT

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The intrathyroidal thymic carcinoma (ITTC) is a rare malignant epithelial tumor with thymic differentiation. It commonly originates in the ectopic thymic tissue, thought to arise in intra- or perithyroidal thymic tissue, remnants of thymo-pharyngeal duct, or the branchial pouch. A 58-year-old woman was referred for a thyroid ultrasound examination. A prominent, solid hard non-mobile mass was present in the lower neck. Thyroid function test and calcitonin level were normal. TPOab was negative. On ultrasound a solid hypoechoic heterogeneous mass was detected arising from the right lobe of the thyroid gland extending to the anterior mediastinum. The borders showed lobulated aspects in contact to the trachea and to the strap muscles. The heterogeneity of the mass was done by the presence of fine echogenic bands and scattered echogenic spots without calcifications. Computed tomography showed a heterogeneous mass with extension to the thoracic operculum. The resected specimen revealed a solid, whitish lobulated mass entirely integrated with thyroid parenchyma. Pathological examination revealed a poorly differentiated carcinoma characterized by polygonal cells with wide amphophilic cytoplasm, gross trabeculae, fibrous strands, and a small nest of lymphoid tissues. Immunohistochemistry results were positive for p40 and CD117 and negative for CD5, CK7, TTF1, PAX8, CD1a and CD99. The final diagnosis was a poorly differentiated squamous cell carcinoma of probably thymic origin. Intrathyroidal thymic carcinoma (ITTC) can originate from ectopic thymic tissue within or adjacent to the thyroid gland. Formerly known as carcinoma showing thymus-like elements (CASTLE), it was recognized by the World Health Organization (WHO) as an independent entity in 2004 and renamed intrathyroidal thymic carcinoma (ITTC), representing less than 0.55% of all thyroid malignancies. In this case, we have described the ultrasonographic features that can aid in considering ITTC in cases of lower neck tumors.

THYROID CANCER CLINICAL

1112663 - UNVEILING ORM1 AS A BIOMARKER IN MEDULLARY THYROID CANCER: INTEGRATING CIRCULATING TRANSCRIPTOME, TISSUE EXPRESSION, AND TUMOR SIZE

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Introduction: Orosomucoid 1 (ORM1), or alpha-1-acid glycoprotein, is a glycoprotein produced by the liver that is abundant in plasma. **Objective:** ORM1 expression has been associated with bladder, colorectal, and kidney carcinoma. On the other hand, there is no data on its association to medullary thyroid cancer (MTC). **Methods:** Patients with active MTC and patients in remission underwent transcriptome analysis from peripheral blood samples. Transcriptome library was constructed using Ion Proton equipment. The differentially expressed genes (DEG) were called using NOISeq. MTC samples from another population were used for tissue microarray (TMA) construction for immunohistochemical analysis and 3 distinct regions of the tissue samples from each patient were collected, one from the center and another from the border of the tumor, and one from nonmalignant tissue. ORM1 expression in the TMA was evaluated by staining intensity and the number of stained cells. The final score combined the intensity of the center and border expression results. **Results:** We constructed 15 transcriptome libraries and identified 427 DEG, from which ORM1 was selected. ORM1 was up regulated in local and distant metastasis, especially those with liver metastasis. TMA analysis identified ORM1 in nearly 100% of the neoplastic cells. The final score correlated moderately with tumor size ($r: 0.595$, $p: 0.019$). Tumor size and ORM1 provided an AUC of 0.865. **Conclusion:** In this pilot study, we detected ORM1 expression in almost all MTC cells. When combined with tumor size, this expression could provide a valuable prognostic biomarker. Further studies are necessary to confirm these results.

THYROID CANCER CLINICAL

1113987 - VALUE OF BRAF V600E IN HIGH-RISK THYROID NODULES WITH BENIGN CYTOLOGY RESULTS

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Introduction: Fine needle aspiration (FNA) cytology has its limitations in the diagnosis of thyroid nodules, as evidenced by undiagnostic specimens, inconclusive cytology results, and false negative and false positive results. **Objective:** The aim of this study was to evaluate the additional diagnostic efficacy of BRAFV600E gene mutation testing in FNA of benign thyroid nodules. **Methods:** A retrospective analysis of 3062 high-risk nodules of PTC found in the Department of Thyroid Surgery, China-Japan Union Hospital of Jilin College from January 2019 to July 2024 was performed. A total of 294 benign FNA nodules were enrolled in this study to analyze the clinicopathological characteristics of patients with BRAFV600E gene mutation. **Results:** Of the 294 benign FNA nodules, 151 nodules tested positive for the BRAFV600E gene mutation. The proportion of nodules with diameter ≥ 1 cm was significantly lower in the mutation-positive group than in the mutation-negative group, and the incidence of aspect ratios >1 , irregular margins and a higher number of suspicious ultrasound features was higher than in the mutation-negative group. Postoperative pathology indicated that 215 thyroid nodules were PTC nodules, and the prevalence of BRAFV600E gene mutation, hypoechoic solid nodules, aspect ratio >1 , and fuzzy margins was significantly higher in the PTC group than in the benign nodule group. The risk of diagnosis of PTC in thyroid nodules with negative BRAFV600E gene mutation was 0.146. The positive predictive value of BRAFV600E gene mutation test for the diagnosis of PTC nodules was 90.7%, and FNA combined with BRAFV600E gene mutation test increased the rate of confirming the diagnosis of PTC in benign nodules with FNA by 41.8%. **Conclusion:** BRAFV600E gene testing reduces the underdiagnosis of PTC nodules in benign FNA nodules. It is recommended that thyroid nodules with TIRADS classification of category 4-5 undergo routine combined FNA and BRAFV600E gene testing in the presence of highly suspicious ultrasound features.

THYROID CANCER CLINICAL

1112579 - VARIATIONS OF THE HYPOTHALAMIC-GONADAL AXIS IN MALES DURING SELPERCATINIB TREATMENT FOR MEDULLARY THYROID CARCINOMA

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Introduction: Selpercatinib, a highly selective RET inhibitor, has shown noteworthy efficacy in patients with metastatic RET-mutated medullary thyroid carcinoma. Despite toxicity profile of selpercatinib treatment is more tolerable compared to multi-kinase inhibitors, peculiar adverse events have been reported. Among the adverse events, erectile dysfunction has been observed. **Objective:** This study aims to evaluate the effects of selpercatinib treatment on the hypothalamic-gonadal axis in male patients with medullary thyroid carcinoma. **Methods:** FSH, LH, and total testosterone serum values were evaluated in 7 patients before the beginning and during the selpercatinib treatment, for a follow-up time of 24 months. **Results:** Six patients received selpercatinib as first-line therapy. At the beginning of selpercatinib treatment, the patients had a median age of 61 years (IQR 55-63). All patients reported the onset of erectile dysfunction during selpercatinib treatment. Comparing pre-treatment and subsequent serum values of FSH, LH, and total testosterone in each patient (Friedman test), a significant decrease in total testosterone serum value was observed during the first year of treatment ($p < 0.01$), which then stabilized. This was associated with a significant increase in FSH and LH serum values ($p < 0.01$) during the selpercatinib treatment. **Conclusion:** In this preliminary study, the initial decrease of testosterone serum value and the simultaneous increase in gonadotropins were frequent adverse events during selpercatinib treatment. Given the high incidence of erectile dysfunction, it is reasonable to hypothesize a possible pathogenic correlation between these two phenomena.

THYROID CELL BIOLOGY

1114125 - A NOVEL cAMP BIOSENSOR-BASED ASSAY TO DETECT TSH BIOACTIVITY AND STIMULATING TSH RECEPTOR ANTIBODIES USING HUMAN THYROID CELL LINES

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Introduction: Thyroid Stimulating Hormone (TSH), produced by the pituitary, binds G-protein coupled TSH receptors (TSHRs) stimulating thyroid hormone synthesis and growth. Cyclic adenosine monophosphate (cAMP) is an important second messenger downstream of TSHR activation. Establishing the activity of TSH or TSHR autoantibodies (TSHR-Abs) is relevant under specific conditions. Luciferase-based cAMP biosensor assays have been developed to determine TSHR activation and are used to measure the bioactivity of stimulating TSHR autoantibodies (TSHR-Abs) in Graves' disease (GD). However, biosensor assays that assess TSH or TSHR-Abs bioactivity in human thyroid cells using the endogenous TSHR signaling pathway are lacking. This study aims to develop assays to measure TSH and TSHR-Ab bioactivity, providing a more precise tool for differential diagnoses in thyroid disorders.

Objective: To develop a cAMP-biosensor-based assay in cells with endogenous TSHR signaling, capable of detecting TSH and TSHR-Ab activity. **Methods:** The human differentiated oncogenic thyroid carcinoma cell line XTC.UC1 and SV40-immortalized normal thyroid epithelial cell line Nthy-ori 3-1, both endogenously expressing TSHR, were lentivirally transduced or stably transfected with cAMP biosensor 22F or 20F. Cells were serum-starved and subsequently stimulated with bovine TSH or the human TSHR-Ab M22.

Results: Our bioassays detected bovine TSH at concentrations as low as 1 mIU/L and M22 at 100 ng/mL. The cAMP biosensor expressing cells showed fold inductions ranging from 2 to 60 versus negative controls. Cells maintained robust signal-to-noise ratios under serum-free conditions for up to 72 hours, with fold inductions comparable to those after 2-hour serum starvation. **Conclusion:** Our study demonstrates that XTC.UC1 and Nthy-ori 3-1 cells with stably expressed cAMP biosensor can measure the bioactivity of bovine TSH and TSHR-Abs. Should further studies show that this bioassay system can reliably detect human TSH and TSHR-Ab activity, our tool may aid in management of thyroid disorders.

THYROID CELL BIOLOGY

1112331 - MODELING OF PATIENT-DERIVED 3D ORGANOID MODELS OF THYROID CANCER: FROM CELLS TO CARE

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Introduction: Recent advances in three-dimensional (3D) organoid technology, derived from patient tissues, provide a more accurate representation of cancer biology, offering an effective tool compared to traditional two-dimensional (2D) models. This study aims to develop patient-derived 3D organoid models for refractory and anaplastic thyroid cancer, with the long-term goal of using these models to guide personalized treatment strategies and improve patient outcomes. **Materials and Methods:** Tumor tissues from refractory and anaplastic thyroid cancer patients were collected, dissociated, and embedded in Matrigel for 3D culture. The cells were then incubated with specific growth factors to establish organoid models, which were monitored for cell growth and subcultured.

Results: Single thyroid cells from refractory and anaplastic thyroid cancer were cultured in a 3D environment using Matrigel and specific growth factors to establish thyroid organoids. The TCO001 sample showed substantial growth up to passage 11 over five months, while the TCO002 sample had limited proliferation and stopped at passage 4 after four months. **Conclusions:** Despite the considerable challenges in cultivating patient-derived 3D organoid models for thyroid cancers, this study achieved meaningful progress by establishing viable cultures. This achievement is expected to provide the foundation for advancing personalized treatment strategies and supporting improved patient outcomes.

THYROID CELL BIOLOGY

1113781 - ROLE OF THE CHLORIDE CHANNEL CLC-3 IN THYROID FUNCTION

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Introduction: CLC-3 is an endosomal chloride channel involved in intracellular protein trafficking. Although its role has been described in various tissues, its function in the thyroid gland remains unknown. **Objective:** To investigate the expression and functional role of CLC-3 in the thyroid, using a CLC-3 knockout (Cln3^{-/-}) mouse model. **Methods:** In this study, the expression and function of CLC-3 in the thyroid were evaluated in 40 CLC-3-KO (Cln3^{-/-}) mice [24 F, 16 M, age 14.5 (5.7) weeks, SVJ129-C57BL/6 background], and 41 heterozygous (Cln3^{+/-}) mice [23 F, 18 M, age 14.7 (5.8) weeks]. **Results:** CLC-3 was detected in the thyroid of Cln3^{+/-} mice with intracellular localization, but was absent in Cln3^{-/-} mice. CLC-3 was also detected by Western blotting in thyroid extracts of Cln3^{+/-} mice and minimally in Cln3^{-/-} mice (molecular mass 102 kDa). Serum FT4 levels were lower in Cln3^{-/-} mice (mean difference -9.9 pg/mL, 95% CI -17.1 to -2.7, P = 0.0072), whereas TSH levels were higher, although not significantly. However, Cln3^{-/-} mice had a higher TSH/FT4 ratio (Mann-Whitney U = 256, P = 0.03053), suggesting the presence of hypothyroidism. Histologically, follicular area was smaller in Cln3^{-/-} mice (mean difference -18.6 pixels/nm², 95% CI -34.2 to -2.9, P = 0.021), as occurs in conditions of TSH-dependent hyperstimulation. By immunofluorescence, Tg was detected in the follicular lumen with no differences between the two groups. However, intracellular thyroglobulin (Tg) was higher in Cln3^{-/-} mice, indicating intracellular retention, as confirmed by Tg measurement in thyroid extracts by Western blotting (mean difference 20.2 pixels/nm², 95% CI 5.6 to 34.8, P = 0.011). **Conclusion:** CLC-3 is expressed in the thyroid and appears to be involved in thyroid hormone synthesis, likely by regulating intracellular thyroglobulin trafficking. Loss of CLC-3 impairs thyroid function and leads to a phenotype suggestive of subclinical hypothyroidism.

THYROID EPIDEMIOLOGY

1112262 - ANALYSIS OF HOSPITALIZATION VARIABLES FOR THYROID CANCER AMONG BRAZILIAN REGIONS IN THE LAST FIVE YEARS

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Introduction: In Brazil, the impact of thyroid cancer is influenced by factors such as level of access to healthcare services and lifestyle habits. Treatment usually begins with thyroidectomy, followed by radioiodine therapy, and in some cases, the use of medications to suppress thyroid function is necessary. For this, hospitalization is crucial to acquire adequate treatment, however, the frequency and duration of stay depend on each patient. **Objective:** To analyze thyroid cancer hospitalization patterns across Brazilian regions from 2019 to 2023. **Methods:** Data were sourced from the Department of Informatics of the Unified Health System (DATASUS), through a quantitative approach to assess hospitalizations for thyroid cancer in Brazilian regions from 2019 to 2023. Variables included type of treatment, regional distribution, age group, gender, and annual diagnostic trends. **Results:** The data highlight surgery as the most adopted method, with 20,667, followed by radiotherapy with 500 occurrences. Regionally, the highest number of surgeries was in the southeast, with 7,332, compared to the north 986 surgeries. In terms of age group, the highest number of malignant neoplasms of the thyroid gland was between 50 and 59 years old, with 5,036, especially in the southeast with 2,186 cases in the analyzed period. In relation to the lowest number, it was evident in the population aged 0 to 19 years, in the north region, expressing 35 cases in this period. In addition, with regard to diagnosis, there was a quantitative increase from 2020 to 2023, approximately 21%, 17% and 3% respectively. Finally, the highest prevalence of cases of malignant thyroid neoplasm occurs in females, mainly in the southeast. **Conclusion:** Data suggest surgical treatment as the method of choice, especially where therapeutic resources are available. Controlling risk factors for thyroid cancer development is crucial.

THYROID EPIDEMIOLOGY

1112281 - ANALYSIS OF MORTALITY PROFILES FROM MALIGNANT THYROID NEOPLASM IN BRAZIL: A DECADE OF DATA

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Introduction: Malignant thyroid neoplasm refers to the uncontrolled growth of malignant cells in the thyroid gland. The rising incidence in Brazil highlights the importance of epidemiological studies to guide better clinical management strategies. **Objective:** This study aims to conduct an epidemiological analysis of malignant thyroid neoplasm in Brazil from 2013 to 2023, focusing on demographic health patterns. **Methods:** This descriptive study used data from DATASUS TABNET (20132023) on mortality profiles from malignant thyroid neoplasm in Brazil. The analyzed variables included year, age, sex, race/ethnicity, and educational level. **Results:** An analysis of 9,058 patients revealed that the Southeast region accounted for the highest number of cases during the studied period, representing 39.97% of the total. Mortality was most prevalent among individuals aged 70 to 79 years (27.39%). Women constituted the majority of cases (65.98%) compared to men (34.12%). Regarding race/ethnicity, white individuals were the most affected (54.95%). Most deaths occurred among those with 1 to 3 years of education (23.49%). Women and individuals with lower educational levels were the most affected groups. However, this differs from the age factor, as mortality was highest among those aged 70 to 79 years, demonstrating the influence of aging on poor prognosis. **Conclusion:** This investigation highlights that thyroid carcinoma in Brazil predominantly affects women and white individuals, with high mortality rates among patients aged 70 to 79 years in the Southeast region. These findings underscore the importance of public policies aimed at early detection and adequate therapeutic interventions.

THYROID EPIDEMIOLOGY

1112203 - ANALYSIS OF THE EPIDEMIOLOGICAL PROFILE OF MORTALITY FROM MALIGNANT THYROID NEOPLASM IN THE MUNICIPALITY OF SÃO PAULO BETWEEN THE YEARS 2013 TO 2023

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Introduction: Thyroid neoplasia is characterized by the abnormal growth of cells, forming benign or malignant tumors. According to U.S. projections, it will rank as the 4th most common neoplasm by 2030. In this context, understanding its epidemiology becomes essential, especially given the scarcity of studies. **Objective:** To analyze and describe the epidemiological profile of mortality due to thyroid neoplasia in the last decade in São Paulo's municipality. **Methods:** A quantitative, retrospective, and descriptive study was conducted on mortality due to malignant thyroid neoplasia in São Paulo from 2013 to 2023. Data were obtained from the Outpatient Information System (SIA) of TABNET (DATASUS), analyzing variables such as sex and age. **Results:** During the analyzed period, 3,509 deaths from thyroid neoplasia were recorded in São Paulo, with a predominance in females (59.2%) compared to males (40.8%). The highest number of male deaths occurred in 2022 (147), while for females, it was in 2023 (209). The smallest percentage difference between sexes was in 2014 (12.3%), while the largest was in 2020 (26.98%). Regarding age groups, 45.7% of deaths (1,604) occurred between 60 and 79 years, with the 70 to 79 age group standing out with 766 deaths (21.9% of the total). Among individuals under 19 years, 265 deaths (7.6%) were recorded, with the highest incidence between 1 to 4 years. There was slight annual fluctuation in the number of deaths, peaking in 2018 (349 deaths). **Conclusion:** The data highlight a predominance in females and a higher incidence in 2023, with the 60 to 79 age group being most affected. This pathology has led to a growing mortality rate, underscoring the need for further studies on contributing factors. Thus, research is crucial to developing strategies to reduce mortality from this neoplasia.

THYROID EPIDEMIOLOGY

1113705 - ASSOCIATION BETWEEN SERUM SELENIUM AND URINARY IODINE WITH THE RISK OF PAPILLARY THYROID CANCER IN KOREA: A CASE-CONTROL STUDY

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Introduction: Selenium is involved in the production of thyroid hormones in conjunction with iodine. Several studies have reported a relationship between selenium deficiency and the risk of thyroid cancer, but the results have been inconsistent. **Objective:** We aimed to investigate the relationship between selenium and the risk of papillary thyroid cancer (PTC), as well as the impact of iodine on this relationship. **Methods:** A hospital-based case-control study was conducted in a tertiary hospital with high volume of thyroid cancer patients in Seoul Korea, between November 2011 and June 2016. We interviewed the participants on lifestyle and dietary intake, and collected blood/urine samples. A total of 498 cases with newly diagnosed PTC and 573 controls who donated fasting blood and spot urine were included in this study. Serum selenium levels were categorized into four groups: deficient ($<110 \mu\text{g/L}$), low normal (≥ 110 - $<122.74 \mu\text{g/L}$), mid normal (≥ 122.74 - $<141.14 \mu\text{g/L}$), high normal ($\geq 141.14 \mu\text{g/L}$). Urinary iodine concentration (UIC) was categorized into quartiles. **Results:** After adjusting for the covariates, the high normal selenium group had a lower risk of PTC compared to the deficient group (odds ratio [OR] = 0.55, 95% confidence interval [CI]: 0.38-0.81, P trend = 0.003). The association was not modified by sex and age (<45 years vs. ≥ 45 years). There was no association between selenium levels and tumor size. UIC increased the risk of PTC only when the level of selenium was low normal (q4 vs. q1 of UIC, OR = 3.45, 95% CI: 1.32-9.07) or deficient (q4 vs. q1 of UIC, OR = 4.54, 95% CI: 1.91-10.98). **Conclusion:** We found a negative association between serum selenium levels and the risk of PTC. A deficiency in selenium combined with excessive iodine intake may increase the risk of PTC. Additional large-scale prospective studies are needed to clarify these associations.

THYROID EPIDEMIOLOGY

1114192 - BIDIRECTIONAL CANCER RISKS BETWEEN THYROID AND BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Thyroid cancer (TC) and breast cancer (BC) represent common malignancies affecting mainly females. Growing evidence suggests a higher-than-expected co-occurrence of these cancers within the same individuals. **Objective:** We evaluated the relationship between TC and BC and examined the likelihood of developing BC following TC (TC1-BC2) and vice versa (BC1-TC2). **Methods:** A systematic review and meta-analysis were performed using the PubMed and Embase databases according to current guidelines (MOOSE). We included articles containing epidemiological evidence of TC after BC and vice-versa, published until 2024. For BC1-TC2 studies subgroup analysis regarding age at the time of BC diagnosis and type of treatment (radiotherapy and chemotherapy) was performed. The standardized incidence ratio (SIR) was used to calculate the risk of second primary malignancy. **Results:** Sixteen studies comprising 511,787 patients were included in the meta-analysis of TC1-BC2 and showed an increased risk of BC after TC when compared to the adjusted population risk (SIR = 1.4, 95% CI 1.2-1.6, $p < 0.01$). Moreover, for BC1-TC2, 28 studies with 2,486,870 patients were included in the meta-analysis and demonstrated an increased risk of developing TC following BC (SIR = 1.5, 95% CI 1.3-1.7, $p < 0.01$). The risk of TC was also higher in BC patients under 50 (SIR = 1.8, 95% CI 1.2-2.3) and in those treated with chemotherapy (SIR = 1.6, 95% CI 1.5-1.7). Radiotherapy for BC was not associated with an increased risk of TC. **Conclusion:** This study demonstrated an increased risk of developing TC or BC as secondary malignancies. Further studies are needed to provide a more in-depth understanding of the mechanisms that underpin this association, potentially impacting patient follow-up and management strategies.

THYROID EPIDEMIOLOGY

1112407 - CLINICAL-EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH THYROID EYE DISEASE FROM A TERTIARY HEALTHCARE SERVICE

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Objective: Evaluate the clinical and epidemiological profile of patients with Thyroid Eye Disease (TED) in a tertiary hospital. **Methods:** This is an observational and retrospective study aimed at evaluating the medical records of 164 patients with TED from January 2018 to September 2023. Epidemiological data were collected, including sex, age, race, thyroid and ocular disease history. Patients were stratified according to the severity (EUGOGO) and activity (CAS). **Results:** We identified 164 patients, of whom 116 (70.7%) were female and the average age was 46.66 years (SD 14.24). Ninety patients were smokers (54.87%). The three main symptoms reported at the beginning of the ocular condition were proptosis (72.2%), pain (7.2%) and diplopia (6.6%). 92% were hyperthyroidism, 6.2% hypothyroidism and 1.8% euthyroidism upon arrival at our service. The majority used ATD (89%) for systemic control, 22.5% RAI and 9.75% thyroidectomy. 22% required treatment with steroids (81.12% intravenously). Strabismus and diplopia were present in more than 30% of patients, asymmetry in 46.9% of the sample and 42% had eyelid retraction greater than 2mm. Almost 62% had a predominant lipogenic pattern on tomography and 84.15% were in the chronic or stable phase. As for severity, 55.48% had mild orbitopathy, 35.36% moderate-to-severe and 9.16% sight threatening. **Conclusion:** The characteristics of TED in the Brazilian population are very similar to international publications, however very severe cases were higher in our practice.

THYROID EPIDEMIOLOGY

1112642 - COMPARISON BETWEEN RADIOTHERAPY AND CHEMOTHERAPY IN SOUTHEASTERN ADULTS WITH MALIGNANT THYROID NEOPLASM OVER A DECADE

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Introduction: Thyroid gland neoplasms represent a challenge in modern medicine, from diagnosis to treatment due to the high risk of malignization. Radiotherapy is currently the most widely treatment used, specially as an adjuvant to surgery for larger tumors or to resolve unoperable ones, whereas, chemotherapy is casually introduced in anaplastic tumors or in cases of distant metastases. **Objective:** To collect and analyze data on chemotherapy and radiotherapy treatments for malignant thyroid neoplasms in the population of the southeastern region of Brazil. **Methods:** This is an epidemiological study that analyzed data from the SUS Outpatient Information System (SIA) and Hospital Information System (SIH), collected between 2014 and 2023. The focus was on cases of malignant neoplasia of the thyroid gland in adults in the Southeast region of Brazil, aged between 20 and 59 years, according to the data available in the Oncology-Panel. In addition, the data was stratified by gender, allowing an analysis of the distribution of cases. **Results:** The comparison between chemotherapy and radiotherapy treatments shows that the Southeast concentrates the greatest use of both therapeutic methods, covering approximately 38.7% of the patients analyzed from all regions of Brazil. Of the 252 cases examined, 110 patients underwent chemotherapy, while 142 received radiotherapy, corresponding to 43.7% and 56.3% of cases, respectively. The gender distribution analysis showed a balance between the sexes, with 128 cases in women (50.8%) and 124 in men (49.2%). With regard to age group, 252 patients were analyzed and the highest incidence was observed among middle-aged adults, especially in the 50-54 age group, representing 28.57% of all cases, followed by patients aged 55-59, 25% of the sample from this region. **Conclusion:** The analysis reveals a predominance of radiotherapy, highlighting its effectiveness as an adjuvant treatment and as an option for inoperable patients.

THYROID EPIDEMIOLOGY

1112318 - COMPARISON OF THYROTOXICOSIS CASES IN THE STATE OF RIO DE JANEIRO AND BRAZIL DURING THE PERIOD FROM 2019 TO 2024

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Introduction: Thyrotoxicosis is a complex clinical syndrome characterized by an excess of thyroid hormones. Its symptoms include unintentional weight loss, tachycardia, and severe complications such as psychiatric alterations and thyrotoxic crisis. This condition represents a significant health issue, necessitating effective medical interventions for proper management¹. The primary causes include Graves' disease, toxic multinodular goiter, and excessive use of thyroid hormones. Understanding the epidemiological characteristics of this condition is crucial for developing prevention and treatment strategies. **Objective:** To compare the epidemiological characteristics of thyrotoxicosis cases between the state of Rio de Janeiro and Brazil from 2019 to 2024. **Methods:** An observational, cross-sectional, descriptive, and comparative epidemiological study was conducted using data extracted from DATASUS (SIH/SUS) for the period from 2019 to 2022. The analysis encompasses all age groups and considers variables such as race and gender. **Results:** Between 2019 and 2024, the state of Rio de Janeiro recorded 334,584 cases of thyrotoxicosis (13.15% of the national total). The year with the highest number of cases was 2022 (79,792), while the lowest was in 2024 (29,882). The most affected age group was 50 to 59 years (29.20%), with the mixed-race population being the most affected (29.17%). In Brazil, there were 2,542,917 reported cases, with 76.90% in women and 23.10% in men. **Conclusion:** The analysis reveals that thyrotoxicosis has a higher incidence among mixed-race women aged 50 to 59 years; Brazil shows a similar statistic, differing only in the predominant age group among patients aged 40 to 49 years. These data highlight epidemiological patterns that underscore the importance of implementing public policies aimed at the prevention and treatment of thyrotoxicosis in vulnerable populations.

THYROID EPIDEMIOLOGY

1112481 - DISTRIBUTION OF THYROID CANCER MORTALITY BY AGE GROUP AND BIOLOGICAL SEX IN BRAZIL: AN ANALYSIS OF EPIDEMIOLOGICAL BEHAVIOR FROM 2012 TO 2022

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Introduction: Thyroid cancer, although rare, has seen a significant rise in incidence since the 1990s, especially among women of reproductive age. In Brazil and Latin America, annual increases in diagnosis rates raise concerns about fertility and the need for strict monitoring during pregnancy to prevent complications. Papillary and follicular carcinoma are the most common subtypes, with low mortality rates. However, their heterogeneity demands personalized treatments, particularly for intermediate-risk patients. Advances in molecular imaging and genetic analysis enhance understanding of risk factors and guide therapies, emphasizing early detection and tailored care. **Objective:** To evaluate thyroid cancer mortality trends in Brazil, considering methodological and data heterogeneity. **Specific Objectives:** To identify temporal and epidemiological patterns. To compare adjusted mortality rates. To highlight discrepancies in results. **Methods:** This epidemiological study analyzed thyroid cancer mortality trends in Brazil (2012-2022), focusing on age and biological sex distribution. Data were obtained from DATASUS and international databases, including PubMed, SciELO, Google Scholar, and LILACS, using descriptors in Portuguese and English, such as thyroid cancer, mortality rate, and age distribution. Inclusion criteria required complete records on age, sex, and adjusted mortality rates. Inconsistent data and non-Brazilian populations were excluded. Mortality rates were standardized using the global standard population, enabling comparisons. Trends were analyzed using the Joinpoint Regression Program. Ethical approval was unnecessary, as publicly available data were used. **Results:** The study analyzed 100 cases, predominantly women (70%) aged 20-80 years. Histological analysis showed 85% were papillary carcinoma, 10% follicular carcinoma, and 5% rare subtypes. BRAF V600E mutations were present in 60% of cases, linked to recurrence and lower survival ($p < 0.01$). **Conclusion:** Thyroid cancer incidence is rising, especially among women, necessitating prevention and tailored therapies. Advances in molecular diagnostics enhance understanding and stratification. Early diagnosis and integrated approaches improve outcomes and quality of life in Brazil.

THYROID EPIDEMIOLOGY

1112638 - EPIDEMIOLOGICAL AND FINANCIAL ANALYSIS OF TOTAL THYROIDECTOMY IN ADULTS IN THE STATE OF RIO DE JANEIRO FROM 2017 TO 2023

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Introduction: Thyroidectomy is the total surgical resection of the thyroid gland, indicated in cases of neoplasms or certain benign diseases. The analysis of epidemiological and financial data related to this procedure can help reduce excessive and potentially avoidable surgeries. **Objective:** To assess the epidemiological and financial profile of total thyroidectomy in adults in the State of Rio de Janeiro from 2017 to 2023. **Methods:** Data from government sources were analyzed, including the number of procedures performed annually from 2017 to 2023, hospitalizations by municipality in 2023, total costs by municipality between 2017 and 2023, and recorded deaths associated with the procedure of interest during the same period in the State of Rio de Janeiro. Additionally, a review of five studies on the effects, management, and costs of thyroidectomy in adult and pediatric patients was conducted. **Results:** The epidemiological and financial analysis of total thyroidectomy in adults in the State of Rio de Janeiro from 2017 to 2023 revealed significant trends. There was a gradual increase in the number of procedures, possibly reflecting greater detection of thyroid diseases. Associated costs showed a steady rise, varying by municipality and year, suggesting regional differences in demand and treatment expenses. Furthermore, the associated mortality rate was low, indicating advancements in perioperative care. **Conclusion:** This detailed analysis highlights the importance of continuous monitoring and efficient resource allocation in the healthcare sector. The increase in procedures and costs, along with the low mortality rate, emphasizes both advancements in medical care and the need for tailored regional strategies to address variations in demand and expenses. Thus, a planned approach is essential to ensure the sustainability and efficiency of the state healthcare system.

THYROID EPIDEMIOLOGY

1112639 - EPIDEMIOLOGICAL AND FINANCIAL OVERVIEW OF SURGICAL THYROID BIOPSY IN RIO DE JANEIRO OVER 5 YEARS (2019-2023)

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Introduction: The thyroid is an essential gland for the proper functioning of metabolism. However, the appearance of thyroid nodules, characterized by abnormal cell growth, is common in the Brazilian population and can affect individuals of various age groups. In these cases, surgical biopsy is often used as a diagnostic method to differentiate benign from malignant lesions. **Objective:** To analyze the epidemiological and financial overview of surgical thyroid biopsy in Rio de Janeiro between 2019 and 2023. **Methods:** This study aimed to outline the epidemiological and financial panorama of surgical thyroid biopsy in Rio de Janeiro over a 5-year period, using data extracted from the public DATASUS database. **Results:** From 2019 to 2023, a total of 66 hospitalizations were recorded for surgical thyroid biopsy, with 35 in 2019, 16 in 2020, 4 in 2021, 3 in 2022, and 8 in 2023. The average cost per hospitalization, according to the year of processing, was 232.92, distributed as follows: 231.62 in 2019, 229.31 in 2020, 295.11 in 2021, 233.08 in 2022, and 214.71 in 2023. **Conclusion:** The study revealed a significant variation in the number of hospitalizations for surgical thyroid biopsy in Rio de Janeiro between 2019 and 2023, with a sharp decline between 2021 and 2022, followed by a recovery trend in 2023. The average hospitalization cost per year during the period was 232.92, with 2023 registering the lowest value and 2021 the highest. Surgical biopsy plays a crucial role in identifying potential malignancies in thyroid nodules. Early diagnosis, combined with appropriate treatment, is essential for effective management of this condition. Additionally, considering the patients context is vital to ensure individualized diagnoses and treatments. Therefore, a personalized approach is necessary to ensure that patients receive appropriate and high-quality care.

THYROID EPIDEMIOLOGY

1112651 - EPIDEMIOLOGICAL OVERVIEW OF ADULT MORTALITY DUE TO MALIGNANT THYROID GLAND NEOPLASMS IN BRAZIL FROM 2017 TO 2023: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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Introduction: Thyroid cancer (TC) is one of the most common endocrine malignancies, characterized by one of the best prognoses among cancers. TC is classified into papillary thyroid carcinoma (PTC), anaplastic thyroid carcinoma (ATC), follicular thyroid carcinoma (FTC), and medullary thyroid carcinoma (MTC), with PTC being the most prevalent. Common clinical manifestations include neck masses, lymphadenopathy, thyroid dysfunction, and obstructive effects. **Objective:** To analyze the evolution of mortality rates from TC in the adult Brazilian population between 2017 and 2023. **Methods:** A time-series ecological study with a quantitative, descriptive, and exploratory approach was conducted using public data on general hospital mortality due to Malignant Neoplasm of the Thyroid Gland from 2017 to 2023. Data were obtained from the Mortality Information System (SIM) of the Brazilian Unified Health System (SUS) and organized into a Microsoft Office Excel® spreadsheet. Descriptive analysis was performed through absolute incidence and percentages. **Results:** During the study period, 6,105 deaths from malignant thyroid gland neoplasms were recorded in Brazil. Of these, 2,396 were reported in the Southeast region (representing 39.24% of cases), followed by the Northeast with 1,838 (30.1%) and the South with 977 (16%). Mortality rates increased with population aging, with the 7079 age group showing the highest number of deaths (1,671 cases). Women were the most affected across all regions, notably in the Southeast, with 1,548 deaths. **Conclusion:** The analyzed data indicated a higher number of deaths among women and older age groups, with the Southeast region showing the highest mortality rates. These findings highlight the relationship between population aging and increased mortality, as well as regional disparities in death patterns. Thus, it is imperative to implement public policies aimed at improving access to early diagnosis and specialized treatment, particularly in the most affected areas and among vulnerable population groups, to reduce inequalities.

THYROID EPIDEMIOLOGY

1112425 - EPIDEMIOLOGICAL PROFILE OF HOSPITALIZATIONS FOR THYROID DISORDERS RELATED TO IODINE DEFICIENCY IN THE STATE OF SÃO PAULO

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Introduction: Iodine deficiency is one of the leading causes of thyroid disorders, such as goiter and hypothyroidism, affecting approximately 2 billion people globally, with significant impacts in regions where iodine intake is insufficient. In Brazil, despite the implementation of salt iodization in the 1950s, hospitalizations related to iodine deficiency remain a challenge for the healthcare system, particularly in terms of prevention and appropriate management. **Objective and Methods:** This study aimed to analyze the distribution of hospitalizations due to thyroid disorders associated with iodine deficiency in the state of São Paulo between 2020 and 2024, based on data extracted from DATASUS (SIH/SUS). It is a cross-sectional and descriptive epidemiological study that considered demographic variables such as age group, sex, and race/skin color. The data were tabulated and analyzed using a quantitative approach. **Results:** During the analyzed period, 170 hospitalizations for iodine deficiency-related thyroid disorders were recorded, with a predominance of cases among women (81.18%). The most affected age group was 5059 years (23.53%), followed by the 4049 and 6069 age groups, both at 17.64%. Regarding race/skin color, white patients accounted for 54.11% of hospitalizations, followed by mixed-race individuals (25.88%) and black individuals (7.68%), with 10% of cases missing information. **Conclusion:** The results reveal significant inequalities related to gender and race/skin color, highlighting the need for more effective public policies for prevention and management. Furthermore, socioeconomic and environmental factors influencing these disorders should be investigated to support targeted interventions. Comprehensive strategies are essential to mitigate the impacts of these disorders on the healthcare system and improve the populations quality of life, reinforcing the importance of continuous monitoring and the promotion of preventive health practices.

THYROID EPIDEMIOLOGY

1112445 - EPIDEMIOLOGICAL PROFILE OF HYPERALDOSTERONISM IN BRAZILIAN REGIONS FROM 2019 TO 2023

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Introduction: Hyperaldosteronism is a dysregulation of aldosterone produced by the adrenal glands. Aldosterone, through the renin-angiotensin-aldosterone system, promotes sodium retention and potassium excretion, increasing blood volume and blood pressure. Conditions like adrenal tumors or generalized adrenal hyperactivity can lead to hypertension. Screening for aldosterone imbalances is vital due to its link with hypertension, a prevalent condition. **Objective:** To analyze and compare new hyperaldosteronism cases across Brazilian regions from 2019 to 2023. **Methods:** Epidemiological study of the Brazilian regions, using the DATASUS (Department of Informatics of the Unified Health System) database in the period from 2019 to 2023, considering deaths from hyperaldosteronism by residence and by occurrence and the variables sex, color/race, schooling, place of occurrence, age group and region. **Results:** Equivalent data was observed both for deaths by occurrence and by residence. 38 deaths were reported, with a Southeast region predominance (16 cases). Hospitals accounted for 80% of occurrences. Most victims were white, female (21 deaths), aged 80 and over, with schooling from 8 to 10 years. **Conclusion:** Hyperaldosteronism remains a significant health challenge in Brazil, particularly among elderly women in the Southeast. Strengthening public health policies for early diagnosis and effective management is crucial to improving population outcomes.

THYROID EPIDEMIOLOGY

1112440 - EPIDEMIOLOGICAL PROFILE OF HYPOPARATHYROIDISM IN BRAZILIAN REGIONS FROM 2019 TO 2023

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Introduction: Hypoparathyroidism is a rare endocrine disorder characterized by deficient production of parathyroid hormone, leading to disturbances in calcium and phosphorus metabolism. Understanding the geographic distribution and demographic profile of affected patients is essential for developing public health intervention strategies and improving clinical management. This study examines epidemiological data on hypoparathyroidism in different Brazilian regions from 2019 to 2023. **Objective:** To describe the epidemiological profile of hypoparathyroidism in Brazilian regions from 2019 to 2023. **Methods:** This is an epidemiological study with a quantitative approach, characterized as descriptive and retrospective, that focused on deaths caused by hypoparathyroidism. The study was conducted by extracting data from the Department of Informatics of the Unified Health System (DATASUS) for the time series spanning 2019 to 2023. The variables included death, ethnicity/race, sex, age group, stratified by Brazilian regions. The data were imported from the Hospital Information System into Microsoft Excel, where they were tabulated and used to create charts and tables for descriptive statistical analysis. **Results:** Analysis of mortality associated with hypoparathyroidism in Brazil showed the Southeast region had the highest occurrence (14 cases). The North, Northeast, and South regions each recorded 4 deaths, while the Central-West had 2. Regarding ethnicity, approximately 57% of deaths occurred among white individuals, 32% among mixed-race individuals, and 10% among black individuals. Additionally, 75% of deaths occurred in individuals over 60 years old, with a predominance of about 68% among women. **Conclusion:** The study revealed a higher prevalence of cases and deaths in the Southeast region, especially among women and the elderly. The majority of deaths occurred among white individuals, highlighting regional and demographic disparities. These findings underscore the need for public health strategies focused on vulnerable groups and further research to improve the diagnosis and management of the disease.

THYROID EPIDEMIOLOGY

1112303 - EPIDEMIOLOGICAL PROFILE OF MALIGNANT THYROID NEOPLASMS IN THE SOUTHEAST REGION FROM 2020 TO 2024

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Introduction: Thyroid cancer is the most prevalent type of endocrine tumor and plays a significant role among carcinomas affecting the head and neck region. The primary types of malignant thyroid neoplasms are papillary carcinoma and follicular carcinoma, the latter being more aggressive with a higher likelihood of metastasis. According to the most recent Brazilian estimates, thyroid cancer is the third most common cancer among women in the Southeast Region. **Objective:** To analyze the epidemiological profile of malignant thyroid neoplasms in the Southeast Region of Brazil between 2020 and 2024. **Methods:** This is a retrospective, quantitative epidemiological study based on data from the “PANEL-Oncology” platform of the Department of Information Technology of the Unified Health System. Cases of malignant thyroid neoplasms in the Southeast Region from 2020 to 2024 were analyzed. Variables included federative unit, sex, age group, therapeutic modality, and year of diagnosis. Data were tabulated in Microsoft Excel and analyzed using descriptive statistics. **Results:** The analysis identified 17,592 cases of malignant thyroid neoplasms. The state of São Paulo accounted for 72% of the cases, followed by Minas Gerais with 15.5%. Distribution by sex revealed a higher prevalence in women, who represented 86% of the cases. In terms of age, the most affected group was between 50 and 64 years old. Regarding treatment, 37.6% of cases were managed surgically, while chemotherapy and radiotherapy were less commonly used. **Conclusion:** There is a high prevalence of malignant thyroid neoplasms in the Southeast Region of Brazil, particularly in São Paulo. A notable disparity exists between the incidence in women and men. Surgery was the predominant treatment modality; however, the lack of comprehensive data limits further analysis. Therefore, it is crucial to examine data from other regions of the country to improve infrastructure, optimize resources, and develop targeted treatment strategies.

THYROID EPIDEMIOLOGY

1112645 - EPIDEMIOLOGICAL PROFILE OF THYROTOXICOSIS IN THE PEDIATRIC POPULATION BETWEEN 2019 AND 2023

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Introduction: Thyrotoxicosis, a disorder marked by excessive thyroid hormones, presents varied and subtle symptoms, especially in children, complicating early diagnosis. Undetected, it risks severe neurological damage or acute emergencies. Autoimmune diseases primarily cause thyrotoxicosis in children, with a notable correlation to chromosomal disorders. Although less prevalent in this age group, its severity demands further research on risk factors, prevention, and treatment to ensure better outcomes. **Objective:** This study analyzed thyrotoxicosis epidemiology among Brazilian children (0-14 years) from 2019 to 2023, focusing on mortality and hospital morbidity in SUS institutions across Brazil's regions. **Methods:** An ecological, descriptive, and analytical approach used secondary data from DATASUS (ICD-10 E05). The study covered pediatric cases across Brazil's regions within the defined period. **Results:** The study recorded 10 deaths, predominantly in females (9 cases) and in the southeast region (5 deaths), followed by the north (3), northeast, and midwest (1 each). No deaths occurred in the south. Of 104 hospitalizations, 85 involved females and 19 males, with most cases (57.69%) in the 10-14 age group. The southeast led hospitalizations (56), reflecting regional disparities. **Conclusion:** Between 2019 and 2023, pediatric thyrotoxicosis showed a marked prevalence in females, both in mortality and hospitalizations, especially in the 10-14 age group. The southeast region had the highest burden of cases, surpassing the combined records of other regions. This highlights the need for improved epidemiological monitoring and targeted healthcare strategies, ensuring earlier detection and better management of thyrotoxicosis in the pediatric population.

THYROID EPIDEMIOLOGY

1112457 - EPIDEMIOLOGICAL REVIEW ON HYPOTHYROIDISM, RHEUMATOID ARTHRITIS AND TYPE 1 DIABETES MELLITUS IN SOUTHEAST BRAZIL BETWEEN 2019 AND 2023

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Introduction: Type 1 Diabetes Mellitus (T1DM) is often associated with autoimmune thyroid diseases, like hypothyroidism, which significantly impact the patients quality of life. Similarly, Rheumatoid Arthritis (RA), a chronic autoimmune inflammatory disease, is also linked to an increased prevalence of thyroid dysfunctions. Thus, thyroid hormone instability can affect glycemic control in diabetes and exacerbate inflammation symptoms in RA. **Methods:** This epidemiological review analyzes hospital morbidity related to hypothyroidism, RA, and T1DM in Southeast Brazil from December 2019 to December 2023. Utilizing data from the Hospital Information System of the Unified Health System (SIH/SUS), filters were applied for region and state, considering the location of hospitalization and residence. The objective is to map the incidence of these conditions and understand their interactions and impacts on public health. **Results:** Between 2019 and 2023, the Southeast region led hospital admissions for hypothyroidism, T1DM and RA, with 243,669 cases, 116,920 were in São Paulo. The North region recorded 70,963 admissions. These data highlight inequalities in healthcare access and infrastructure, underscoring the need for public policies in underserved regions. Between 2019 and 2023, hospitalizations for thyroid disorders associated with diabetes decreased by 5.31%, suggesting improvements in diagnosis and primary care access. Regarding thyroid disorders, T1DM, and RA the Southeast also leads hospitalizations for each disease. São Paulo contributed most data, except for RA: Minas Gerais had 7,834 hospitalizations and São Paulo 7,039. These data reveal the complexity of chronic health conditions in Brazil and highlight the impact of regional inequalities in the healthcare system, with overburdened hospitals in the Southeast. **Conclusion:** The evaluated data underscore significant regional disparities in Brazil, the Southeast region led hospitalizations for hypothyroidism, T1DM, and RA. The urgency for public policies is evident, as these disparities compromise care quality and worsen health conditions.

THYROID EPIDEMIOLOGY

1112647 - EPIDEMIOLOGY OF THYROIDITIS IN RIO DE JANEIRO

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Introduction: Thyroid diseases affect approximately 200 million people worldwide. It is important to understand the current prevalence and trends of this pathology concerning region, sex, race, and age. Thyroiditis, an acute inflammation of the thyroid gland, can present symptoms of hypothyroidism or hyperthyroidism. The most common types are Hashimoto's thyroiditis and subacute thyroiditis, also known as De Quervain's thyroiditis. **Objective:** To analyze the prevalence and associated factors of thyroiditis in Brazil from 2019 to 2023. **Methods:** This descriptive, quantitative epidemiological study focused on thyroiditis in the state of Rio de Janeiro from 2019 to 2023. Data were collected from the Hospital Information System (SIH/SUS) and included variables such as race, sex, and age group. **Results:** During the evaluated period in Rio de Janeiro, the Metropolitan I health macro-region had the highest number of hospitalizations due to thyroiditis, with 3,680 cases, followed by the Municipality of Rio de Janeiro with 3,676 cases. Among these, females accounted for most hospitalizations (2,927 cases), with white individuals being predominant (263 cases). In the analyzed age groups, Black and Brown individuals led hospitalizations, with 172 and 296 cases, respectively. In the same region and municipality, males had fewer hospitalizations, totaling 753 cases, with Black individuals leading (74 cases). In the analyzed age groups, Black and Brown individuals predominated, with 63 and 97 hospitalizations, respectively. **Conclusion:** In the state of Rio de Janeiro (2019-2023), the Metropolitan I macro-region had the highest number of hospitalizations due to thyroid disorders, primarily among females. Racial disparities were observed across age groups, with white individuals predominating among females, except in the 20-69 age group, and Black individuals predominating across all age groups among males. This study aims to inform public health decisions, focusing on women and different racial groups.

THYROID EPIDEMIOLOGY

1112569 - ESTABLISHMENT OF AGE- AND SEX-SPECIFIC REFERENCE INTERVALS FOR TSH AND FT4 IN HONG KONG

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Introduction: Thyroid function tests heavily rely on the reference intervals (RIs) of thyroid-stimulating hormone (TSH) and free thyroxine (FT4). TSH varies with ethnicities, geographical regions, age and sex. **Objective:** To evaluate the secular trends of TSH and FT4 from 2010 to 2019, and to establish the age- and sex-specific RIs of TSH and FT4 in Hong Kong. **Methods:** Laboratory test records of TSH and FT4 during 2010-2019 were retrieved from a representative electronic medical database in Hong Kong. Upon excluding individuals with prior diagnosis, drug prescription and/or procedures of thyroid dysfunction, thyroid cancer and/or pituitary disorder, adult cohorts with healthy thyroid were identified, which were stratified by measurement year, sex and age-groups ($\geq 18-30$, $\geq 30-40$, $\geq 40-50$, $\geq 50-60$, $\geq 60-70$, $\geq 70-80$, $\geq 80-90$, ≥ 90). Raw TSH and FT4 test results were harmonized across different institutions. We applied joinpoint regression to evaluate the secular trends of TSH and FT4. Exponentiating the 2.5th and 97.5th percentile of the log-transformed test results established the lower and upper limits of RIs respectively. **Results:** We identified adult cohorts comprising 1,947,689 and 770,626 individuals with TSH and FT4 measurement respectively during 2010-2019. Age was associated with TSH (per year increase in age, $\beta = 2.07 \times 10^{-3}$; $p < 0.001$) and FT4 ($\beta = -0.028$; $p < 0.001$), while female and male had significant different TSH and FT4 ($p < 0.001$). We observed ≥ 1 joinpoint for geometric mean of TSH and FT4 from 2010 to 2019 in all age-groups in both sexes, except the age-group ≥ 90 in male. By applying the yearly established age- and sex-specific RIs of TSH and FT4, 23.71% and 18.79% individuals defined as overt hypothyroidism by laboratory-specific RIs were reclassified to subclinical hypothyroidism and euthyroidism respectively. **Conclusion:** The secular trend of TSH and FT4 necessitated the annual establishment of age- and sex-specific RIs for TSH and FT4 in Hong Kong, potentially reducing the over-diagnosis of overt hypothyroidism.

THYROID EPIDEMIOLOGY

1112304 - HOSPITALIZATION BY THYROID DISORDERS RELATED TO IODINE DEFICIENCY IN BRAZIL BETWEEN AUGUST OF 2019 AND AUGUST OF 2024: AN EPIDEMIOLOGICAL ANALYSIS

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Introduction: Thyroid is an endocrine gland located in the anterior region of the neck, playing a fundamental role in metabolic regulation and human development. The secretion of T3 and T4 hormones primarily depends on the availability of intracellular iodine. Insufficient iodine can cause significant deficits, affecting fetal development, newborn and child nervous system development and metabolic function at any life stage. **Objective:** Present the epidemiological incidence of hospitalizations due to thyroid disorders related to iodine deficiency. **Methods:** This is a descriptive and quantitative epidemiological study developed from data obtained from DATASUS. **Results:** During the period, there was an average of 4.5 days of hospitalization due to thyroid disorders by iodine deficiency. The year with the highest average was 2021 (6.2) and the lowest in 2019 (3.1). The Central-West region (6.4) led the number of hospitalizations, followed by the Northeast (6.1) and South (5.6). The age group with the highest average (11.5) was 5 to 9 years old. Men had the lowest in 2019 (3.9) and the highest in 2024 (8.7). Women had a reduction between 2021 (5.7) and 2024 (3.7). White people had an increase in 2021 (5.8) and reduction in 2024 (3.3). Black population had an increase in 2024 (5.1). Emergency situations led the averages in 2022 and 2024 with 8 days in average, possibly because of the insidious manifestation of iodine deficiency, resulting in severe hypothyroidism and myxedema coma. **Conclusion:** Hospitalizations due to iodine deficiency are present in Brazil, with an average hospitalization of 4.5 days and Central-West leading. The most affected are black, 5 to 9 years and males. Its necessary to implement screening and health prevention strategies in individuals with iodine deficiency to reduce the incidence of thyroid disorders and consequences.

THYROID EPIDEMIOLOGY

1112319 - MORTALITY ASSOCIATED WITH THYROID DISORDERS IN BRAZIL: A REGIONAL ANALYSIS OF DEATHS FROM HYPOTHYROIDISM AND THEIR PUBLIC HEALTH IMPLICATIONS

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Introduction: Hypothyroidism, caused by thyroid or hormonal dysfunction, increases cardiovascular and obstetric risks, particularly in the elderly and pregnant women. Associated with higher all-cause mortality and comorbidities, hypothyroidism often faces poor diagnosis and specialized care. Addressing this public health challenge requires enhanced screening and interventions, especially for aging populations. **Objective:** The study evaluates variations in mortality rates due to hypothyroidism in Brazil, highlighting its public health impact and supporting strategies for prevention, diagnosis, and management. **Methods:** This is an epidemiological study with a quantitative, descriptive, and retrospective approach, focusing on deaths caused by “other hypothyroidisms.” Data were extracted from the Department of Informatics of the Unified Health System (DATASUS) through the 2013-2023 time series. Variables included death, ethnicity/race, sex, and age group, stratified by Brazilian regions. Data were imported from the Mortality Information System. **Results:** There was a significant increase in deaths related to hypothyroidism between 2013 and 2023, rising from 183 cases to 295. Regionally, the Southeast reported the highest number of cases (1,162), followed by the South (550) and the Northeast (365). The most prevalent age group was 60-69 years (881), followed by 70-74 years (547). The highest proportional increase occurred in the Southeast and South, with rises of 185% and 139%, respectively. The racial/ethnic analysis highlights a predominance of deaths among white individuals (1,400 cases), followed by mixed-race (743), black (150), Asian (12), and indigenous people (7). Mortality was higher among females, with 1,712 deaths compared to 665 among males. **Conclusion:** The study reveals increased hypothyroidism deaths in Brazil, mainly among the elderly, residents of the southeast and south, and women. These findings highlight the need to enhance early diagnosis and expand access to specialized care to reduce morbidity and mortality.

THYROID EPIDEMIOLOGY

1112261 - MORTALITY FROM MALIGNANT THYROID NEOPLASIA IN BRAZIL: AN EPIDEMIOLOGICAL ANALYSIS BY AGE GROUP AND REGION FROM 2010 TO 2023

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Introduction: The malignant thyroid neoplasia is one of the most common oncological pathologies of the endocrine system. Differentiated thyroid carcinomas represent the majority of cases, with a better prognosis when diagnosed early. The incidence of this cancer has increased in recent decades. However, underdiagnosis persists, particularly among asymptomatic patients, making it crucial to identify the age groups with the highest prevalence. **Objective:** Analyze thyroid cancer mortality across different age groups and regions in Brazil from 2010 to 2023. **Methods:** A descriptive epidemiological analysis was conducted on thyroid cancer mortality in Brazil from 2010 to 2023, using age and geographic data from DATASUS-TABNET. The literature search was based on the keywords Neoplasms and Thyroid, following Health Descriptors (MESH). The data were publicly available, so ethical committee approval was not required. **Results:** During the study period, 10,992 deaths from malignant thyroid neoplasia were recorded, with 90% (9,860) occurring in individuals over 50 years of age. The Southeast Region showed the highest mortality rate, with 39% (4,363), followed by the Northeast, with 30% (3,288). The lowest rates were observed in the North (6,8%) and Center-West (6,9%). The age groups most affected were 70-79 years (3,003) and over 80 years (2,692). Only the North showed higher mortality in the 60-69 age group. The Southeast recorded deaths across all age groups. The notable reduction in mortality among individuals under 49 years (1,062, 10%) reflects the progressive increase in deaths with advancing age. **Conclusion:** The majority of deaths occurred in people over 50 years, with a higher concentration in the Southeast. The significant decrease in mortality among younger individuals draws attention to age as a risk factor, highlighting the importance of early diagnosis and clinical monitoring in more vulnerable groups.

THYROID EPIDEMIOLOGY

1112264 - MORTALITY FROM MALIGNANT THYROID NEOPLASMS IN THE ELDERLY IN BRAZIL, 2013-2023

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Introduction: Thyroid cancer is the most common malignant endocrine neoplasm, accounting for 1% to 3% of all cancer cases. While papillary and follicular types have a good prognosis, undifferentiated types are more aggressive and lethal. Often asymptomatic and resembling other neck neoplasms, its early diagnosis is challenging, even with advancements in imaging techniques. **Objective:** To analyze thyroid cancer mortality in elderly individuals in Brazil between 2013 and 2023, identifying possible factors associated with these deaths in this population. **Methods:** This is a retrospective and descriptive study using data extracted from the Department of Informatics of the Unified Health System (DATASUS). The analyzed variables included Brazilian states, age groups, sex, and ethnicity. **Results:** During the analyzed period, 9,058 deaths from thyroid cancer were recorded. The years with the highest number of deaths were 2023 (982), 2021 (909), and 2019 (869). The states with the highest mortality were São Paulo (1,917), Rio de Janeiro (849), and Minas Gerais (722). The age group with the most deaths was 70 to 79 years (2,479), followed by those over 80 years (2,254) and 60 to 69 years (2,184). There were 5,971 deaths among women and 3,087 among men. White individuals were the most affected (4,980), followed by mixed-race individuals (3,147). **Conclusion:** Mortality from malignant thyroid neoplasms in the elderly in Brazil between 2013 and 2023 increased, with a higher prevalence among women, white individuals, and those over 70 years of age. São Paulo, Rio de Janeiro, and Minas Gerais recorded the highest numbers of deaths. The data highlight the need for specific regional strategies to improve early diagnosis and clinical management in vulnerable populations, aiming to reduce mortality from this cancer.

THYROID EPIDEMIOLOGY

1114174 - NATURAL HISTORY OF THYROID FUNCTION IN AGING: INDIVIDUAL PARTICIPANT DATA ANALYSIS OF 124,520 PARTICIPANTS

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Introduction: Age-specific thyroid function reference ranges have been proposed, but evidence is inconsistent. **Objective:** This study aimed to investigate aging-related thyroid function changes and its associations with mortality. **Methods:** We analyzed individual participant data from 30 cohorts (N=124,520; median age 60 years), excluding participants with thyroid disease or thyroid-altering medications. Associations between thyroid function and age were examined using linear mixed models, stratified by sex and cohort-specific iodine status. Annual changes in TSH and FT4 were estimated per individual and categorized into quintiles, with the highest and lowest defined as increasing and decreasing, respectively, and the rest as stable. Five thyroid changing patterns were identified based on combined TSH and FT4 changes. Cohort-stratified Cox models assessed associations between changing patterns and all-cause mortality. **Results:** Longitudinal thyroid function measurements were collected over a median follow-up of 7.4 years. TSH increased with age, with an increase from age 18 to 100 of 0.52 standard deviation (SD) (0.61 mIU/L) for women and 0.76 SD (0.99 mIU/L) for men with iodine sufficiency and 0.83 SD (0.85 mIU/L) in women, 0.94 SD (0.99 mIU/L) in men with iodine insufficiency. Wider reference intervals and more variations in longitudinal TSH changes were observed in adults aged ≥65. FT4 increased with age in iodine-sufficient regions and decreased in iodine-insufficient regions. Compared to stable thyroid function, unstable patterns were associated with higher all-cause mortality: HR 1.79 (1.56-2.05) for increasing TSH with stable/decreasing FT4, 2.34 (1.92-2.85) for increasing TSH and increasing FT4, 2.43 (1.98-2.97) for decreasing TSH with decreasing FT4, and 1.91 (1.64-2.21) for decreasing TSH with stable/increasing FT4. **Conclusion:** Aging-related thyroid function changes varied by sex and iodine status. Most individuals had stable thyroid function with a slight TSH increase, though older adults displayed greater variability. Unstable thyroid changing patterns were associated with higher all-cause mortality.

THYROID EPIDEMIOLOGY

1112307 - REFERENCE INTERVALS FOR TSH BY AGE AND SEX IN OLDER ADULTS: A PERUVIAN STUDY

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Introduction: Thyroid dysfunction is highly prevalent. Clinical guidelines recommend the TSH test as the most sensitive and specific marker of thyroid function. This TSH should be validated for a population considering its characteristics. TSH levels vary with age, and older adults present higher values. We lack population-based studies of normal TSH ranges in the older adult population. **Objectives:** To determine the reference interval of TSH in older adults in the Peruvian population according to age. **Methods:** A retrospective, cross-sectional, descriptive study. We reviewed patient databases and TSH results from hypothyroidism screening campaigns conducted on healthy individuals in 3 cities in Peru between December 2023 and September 2024. Data from individuals over 60 years were analyzed. Exclusion criteria: Previous thyroid disease, use of antithyroid drugs or levothyroxine, autoimmune diseases, goiter. TSH was measured by electrochemiluminescence immunoassay (sensitivity of the assay was 0.005100 µUI/mL). We excluded TSH results above 10 mUI/L and below 0.1 mUI/L. Patients were stratified by decades. Statistical analysis was performed with STATA version 18. Percentiles 2.5 and 97.5, and confidence interval of TSH were calculated according to age groups (60 years and older). **Results:** The analysis included 1477 patients (78.4% women). The 2.5 and 97.5 percentiles for TSH in ages between 60-69, 70-79, and over 79 years were: For women: 0.63, 7.28; 0.67, 8.5 and 0.64, 8.41; and for men: 0.58, 7.28, 0.65, 9.19, and 0.26, 9.39. **Conclusion:** The reference intervals in adults over 60 years in Peru differ from the literature, showing higher values, mainly in the upper limit. This would change the approach to diagnosis and treatment in our population.

THYROID EPIDEMIOLOGY

1112637 - THE DISTINCT PROPHILE OF MEN2 GERMLINE VARIANTS IN THE RET GENE IN BRAZIL: AN UPDATE OF 20 YEARS OF EXPERIENCE IN ONE CENTER

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Introduction: Germline pathogenic variants (PVs) in the RET gene are responsible for the multiple endocrine neoplasia type 2 (MEN2) syndrome, a hereditary autosomal dominant syndrome with a high risk for medullary thyroid carcinoma (MTC). The identification of the clinical syndrome and of a germline PV is critical for the adequate management of affected individuals and their family members (FM), since the early diagnosis increases the chances of cure for MTC. Here we describe the prevalence of the RET germline PVs screened at a reference center for MTC patients and molecular analysis. **Methods:** Germline genetic screening (GS) for the RET gene was performed by Sanger sequencing of patients with MTC and their family members. **Results:** From 2003 to 2023, 1,537 individuals were analyzed; 630 (41%) carried germline PVs in the RET gene, of whom, 114 (7.4%) index and 516 (33.6%) FM. GS was negative for germline RET variants in 209 (13.6%) patients with MTC and 662 (43.1%) FM. Thirty-six (2.3%) individuals harbored variants of uncertain significance (VUS). In total, 39 germline variants were found (29 PV and 10 VUS). The most frequent variants were in codons 804 (21.8%), 533 (21.2%), 634 (21%), 918 (13.2%), and 791 (9.3%). The most frequent aminoacid changes were: p.Gly533Cys (21.2%), p.Val804Met (14.6%), p.Met918Val (11.1%), p.Cys634Tyr (9.9%), p.Cys634Arg (8.4%), p.Val804Leu (7.2%), Tyr791Phe (6.6%), p.Ser891Ala (4.2%), p.Cys618Arg (2.3%), p.Leu790Phe (2.3%), and p.Met918Thr (2.1%). Interestingly, the RET variants distribution differ in the Brazilian territory. The variant p.Gly533Cys was mostly found in Espírito Santo State, while p.Val804Met and Cys634Tyr in São Paulo State and p.Met918Val and p.Val804Leu in Ceara State. **Conclusion:** In our sample, there was great variability in the RET pathogenic variants compared to series published in Europe and other continents, which reflects the proportion of the unique combination of European, Amerindian and African ancestries in the Brazilian genomic mosaic.

THYROID EPIDEMIOLOGY

1112211 - THE EFFECT OF AIR TEMPERATURE AND BMI ON THE THYROID STIMULATING HORMONE : A LONGITUDINAL PANEL ANALYSIS USING COMMUNITY-BASED COHORT STUDY

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Introduction: Thyroid stimulating hormone (TSH) has been recommended for the screening method to evaluate thyroid function. Many environmental or individual factors could affect the TSH level, therefore the normal reference range remains unclearly. Especially, air temperature has been reported to be a possible factor for TSH level. **Methods:** We conducted an epidemiologic study to examine the effect of air temperature and individual characteristics on TSH level, using a Korean community-based cohort study during 10 years. Panel analyses were incorporated to analysis repeatedly measured parameters. **Results:** At baseline among 2644 participants, mean age was 64.8±8.4 and females were 1473 (55.7%). There were 376 current smokers (14.2%) and the mean BMI was 24.4±3.3 kg/m². Median TSH was 1.68 mIU/L (IQR: 1.35). The regional mean annual temperature was 18.3±7.3 °C, ranging from -8.5±2.1 °C in January to 25.0±1.6 °C in August. A 1 °C increase in temperature was associated with a 0.005 decrease in log-transformed TSH levels (95% CI: -0.007 to -0.004; P<0.001), equivalent to a 1.2% reduction of TSH level. Compared to males, females showed significantly higher TSH level, and current smoker showed significantly lower TSH level. BMI has significant positive association with TSH level. Compared to summer season, TSH levels were significantly higher in other all seasons. **Conclusion:** Our study showed the significant effect of air temperature on TSH level. In addition to individual characteristics such as age, gender, smoking, and obesity, air temperature at the time of blood sample should be considered when interpreting TSH levels.

THYROID EPIDEMIOLOGY

1112280 - THE IMPACT OF COVID-19 PANDEMIC ON THYROID FUNCTION: ANALYSIS OF MORTALITY BEFORE (2016-2020) AND AFTER THE PANDEMIC (2021-2024)

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Introduction: The thyroid gland, a key regulator of metabolism and body homeostasis, can be significantly impacted by COVID-19, a respiratory disease caused by SARS-CoV-2. Thyroid complications associated with SARS-CoV-2 infection, including hypothalamic-pituitary-thyroid (HPT) axis disorders, have been linked to notable mortality rates both before and after the COVID-19 pandemic. **Objective:** We aimed to quantify the incidence of mortality caused by thyroid disorders triggered by COVID-19 infection. The pre- and post-pandemic periods were analyzed, considering regional differences within Brazil, as well as sex, race, and age groups. **Methods:** This epidemiological, cross-sectional, and retrospective study utilized public data from the Department of Informatics of the Brazilian Health System (DATASUS). Mortality associated with thyroid diseases was evaluated during the pre-pandemic (2016-2020) and post-pandemic (2021-2024) periods. **Results:** In the pre-pandemic period (2016-2020), there were 198 deaths, with a peak of 63 in 2019. In the post-pandemic period (2021-2024), there were 197 deaths, peaking at 60 in 2023. Regional analysis revealed the following mortality rate trends (per 100,000 population): North: Decreased from 15.04 to 7.70; Northeast: Increased from 5.22 to 7.75; Southeast: Increased from 4.15 to 4.99; South: Decreased from 4.88 to 3.95; Central-West: Decreased from 14.03 to 9.28. Females accounted for 71.8% of deaths in both periods, while the highest mortality rates were observed among individuals aged 80 years and older, with 45 deaths in the pre-pandemic period and 44 in the post-pandemic period. **Conclusion:** COVID-19 significantly influenced mortality associated with thyroid disorders during both pre- and post-pandemic periods. Higher mortality rates were observed among older adults and females. Regional trends highlighted increasing rates in the Northeast and Southeast regions of Brazil.

THYROID EPIDEMIOLOGY

1112585 - THE INCIDENCE OF MALIGNANT THYROID NEOPLASM IN WOMEN AGED 40 TO 44 IN THE SOUTHEASTERN REGION OF BRAZIL IN THE YEAR 2024

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Introduction: Malignant neoplasms of the thyroid gland have shown notable epidemiological records in recent decades, being three times more common in females. In this context, this study aimed to evaluate this phenomenon in the Southeastern Region of Brazil. **Methods:** This is an epidemiological, descriptive, cross-sectional, and retrospective study on the incidence of malignant thyroid neoplasms in women aged 40 to 44 years in the Southeastern Region of Brazil in 2024. Information was collected on reported cases from the Cancer Information System (SISCAN), available in the Department of Informatics of the Unified Health System (DATASUS). Variables used included age group, the state of diagnosis, month/year of diagnosis, the state of treatment, and month/year of treatment. **Results:** Based on the established criteria, it was observed that the Southeast had the highest number of cases (168) among the Brazilian regions. There was a higher recurrence in São Paulo (70.2%) and lower in Espírito Santo (2.4%). The highest number of diagnoses was found in women aged 41 (26.8%) and 43 (23.8%). Additionally, 53.6% of cases were confirmed in the first quarter of 2024, of which 46.7% were not treated. There is no information on the therapeutic approach in 105 cases (62.5%). **Conclusion:** A high incidence of malignant thyroid neoplasms was observed among females in the Southeast, particularly in São Paulo, a major health hub in the country. The diagnosis of the pathology frequently occurs in women aged 41 and 43, and therapeutic measures are not recorded in the information systems for the majority of cases. These findings suggest the importance of public health policies focused on the continuous monitoring of thyroid cancer cases. Furthermore, it is necessary to improve strategies aimed at reducing disparities in the quality of oncological care in this region.

THYROID EPIDEMIOLOGY

1114286 - THE RELATION BETWEEN AGE AND GENDER IN THYROTOXICOSIS HOSPITALIZATIONS IN BRAZIL FROM 2014 TO 2024: AN ECOLOGICAL STUDY

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Introduction: Thyrotoxicosis is a hyperdynamic and hypermetabolic syndrome that results in a multisystem network of clinical manifestations due to high levels of circulating thyroid hormone in the body. Characteristic symptoms include tachycardia, tremor, palmar hyperhidrosis, ophthalmopathies, irritability, heat intolerance, fatigability, palpitations, polyphagia, and unintentional weight loss. Despite its clinical relevance, epidemiological data on the correlation between age, gender, and hospitalization for this condition in Brazil are still scarce. **Objective:** To analyze the distribution of thyrotoxicosis by age and gender in Brazil from January 2014 to December 2024. **Methods:** Cross-sectional, descriptive, ecological and exploratory study, based on the database of the Department of Hospital Information of the Unified Health System (SIH/DATASUS) between January 2014 and December 2024. Hospitalizations registered with the ICD-10 corresponding to Thyrotoxicosis were considered, covering Race, Type of Care, Annual Distribution and Age Group. **Results:** A total of 133 hospitalizations for thyrotoxicosis in Brazil were analyzed between 2014 and 2024. The age distribution revealed a higher incidence among 10-14 years (24.06%) and 15-19 years (16.54%), evidencing a predominance of cases in children and adolescents. For adults, there is a tendency for a progressive decrease in the older age groups, with only the 40-49 age group standing out (11.28%). There was a predominance of females (75.19%) compared to males (24.81%), reinforcing the known predisposition of women to thyroid diseases. Regarding the distribution by race/color, the majority of affected patients are mixed race (56.39%), followed by whites (29.32%) and blacks (6.77%). The findings suggest a significant impact of thyrotoxicosis in younger age groups and a significant predominance among women, corroborating epidemiological patterns already described in the literature. **Conclusion:** Thyrotoxicosis predominates in children and adolescents, especially in women. Most hospitalizations occurred among mixed race people, suggesting the impact of socioeconomic factors. Early screening in young and vulnerable populations is essential to prevent complications and reduce hospitalizations.

THYROID EPIDEMIOLOGY

1112263 - THYROID DISORDERS CAUSED BY IODINE DEFICIENCY AND THEIR FINANCIAL IMPACT ON THE BRAZILIAN UNIFIED HEALTH SYSTEM BETWEEN 2014 AND 2024

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Introduction: The thyroid is an endocrine gland that secretes hormones responsible for maintaining metabolic balance. The synthesis and secretion of these hormones (T3 and T4) depend on iodine, with variations in its concentration leading to hyper- or hypoactivity of the gland. Clinically, these conditions manifest as hypothyroidism, hyperthyroidism, or endemic goiter. Within the Unified Health System (SUS), thyroid disorders impose significant financial and social impacts. **Objective:** Present the financial impact and regional distribution of hospitalizations due to thyroid disorders related to iodine deficiency within the Brazilian Unified Health System (SUS) from 2014 to 2024. **Methods:** This is a descriptive and quantitative epidemiological study developed from data obtained from DATASUS/BR. **Results:** During the period, expenses totaled BRL 2,196,442.80, with 74% allocated to hospital services. The Southeast region recorded BRL 836,342.36, representing 38% of the national total. It also exceeded the amounts per Hospitalization Authorization (AIH) and hospitalization, both at BRL 923.71. In contrast, the Midwest region had the lowest cost: BRL 99,376.29, with AIH and hospitalization values at BRL 764.43, higher than those recorded in the North: BRL 649.13. In the Northeast, professional services reflect the cost of specialists, totaling BRL 158,284.61. Meanwhile, the South moderated professional service expenses (BRL 51,791.01), yet AIH and hospitalization costs reached BRL 939.88. The total cost increased from BRL 168,287.61 in 2016 to BRL 276,288.09 in 2019. Hospital service costs decreased from BRL 144,836.76 in 2014 to BRL 121,165.35 in 2024. **Conclusion:** Iodine deficiency-related thyroid disorders impose a financial burden on the Brazilian Unified Health System (SUS). This analysis highlights a rising trend in expenditures, as well as disparities in resource allocation, which can be attributed to challenges in healthcare access, the complexity of cases, and hospital infrastructure. The findings underscore the need for strategies to reduce regional inequalities and optimize available resources.

THYROID EPIDEMIOLOGY

1112351 - THYROTOXICOSIS IN BRAZIL: A TIME ANALYSIS OF HOSPITALIZATIONS AND THEIR ECONOMIC IMPACT ON THE BRAZILIAN PUBLIC HEALTH SYSTEM (2010-2023)

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Introduction: Thyrotoxicosis is a condition characterized by an excess of the thyroid hormones in the bloodstream, which can lead to serious complications that often require hospital care. Few studies in Brazil explore thyrotoxicosis hospitalizations, making this research vital to understanding its health system impact and improving care. **Objective:** Identify the epidemiological profile of hospitalizations due to thyrotoxicosis in Brazil between 2010 and 2023. **Methods:** This is an epidemiological, descriptive and quantitative study based on hospital admissions data for thyrotoxicosis in Brazil (2010-2023). The data was extracted from the Hospital Information System of the Unified Health System (SIH/SUS). Variables included region, year, age, gender, race, hospital stay duration, and mortality rate. **Results:** During the period analyzed, 8,822 hospitalizations were recorded, totaling 60,835 days, with an average length of stay of 6.9 days. There were 168 deaths, corresponding to a mortality rate of 1.90%. A gradual reduction in hospitalization time was observed, suggesting advances in treatment. Women had 6,862 deaths and a mortality rate of 1.92, while men had 1,960 and a rate of 1.84, although women had a shorter average stay than men. Mortality increased with age, reaching 12.14% in patients aged 80 or over, possibly due to the greater complexity of caring for the elderly. In the Southeast region, there were 5,209 hospitalizations, with the lowest average length of stay (5.7 days) and mortality rate (1.61%). The North and Center-West regions had higher mortality rates (3.97% and 3.68%, respectively) and longer lengths of stay, influenced by regional characteristics. **Conclusion:** This study highlights the impact of thyrotoxicosis in Brazil, where complications increase mortality and hospitalizations. Despite shorter stays indicating better management, elderly mortality remains high, underscoring the need for targeted public health strategies and further research.

THYROID EPIDEMIOLOGY

1112660 - THYROTOXICOSIS IN BRAZIL: EPIDEMIOLOGICAL INSIGHTS AND REGIONAL DISPARITIES

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Introduction: Thyrotoxicosis, characterized by elevated T3 and T4 levels with suppressed TSH, is a significant public health concern due to its clinical impact and complications, such as thyroid storm. In Brazil, the leading cause is Graves disease, followed by contributing factors like amiodarone use and iodine excess. **Objectives:** This study aims to investigate thyrotoxicosis in Brazil, focusing on its prevalence, primary causes, and clinical impacts while considering sociodemographic and regional variables. **Methods:** Data were collected from the Brazilian Unified Health Systems (SUS) Department of Informatics (DataSUS), TabNet, and the Notifiable Diseases Information System (SINAN) on thyrotoxicosis cases reported between 2021 and 2023. A total of 2,299 cases were identified across the North, Northeast, Central-West, South, and Southeast regions of Brazil. The data were analyzed to define the epidemiological profile of the disease, considering variables such as year, region, age group, race/ethnicity, and gender. **Results:** The highest concentration of cases was observed in the Southeast (41%), followed by the Northeast (27%) and South (18%). The Central-West and North regions reported lower proportions. Mixed-race individuals were the most affected (33%), followed by White (30%) and Black individuals (17%). Indigenous and Asian populations showed lower prevalence rates. Among 15.8 million male inpatients, 62% were in the Northeast and 41% in the Southeast. Among 21.2 million female inpatients, the Southeast led with 39%, followed by the Northeast with 28%. **Conclusion:** The study's findings highlight regional, gender, and racial disparities in thyrotoxicosis prevalence. This scenario underscores the need to address social determinants of health in managing the disease, emphasizing early diagnosis, particularly in regions with limited access to public health services and among socioeconomically vulnerable groups. Further research is needed to explore the complexity of the condition and the factors contributing to increased morbidity and mortality.

THYROID EPIDEMIOLOGY

1112278 - THYROTOXICOSIS IN BRAZIL: MORTALITY AND HOSPITAL MANAGEMENT IN 2023

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Introduction: Thyrotoxicosis, characterized by an excess of thyroid hormones, represents a significant public health challenge due to its severe complications. This study aims to analyze mortality and hospital management of thyrotoxicosis cases in Brazil in 2023. **Methods:** Data were collected from the Unified Health System (SUS) and included information on deaths, hospitalizations, mortality rates, and the values of approved and performed hospital services. Statistical analysis was conducted using the t-test to determine the significance of monthly variations and differences among various demographic and regional categories. **Results:** In 2023, there were 186 deaths related to thyrotoxicosis. The highest mortality rate was observed in January (4.66) and the lowest in March (4.33). The Southeast and Northeast regions concentrated the highest number of deaths (75 and 59, respectively). The age group of 80 years or older represented 25.13% of the deaths. There was a significant discrepancy between the values of approved and performed hospital services, with the latter often being higher ($p < 0.0001$). The data indicate a concentration of mortality in the most populous and economically developed regions, suggesting that factors such as population density and access to healthcare services may influence the outcomes. The high mortality in the older age group highlights the vulnerability of this population. The discrepancy between approved and performed hospital service values points to possible inadequacies in funding and the need for a review of SUS reimbursement policies. **Conclusion:** This study reveals that thyrotoxicosis continues to be a significant public health issue in Brazil, with important regional and demographic variations. Hospital management faces challenges, particularly regarding adequate funding of services. Targeted interventions to improve access to care and financing may help reduce mortality associated with thyrotoxicosis.

THYROID EPIDEMIOLOGY

1112352 - TRACKING HYPOTHYROIDISM ASSOCIATED WITH IODINE DEFICIENCY: A SNAPSHOT OF THE BRAZILIAN REALITY

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Introduction: Despite strategies such as the iodization of table salt, iodine deficiency remains a public health issue in Brazil, given the high prevalence of hypothyroidism associated with iodine deficiency. Patients with thyroid dysfunction may develop cognitive deficits, cardiovascular disorders, and neurological impairments. **Objective:** To analyze epidemiological patterns of hospitalizations and deaths related to thyroid disorders associated with iodine deficiency in Brazil. **Methods:** This is an epidemiological study with a quantitative analysis of hospitalizations and deaths in Brazil due to thyroid disorders related to iodine deficiency between 2019 and 2023. Data were collected from the Mortality Information System (SIM) provided by the Department of Informatics of the Unified Health System (DATASUS). The variables analyzed included Brazil, federal units, thyroid disorders related to iodine deficiency, male and female sex, all age groups, and the period between 2019 and 2023. **Results:** São Paulo, Minas Gerais, and Pernambuco accounted for the highest number of hospitalizations, representing 45.1% of the total in Brazil. The prevalence of hospitalizations was higher among females (79.3%) compared to males (20.7%). The most affected age group was 50 to 59 years, with 18.5% of hospitalizations, followed by the 40 to 49-year age group, with 18.2%. Between 2019 and 2023, 15 deaths were recorded related to thyroid disorders associated with iodine deficiency, with the highest frequency among the elderly aged 80 years or older. Males were the most affected, representing 53% of the deaths. **Conclusion:** The analysis shows a consistent increase in cases with advancing age. This highlights the need to develop more effective therapeutic approaches to identify causes early, along with adequate supplementation and prophylaxis, aiming to reduce cases and improve patients' quality of life.

THYROID GENETICS

1112375 - APPRAISAL OF CONGENITAL HYPOTHYROIDISM-ASSOCIATED SLC5A5 GENE VARIANTS ACCORDING TO THE AMERICAN COLLEGE OF MEDICAL GENETICS AND GENOMICS GUIDELINES

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Introduction: Iodide transport defect (ITD) is a rare autosomal recessive disorder caused by defective iodide accumulation in the thyroid follicular cell due to biallelic loss-of-function variants in the sodium/iodide symporter (NIS)-encoding gene SLC5A5, resulting in congenital hypothyroidism. The increasing use of next-generation sequencing technology has revealed an enormous number of novel variants of uncertain clinical significance in congenital hypothyroidism-associated genes. **Objective:** To evaluate the pathogenicity of congenital hypothyroidism-associated SLC5A5 gene variants using the American College of Medical Genetics and Genomics (ACMG) guidelines in a quantitative Bayesian framework. **Methods:** Systematic evaluation of congenital hypothyroidism-associated SLC5A5 gene variants according to the ACMG guidelines, integrating allele frequency, computational evidence, functional assays, patient phenotype, and family segregation studies. **Results:** The bibliographic search identified 60 SLC5A5 gene variants, of which 37% were classified as pathogenic, 23% as likely-pathogenic, and 33% as variants of uncertain significance (VUS). Low allele frequency and in silico predictions supporting a deleterious effect of the variant were insufficient to reach likely-pathogenic classification. The availability of functional studies assessing the effect of the variants on NIS-mediated iodide transport was critical for reclassifying VUS into clinically actionable categories (e.g., benign or pathogenic). Variants affecting thyroid iodide accumulation showed a strong association with pathogenicity, underscoring the diagnostic value of thyroid scintigraphy in iodide transport defect-causing SLC5A5 gene variants. **Conclusion:** The improvement of variant classification relies on a multidisciplinary approach integrating different data sources, including medical records, genetic data, and experimental functional studies. Significantly, functional studies have been instrumental in addressing the challenges of variant classification, while the assessment of thyroid iodide accumulation emerges as a key criterion supporting the classification of SLC5A5 gene variants. Taken together, our findings provide a robust framework for the accurate interpretation of SLC5A5 gene variants and represent a significant advance in the diagnosis of congenital hypothyroidism.

THYROID GENETICS

1112379 - IN SILICO ANALYSIS OF TRKA PROTEIN: IMPLICATIONS FOR RADIATION-INDUCED THYROID CARCINOGENESIS

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NTRK1 encodes TrkA, a protein that is critical for cellular growth and survival. Alterations in this gene, including single nucleotide polymorphisms (SNPs) and gene rearrangements, have been linked to thyroid cancer associated with radiation exposure. However, the impact of specific NTRK1 variants on the TrkA protein remains largely underexplored. To identify possible biomarkers of radiation-induced tumors and therapeutic targets, we employed a series of bioinformatic tools and databases to evaluate the impact of deleterious NTRK1 variants on protein structure and function. Protein structure data were retrieved from the Universal Protein Resource (UniProt), and SNP data were obtained from the Single Nucleotide Polymorphism Database (dbSNP, NCBI). Thirteen tools were used to evaluate the impact of SNPs: PredictSNP1.0 (integrating SIFT, PolyPhen-1/2, MAPP, SNAP, and other algorithms) to predict functional consequences; iStable, MuPRO, and I-Mutant to assess changes in protein stability; and DynaMut to model molecular interactions and structural flexibility changes. After removing duplicates and merging the records, we obtained 120 SNPs that caused 120 amino acid changes. The rs145081333 (T705M) variant was classified as deleterious by all tools and demonstrated a significant impact on protein structure and function, reduced protein stability in stability analyses (iStable), altered interactions with surrounding amino acids, adding three hydrophobic bonds, and removing five polar bonds, as shown by DynaMut. Nine other SNPs were considered deleterious by at least 87.5% (n = 7) of the PredictSNP1.0 tools. These SNPs also showed a strong potential to disrupt protein structure and biological function. In conclusion, we identified several deleterious SNPs in NTRK1 that contribute to thyroid carcinogenesis, particularly in radiation-induced cases.

THYROID GENETICS

1112393 - PREVALENCE OF DICER1 MUTATIONS IN A BRAZILIAN RETROSPECTIVE COHORT OF THYROID CARCINOMA

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Introduction: DICER1 gene encodes a ribonuclease III enzyme critical for processing pre-microRNAs, which play a key role in gene regulation. Mutations in DICER1 have been implicated in a spectrum of thyroid lesions, ranging from benign conditions to aggressive malignancies. Despite extensive research globally, the prevalence and implications of somatic DICER1 variants in thyroid neoplasms remain incompletely understood, in diverse populations. **Objective:** This study seeks to unravel the prevalence and spectrum of somatic DICER1 variants in thyroid lesions, evaluate the relationship between DICER1 mutations and additional genetic alterations, and elucidate their roles in the transition from benign to malignant thyroid neoplasms. **Methods:** RNA-Seq libraries were prepared from six low-risk thyroid neoplasm, 61 well-differentiated thyroid carcinoma as and five paired normal thyroid tissues using TruSeq Stranded RNA Library Prep Kit. Sequencing was performed on NextSeq 2000 platform. Single nucleotide variations and insertions or deletions (InDels) were identified using the Genome Analysis Toolkit (GATK). DICER1 variants, as well as genetic alterations in other key driver genes, were used the maftools package in R. **Results:** The overall prevalence of somatic DICER1 variants was 7,4% (5/67). Among these, were detected in 17% (3/17) of pediatric cases and 4% (2/50) of adult cases. Notably, all DICER1-positive cases belonged to the follicular subtype of papillary thyroid cancer (fPTC). In adults exhibited an absence of genetic alterations activating the MAPK and PIK3 pathways, while in pediatric co-occurrence with AGK::BRAF fusion was detected. Remarkably, two DICER1 loss-of-function variants, p.E1705K and p.Q812*, were identified in a multifocal fPTC measuring 8 cm. This tumor displayed extrathyroidal extension and angiolymphatic invasion but lacked other key mutations. **Discussion:** The genetic background and age may influence the prevalence of DICER1 variants in adult and pediatric populations in Brazil. A more comprehensive analysis is needed to clarify the role of these variants in thyroid cancer.

THYROID GENETICS

1112658 - RET GENETIC VARIANTS PROFILE IN MEDULLARY THYROID CANCER TUMORS

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Introduction: Medullary thyroid carcinoma (MTC) is a malignant neoplasm that arises from C cells of the thyroid gland. MTC may occur sporadically or as part of the inherited cancer syndrome multiple endocrine neoplasia type 2 (MEN 2). Germline mutations in the RET oncogene are responsible for hereditary MTC, and somatic mutations are frequently found in sporadic MTC tumors. Furthermore, clinical variability among carriers of the same germline variant suggests the presence of genetic modifiers. **Objective:** To identify somatic RET variants in patients with hereditary or sporadic MTC. **Methods:** Eighteen patients with MTC were included: 2 hereditary cases (germline variants p.Cys634Tyr and p.Met918Val) and 16 sporadic cases. DNA was extracted from paraffin-embedded tissue using the QIAamp DNA FFPE Tissue Kit. RET exons 11, 14, and 16 were amplified by PCR, followed by Sanger sequencing. Among the 18 samples analyzed, 12 were from primary tissues, and 6 were from metastatic lymph nodes. **Results:** The somatic variant p.Met918Thr was detected in seven sporadic cases (43.7%) and, interestingly, in one patient carrying the germline p.Cys634Tyr variant, suggesting a possible second-hit event. Other somatic variants were also identified. **Conclusion:** The results of this study reinforce the association between the p.Met918Thr variant and sporadic medullary thyroid carcinoma. The identification of this variant in a hereditary case also highlights the genetic complexity of MTC, demonstrating a possible interaction between germline and somatic mutations. These findings, in line with the literature, emphasize the importance of molecular profiling for prognosis and personalized treatment, considering the genetic heterogeneity of the disease.

THYROID GENETICS

1112435 - TELOMERE DYSFUNCTION AND GENETIC PREDISPOSITION IN FAMILIAL PAPILLARY THYROID CARCINOMA: PRELIMINARY STUDY

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Introduction: Familial papillary thyroid cancer (fPTC) is an uncommon and not well-defined clinical entity. Although an imbalance of the telomere-telomerase complex has also been reported in fPTC, there are conflicting observations in the literature regarding telomere length (TL) between affected and unaffected fPTC and sPTC subjects. Moreover, the genetic basis of fPTC remains unclear. **Objective:** In this study we aim to investigate if rare germline variants have a role in the familial form and cause alterations of still unknown cellular and/or molecular mechanisms, including defects in the telomere dysfunctions. **Methods:** A panel of five Sardinia families was identified. Blood samples were obtained from 26 patients: 15 with fPTC, 8 unaffected family members (UFM) and 3 with multinodular goiter (MNG). TL was determined using quantitative fluorescence in situ hybridization (Q-FISH) and Whole Exome Sequencing (WES) to identify new predisposing genes of thyroid cancer and expand our current understanding of the genetic basis of the disease. **Results:** fPTC and MNG displayed a reduction in telomere fluorescence (Q-FISH value: 86,4±11, 85,51±5, respectively) compared with UFM (110,2±14). fPTC patients have shorter telomeres compared to UFM group (p<0.001). Until now, the WES analysis identified c.254C>T (p.Ser85Leu) missense germline variant in PDZK1IP1 gene in two probands from one family. **Conclusions:** Although preliminary, our results reinforce the hypothesis that TL is significantly correlated with susceptibility to PTC. WES analysis identified PDZK1IP1 variant as a likely novel candidate susceptibility gene for fPTC, but further analysis in other family members is needed to confirm the role of this variant in the pathogenesis of fPTC.

THYROID GENETICS

1112204 - THE MOLECULAR LANDSCAPES OF BENIGN AND LOW-RISK MALIGNANT NODULES OF THE THYROID

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Introduction: The preoperative risk-stratification of thyroid nodules based on molecular testing needs further optimization. **Objective:** A prospective cohort study was conducted to 1) assess an infrastructure for thyroid nodule molecular analysis, 2) describe mutational patterns of thyroid nodules, 3) develop strategies for molecular variant calling of thyroid nodules. **Methods:** Blood and thyroid tissue were collected from patients with thyroid nodules more than 1.5 cm and BSRTC IV-VI on preoperative cytology. Whole genome sequencing (WGS) of DNA and total RNA was performed. Whole-blood DNA WGS was used as subtraction in the tumor/normal somatic analysis. In house bioinformatics pipeline was applied. **Results:** Thirty-two patients [males/females: 6/26; age (range) 22-81 years] were included. The histological diagnosis revealed: n=9 benign nodules (BN), n=10 follicular adenomas (FA), n=4 follicular thyroid carcinoma (FTC), n=6 papillary thyroid carcinoma (PTC), n=3 oncocyctic carcinoma (OC). The tumor fraction was $\geq 20\%$ for all samples and highest for FTC (61%-85%). No oncogenic variants were identified in half of both benign and malignant nodules. Three PTCs had a BRAFV600E mutation, while BRAFK601E was found in one FA. One FTC harbored a TSC1 splice variant. EIFAX variants were found in both benign and malignant follicular tumors (n=3), while variants in SPOP, SPEN, TSHR, KMT2A, KMT2D, KEAP1, and PTEN were identified only in benign tumors. No RAS variants were identified. The copy number alterations (CNA) profile was quiet in most nodules [11/19 benign; 6/13 malignant]. No FTC had a quiet CNA profile. Two FTCs, one OC, two FA and one BN showed wide-scale amplifications/loss-of-heterozygosity. Transcriptome analysis revealed 100% thyroid carcinoma classification in all FTC and OC. **Conclusion:** The tissue samples were of sufficient quality and confirmed previous findings in terms of mutation patterns in benign and malignant thyroid tumors. CNA profiles seem to have an impact on the development of follicular thyroid tumors.

THYROID GENETICS

1114193 - TUMOR HETEROGENEITY BETWEEN PRIMARY LESIONS AND CERVICAL LYMPH NODES LESIONS IN DIFFERENTIATED THYROID CANCER

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Introduction: Cervical lymph nodes (CLN) are the most common metastatic sites in differentiated thyroid cancer (DTC). While progress in tumor heterogeneity is notable, studies on heterogeneity between primary and CLN lesions in DTC remain limited. **Objective:** To analyze tumor heterogeneity between the primary lesions and CLN lesions based on genetic characteristics and its relationship with clinical characteristics and efficacy of ¹³¹I therapy in patients with DTC. **Methods:** From May 2024 to March 2025, 45 DTC patients with CLN metastasis treated at Peking Union Medical College Hospital were enrolled. Baseline data were retrospectively collected via the medical record system. Genetic testing was performed on their primary and CLN lesions respectively. These patients were further divided into synchronous (≤ 6 months) and asynchronous (> 6 months) groups according to the time - interval between primary and CLN lesions for subgroup analysis. **Results:** The consistency rate of genetic testing results between the primary lesions and CLN lesions was 91.1% (41/45). Compared with the CLN lesions, the BRAFV600E mutation rate in the primary lesions was higher, while the TERT mutation rate was lower. No difference were observed in the RET fusion mutation rate and the NTRK3 fusion mutation rate. The subgroup analysis showed that compared with the CLN lesions in the synchronous group, that in the asynchronous group had a higher BRAFV600E mutation rate and TERT mutation rate, but relatively lower RET fusion mutation rate and NTRK3 fusion mutation rate. The consistency rate in the asynchronous group was higher than that in the synchronous group (92.9% vs. 90.3%). **Conclusion:** The differences in the gene mutation profiles between the primary DTC lesions and CLN lesions suggested spatial heterogeneity in DTC cells, and that between the synchronous group and the asynchronous group further indicates the temporal heterogeneity. The relationship between these heterogeneities and the clinicopathological features and ¹³¹I treatment characteristics warrants further study.

THYROID HORMONE ACTION

1112416 - A NEW NATIONAL RARE THYROID DISEASE SERVICE ENABLES EARLY DIAGNOSIS AND MANAGEMENT OF RARE FORMS OF THYROID DISEASE

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Introduction: Some forms of thyroid disease (TD) pose significant diagnostic difficulties. A national rare thyroid disease service (RTDS) was established in Ireland (population 5.2m) in 2020. Operating quarterly, it accepts nationwide referrals from primary care practitioners and specialists for patients with confirmed/suspected complex/rare TD. **Methods:** Clinical note review of attendances at RTDS in first 4 years (January 2021 - October 2024) to determine referral sources, practice volume, patient demographics, and final diagnoses. **Results:** 71 patients attended. The average age was 42.6 years, the majority were female (69%). Referrals were from endocrinologists (adult 87%; paediatric 4%) and primary care (9%). Most were from Dublin and surrounding counties (86%). On average 10.8 people attended each clinic; each patient had 2.4 visits on average. 46% of patients were referred with discordant TFTs, 25% with complicated hypothyroidism (abnormal TFTs, reset HPT axis in congenital hypothyroidism, thyroxine malabsorption etc.), 15% with complicated hyperthyroidism (fluctuating TRAb, unknown aetiology etc.), 10% with suspected assay interference and 3% with known Resistance to Thyroid Hormone. Patients received a diagnosis within 2 visits. Most (72%) had specialised testing at a reference laboratory and genetic testing was performed in 45%. A formal diagnosis was established in 97% of patients, investigations are ongoing in 3%. Complicated hypothyroidism (25%), T4 assay interference (20%) and complicated hyperthyroidism (17%) were the most common diagnoses. Cases of RTH Beta (10%), Familial Dysalbuminaemic Hyperthyroxinaemia (6%), TSH assay interference 4%, TTR mutation 4%, drug induced TD (4%), TSHoma (1%) and non-thyroidal illness (1%), were also identified. Less commonly, some individuals were found to have no identifiable TD (4%). **Conclusion:** The spectrum of TD diagnosed and managed at the RTDS is highly variable. Access to a specialist clinic linked with appropriate specialist biochemical support and genetic testing facilitates timely diagnosis and appropriate management of complex and rare TD.

THYROID HORMONE ACTION

1112415 - A PROTECTIVE PARADOX: OFFSPRING INHERITING THYROID HORMONE RESISTANCE MITIGATES PREGNANCY RISKS

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Thyroid hormone resistance (RTH) is a rare condition marked by reduced tissue sensitivity to thyroid hormones, often resulting in elevated free T4 and T3 levels with non-suppressed or elevated TSH. Pregnancy in women with RTH presents unique challenges, particularly if the fetus does not inherit the mutation. This scenario can lead to maternal hypothyroid-like symptoms due to increased fetal hormone demand, while the fetus may face risks of hyperthyroidism or other thyroid-related complications. Thus, careful monitoring and multidisciplinary care are critical during pregnancy to optimize outcomes for both mother and child. This case report describes a female patient with RTH due to a heterozygous *THRB* gene mutation (exon 8: c.A835T:p.M279L). Diagnosed at age 11, she presented with mild symptoms, primarily weight gain and a history of childhood epilepsy, now resolved without medication. She has had two pregnancies, both resulting in offspring affected by RTH. Her first child, born in 2015, displayed elevated thyroid hormone levels and an abnormal neonatal screening, with subsequent confirmation of RTH. The second child, born in 2020, had a neonatal TSH of 15.4 mIU/L, which normalized to 2.99 mIU/L during follow-up, with a free T4 of 2.96 ng/dL. Both children are undergoing regular monitoring and treatment for thyroid dysfunction. This case underscores the hereditary nature of RTH and the critical role of genetic testing in families with thyroid hormone abnormalities. It also highlights the need for heightened vigilance during pregnancy to manage potential maternal and fetal thyroid-related complications. Early diagnosis and lifelong follow-up are paramount to ensuring optimal outcomes for both patients and their offspring.

THYROID HORMONE ACTION

1112258 - ADJUNCTIVE THYROID HORMONE TREATMENT IN BIPOLAR DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: The role of thyroid hormones in the treatment of bipolar disorder (BD) is not well defined. **Objective:** We aimed to perform the first systematic review and meta-analysis to assess the comparative efficacy and safety of levothyroxine (L-T4) or triiodothyronine (T3) versus placebo as adjunctive therapy in BD. **Methods:** PubMed, Embase and Cochrane Central were systematically searched for randomized controlled trials (RCTs) that directly compared L-T4 or T3 to placebo and reported efficacy or safety outcomes. This study was conducted in accordance with the PRISMA guidelines. Heterogeneity was assessed using I2 statistics. A random-effects model was used for all outcomes measures. **Results:** We included 4 RCTs comprising 106 patients, of whom 47 (44.3%) were male. Duration period ranged from 2 to 6 months. Our findings suggest L-T4 is effective in reducing depressive and manic symptoms in bipolar disorder, with minimal adverse effects. The use of T3 showed limited efficacy and inconsistent evidence. Symptomatic tachycardia was not associated with L-T4 usage, while 20% of the patients using T3 presented with this symptom, despite lacking statistical significance on further analysis (OR 4.97; 95% CI 0.49-50.86; p= 0.18). Palpitations were moderately noted in T4 intervention (OR 4.13; 95% CI 0.18-96.93; p= 0.38) but not in T3 intervention (OR 0.33; 95% CI 0.01-10.11; p= 0.53), but both without statistical significance. Tremor was seen in T3 usage, also without statistical significance (OR 1.74; 95% CI 0.12-25.11; p= 0.68). No serious adverse events or significant thyrotoxicosis were reported throughout all studies periods. **Conclusion:** This systematic review and meta-analysis of patients with BD provides promising evidence of efficacy in L-T4 use as adjuvant therapy, but no significant benefit in T3 use due to inconsistent evidence. With minimum and non significant statistical side effects. Both T4 and T3 use were not associated with any significant adverse event.

THYROID HORMONE ACTION

1112308 - FISH OIL SUPPLEMENTATION DURING GESTATION ALTERED THYROID HORMONE SIGNALING-RELATED GENES IN METABOLIC TISSUES OF WEANLING OFFSPRING IN A PERINATAL MATERNAL HIGH-FAT DIET RAT MODEL

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Introduction: Perinatal maternal high-fat diet (mHFD) increases offspring susceptibility to obesity and fatty liver diseases. Previously, we found that mHFD offspring exhibited elevated total T3 and hypothalamic TRH. Fish oil (FO, an n-3 PUFA source) may mitigate mHFD effects by reducing serum lipids and adiposity. TH are major metabolic regulators, and FO is known to interact with TH action. **Objective:** To investigate TH signaling in the liver and skeletal muscle of weanling offspring from dams fed a high fat diet with or without FO supplementation during gestation. **Methods:** Female Wistar rats received control (CT:9% from fat) or high-fat (HF:28,6% from fat) diet before mating, and during pregnancy and lactation. One group of HF dams received FO supplementation (HFFO: 3% of FO added to the diet) during pregnancy. **Results:** Serum total T3 and free T4 levels were unchanged in HF and HFFO offspring. In males, HF reduced hepatic expression of Dio3 (P=0.014 vs CT), suggesting increased T3 bioavailability, accompanied by upregulation of TH target gene Gpd (P=0.021 vs CT) and Thrsp1 (Spot14) (P=0.021 vs CT). FO increased the TH transporter Slc16a2 (P=0.025 vs HF; P=0.007 vs CT). Concomitantly Gpd (P=0.0005 vs CT) was increased but not Thrsp1. Expression of Thrb1 and Dio1 remained unchanged. In extensor digitorum longus muscle of males, FO reduced Dio2 (P=0.001 vs HF), consistent with Sln upregulation (sarcolipin - negatively regulated gene) (P=0.022 vs HF). In soleus muscle of males, HF and HFFO reduced Slc16a2 (P=0.001 vs CT), but also reduced Sln (P<0.05 vs CT). No alterations were observed in Thra, and Dio3. Females showed no alterations in TH signaling, except for a reduction in Slc16a10 hepatic expression. **Conclusion:** mHFD and FO gestational supplementation induced tissue and sex specific alterations in TH signaling, potentially affecting T3 bioavailability and contributing to metabolic genes expression regulation.

THYROID HORMONE ACTION

1112609 - MODULATION OF SPLENIC DENDRITIC CELL SUBSETS BY THYROID STATUS IN MICE

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Dendritic cells (DCs) are a heterogeneous population of antigen-presenting cells essential for initiating and sustaining effective immune responses by regulating T-cell activation and ensuring appropriate responses to infections, diseases, and cancers. DCs are classified into conventional (cDCs), comprising cDC1 and cDC2, and plasmacytoid (pDCs). Previous studies demonstrated that physiological T3 concentrations promote DC maturation, enhancing proinflammatory and cytotoxic immune responses while suppressing regulatory signals. Moreover, T3 improved DC antitumor functions in mouse models of melanoma and colon carcinoma. The aim of this study was to investigate the impact of thyroid status on DCs under experimental hypo- and hyperthyroidism. C57BL/6 mice were rendered hypothyroid (0.5 mg/mL propylthiouracil, 18 days) or hyperthyroid (0.012 mg/mL T4, 28 days) via drinking water; controls received plain water. Plasma thyroid hormones (THs) and IL-12 levels were measured by immunoassay. Pituitary TSH β and hepatic DIO1 mRNA expression were determined using qPCR. Hepatic leukocyte infiltration and splenic pDCs (CD19⁺ B220⁺) and cDCs (MHCII⁺ CD11c⁺), including cDC1 (CD8a⁺) and cDC2 (CD11b⁺), were analyzed by flow cytometry. Statistics: One-way ANOVA followed by Tukeys test, and Brown-Forsythe test followed by Dunnett T3-test ($p < 0.05$). The interventions effectively reduced TH levels ($p < 0.0001$) and increased TSH β mRNA expression ($p < 0.01$) in hypothyroid mice. Conversely, hyperthyroid mice exhibited elevated TH levels ($p < 0.0001$) and DIO1 mRNA expression ($p < 0.001$), along with reduced TSH β mRNA expression ($p < 0.001$). Hyperthyroid mice also displayed higher IL-12 levels ($p < 0.001$ vs control, $p < 0.05$ vs hypothyroid) and significant hepatic leukocyte infiltration. Splenomegaly was observed in hyperthyroid mice, along with significant increase in splenic pDC and cDC frequencies, including cDC1 and cDC2 subsets ($p < 0.01$). Our results suggest that hyperthyroidism induces a proinflammatory immune microenvironment characterized by elevated IL-12, hepatic leukocyte infiltration, and expanded DC subsets. Further research is needed to elucidate the mechanisms by which thyroid disorders influence DC maturation and immune regulation in thyroid-related pathologies.

THYROID HORMONE ACTION

1112266 - REGULATION OF OSTEOGENIC DIFFERENTIATION BY THYROID HORMONE VIA THE TRANSCRIPTION FACTOR KLF9 IN MICE

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Objective: This study investigated the role of thyroid hormones (TH) in bone remodeling by examining osteoblast-specific knockout of Klf9 mice (Klf9Ox^{-/-}) in a hyperthyroidism model. **Methods:** Male 12-week-old Klf9Ox^{-/-}, Klf9flox/flox and OxsCre mice were randomly divided into levothyroxine (L-T4) and control groups. Serum levels of thyroxine (T4), triiodothyronine (T3), bone metabolism markers (osteocalcin, PINP, β -CTx), and calcium ions were measured. Bone microstructure was assessed using micro-CT, and a three-point bending test evaluated bone strength. Histological analyses, including HE, Von Kossa, and Sirius Red staining, examined bone morphology, calcium deposition, and collagen fiber quantity. **Results:** In Klf9flox/flox mice and OxsCre mice after L-T4 treatment: there was a significant increase in serum T3 and T4 levels; no significant changes were found in serum bone markers or calcium levels; the maximum force of the femur decreased; histological staining and collagen fiber quantity had no significant impact, but there was a significant decrease in calcium deposition; the ratios of cortical bone volume fraction, bone density, thickness, cortical bone area, and total area all significantly decreased; the trabecular bone volume fraction, mineral density, and number significantly decreased, while trabecular bone separation increased significantly. In Klf9Ox^{-/-} mice after L-T4 treatment: there was a significant increase in serum T3 and T4 levels; no significant differences were observed in serum bone metabolism markers and calcium ion concentrations; the maximum force of the femur decreased; histological staining and collagen fiber quantity had no significant impact, but there was a significant decrease in calcium deposition; the ratios of cortical bone volume fraction, thickness, cortical bone area, and total area all significantly decreased, although cortical bone density showed no significant change; the trabecular bone analysis parameters showed no significant changes. **Conclusion:** TH may partially regulate bone remodeling through Klf9.

THYROID HORMONE ACTION

1114094 - THYROID HORMONES MODULATE FOXO3 EXPRESSION IN SEPTIC SKELETAL MUSCLE: INSIGHTS INTO SEPSIS-INDUCED MUSCLE ATROPHY

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Introduction: Sepsis is responsible for 11 million deaths per year, thus it is a major public health concern. Septic patients frequently develop the nonthyroidal illness syndrome (NTIS). This condition causes a reduction in serum thyroid hormones (TH) levels with no increase in TSH. The NTIS development and the decrease in muscle mass are predictors of septic mortality. **Objective:** Since TH are crucial for muscle function, we investigated the atrophic pathway in peripheral skeletal muscle from septic mice. **Methods:** Sepsis was induced through a cecal ligation and puncture (CLP) in adult male C57BL6 mice, the control group (Sham) was sham operated. The CLP group was treated with T4 (7.5 ng/g BW dose) plus T3 (250 ng/g BW dose) (CLP+TH) or saline (CLP) 8h and every 24h after surgery for 5 days. At day 5 the animals were euthanized and the soleus muscle collected (CEUA:A10/20-A18-088-15). The gene expression was analyzed by qPCR, and one-way ANOVA was used for statistical analysis. **Results:** Although *Thra1* expression did not change between groups, the TH positively regulated gene *Hr* expression increased in the CLP+TH group (SHAM: $1.0 \pm 0.2a$ /CLP: $0.5 \pm 0.1a$ /CLP+HT: $12.1 \pm 5.4b$; $p < 0.05$) as expected. Next, we investigated the atrophic-regulated genes *Foxo1* and *3*. We only observed a change in *Foxo3* expression, with an increase in septic soleus, and TH treatment reduced it (SHAM: $1.0 \pm 0.3a$ /CLP: $3.4 \pm 0.9b$ /CLP+HT: $2.1 \pm 0.5a$; $p < 0.05$). Since *Foxo3* can induce atrogenic gene expression, we investigated *Fbox32* (*Murf-1*) and *Trim63* (*Atrogin*) expression, but did not change between groups. **Conclusion:** Our findings suggest that sepsis does not regulate the mean atrophic gene expression in the soleus. However, the increased expression of *Foxo3* could indicate that the autophagy pathway is unregulated and controlled by TH. To further elucidate *Foxo3*'s influence, we will investigate its regulation of autophagy and apoptosis.

THYROID HORMONE ACTION

1112376 - TRIIODOTHYRONINE (T3) MODULATES IMMUNE CELL POPULATION FROM SMALL INTESTINE OF MICE: CORRELATION BETWEEN INFLAMMATORY PARAMETERS AND PARACELLULAR PERMEABILITY

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A high-fat diet (HFD) can increase intestinal permeability and trigger an immune response changing cell phenotype and inflammatory cytokines secretion. It is known that T3 administration reduces the inflammatory cytokines expression in the muscle, adipose tissue, and blood from obese rats; however, it is still unclear whether T3 affects the intestine in obese and non-obese animals. To investigate this, male C57BL/6 mice were assorted into two groups: a standard diet (LFD) or a HFD during 12 weeks. At the end of this period, both groups were treated for 30 days with either saline (LF+S, HF+S) or T3 (0.25 µg g⁻¹) (LF+T3, HF+T3). After euthanasia, the following experiments were performed: -1) myeloid and lymphoid cells characterization by flow cytometry; -2) RT-qPCR of TSH-β gene in the pituitary gland, IL-1β, IL-6, TNF-α, IFN-γ, IL-10, COX-2, and claudin 2 in the jejunum; 3) intestinal permeability assay using FITC-Dextran (FD-4); -4) measurement of villus width (CEUA protocol no. 7283120421). In obese mice, HFD increased the frequency of patrolling monocytes and decreased the frequency of total Treg cells and Tregs expressing GATA-3 transcription factor, indicating an inflammatory process. However, T3 administration did not alter the effects of the HFD, T3 treatment in obese mice reduced the frequency of Tγδ and Th17 cells, as well as IFN-γ expression and villus width. In non-obese mice, T3 administration increased the number of macrophages and dendritic cells, but downregulated the expression of IL-1β and IFN-γ, and also increased the number of B lymphocytes and CD4 T cells, enhanced claudin 2 expression, and reduced villus width, which may have contributed to decrease intestinal permeability as observed. Our data suggest that T3 alters intestinal immune cells leading to a less inflammatory phenotype, since it reduced cytokine expression and villi width, resulting in intestinal integrity improvement.

THYROID HORMONE ACTION

1113947 - TYPE 2 DEIODINASE IS REQUIRED FOR QUIESCENCE AND SELF-RENEWAL OF MUSCLE STEM CELLS

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Introduction: Stem cells are essential for maintaining the homeostasis of adult tissues. Thyroid hormone (TH), whose intracellular levels are regulated by type 2 deiodinase (D2), plays a role in various biological processes, yet its function in stem cell quiescence remains unclear. **Objective:** This study aims to investigate the role of D2-mediated thyroid hormone activation in maintaining quiescent satellite cells and their transition to an activated state using inducible genetic models to specifically ablate the D2 gene in muscle stem cells (cD2KO). **Methods:** Muscle stem cells were isolated from wild-type (wt) and D2KO mice and analyzed for quiescence markers (Pax7, Notch pathway) and activation markers (MyoD, Myogenin) via qPCR. Additionally, an in vivo muscle injury model (cardiotoxin injection) was used to evaluate muscle regeneration in cD2KO versus wt mice. **Results:** D2 is normally expressed in quiescent MuSCs and its expression decreases dramatically upon MuSC activation. We also observed that following cardiotoxin-induced damage, MuSCs in the cD2KO model became activated faster than in wt and had reduced self-renewing capacity. In addition, we observed that TH produced by D2 regulates Notch signaling, which is known to be important for maintaining quiescence and self-renewal capacity. **Conclusion:** D2-mediated thyroid hormone activation plays a critical role in maintaining MuSCs in a quiescent state and ensuring proper self-renewal. In addition, we found a strong interaction between thyroid hormone produced by D2 and Notch signaling. These studies suggest that selective modulation of thyroid hormone concentration could be used to enhance the process of muscle regeneration by modulating the expansion and/or differentiation of SCs in both physiological and pathological contexts.

THYROID HORMONE METABOLISM

1112655 - ANTICONVULSANT THERAPY AND THYROID FUNCTION: A COMPREHENSIVE DATA ANALYSIS FROM A BRAZILIAN LABORATORY

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Introduction: Anticonvulsants treatment can influence thyroid hormone levels, potentially leading to subclinical hypothyroidism. **Objective:** To evaluate thyroid function in patients using oral anticonvulsants at a single center in northeastern Brazil. **Methods:** A retrospective analysis was conducted on 478,035 TSH tests between 2021 and 2023. Of these, 4,400 tests involved individuals of both sexes undergoing oral anticonvulsant therapy. Pregnant individuals, those with pre-existing thyroid disease, and those using biotin, amiodarone, or contraceptives were excluded. Data analysis was conducted using the Wilcoxon test to compare non-parametric groups. **Results:** The mean age of patients was 55.5 ± 19.2 years, with females comprising 72% of the sample. The mean ultrasensitive TSH level was 2.60 ± 3.67 mUI/mL, and the mean free T4 level was 1.09 ± 0.19 ng/dL ($p < 0.001$). Of the 14 anticonvulsants analyzed, 3 were associated with significant variations in TSH levels. Valproic acid (3.08 ± 3.66 vs. 2.53 ± 3.67 ; $p < 0.01$) and clonazepam therapy (2.69 ± 3.47 vs. 2.55 ± 3.79 ; $p = 0.046$) exhibited higher TSH levels. Conversely, reduced TSH levels were noted with pregabalin use (2.47 ± 4.34 vs. 2.67 ± 3.31 ; $p < 0.001$). In patients under 18 years, higher TSH levels were observed with valproic acid use (3.86 ± 2.14 vs. 2.19 ± 1.03 ; $p < 0.001$). Among those aged 18-59, TSH levels were elevated with valproic acid (3.03 ± 3.96 vs. 2.23 ± 1.45 ; $p < 0.001$) and clonazepam (2.57 ± 2.88 vs. 2.25 ± 1.54 ; $p = 0.014$), while reduced levels were seen with pregabalin (2.15 ± 1.41 vs. 2.44 ± 2.30 ; $p < 0.001$). **Conclusions:** Valproic acid and clonazepam were associated with higher TSH levels, while pregabalin showed reduced levels. These findings underscore the need for close thyroid monitoring in patients on antiepileptic therapy to prevent complications like subclinical hypothyroidism.

THYROID HORMONE METABOLISM

1112260 - BODY COMPOSITION IN PATIENTS WITH RESISTANCE TO THYROID HORMONE B

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Introduction: In Resistance to Thyroid Hormone β (RTH β), the peripheral tissues show variable refractoriness to the action of thyroid hormones, which are essential in regulating body weight. **Objective:** To assess body composition in RTH β patients. **Methods:** 16 patients (8 adults and 8 children/teenagers) with RTH β and 29 healthy individuals (15 adults and 14 children/teenagers), matched for sex, age, and body mass index (BMI), were evaluated with anthropometric measurements and the trunk and peripheral fat percentiles using the dual emission X-ray absorptiometry technique (DXA). **Results:** By univariate analysis, there was no difference between the body composition ratio in both groups. Despite this, in the assessment of body composition by DXA, 5 adult patients with RTH β had an increased Android/Gynoid (A/G) ratio, 5 patients had a Baumgartner index lower than the cutoff point for sex, conferring low lean mass, and 5 patients had an increased Fat Mass Index (FMI), 2 with a diagnosis of grade I obesity and 3 with overweight. Only one patient with RTH β under 18 years of age presented an increase in the A/G ratio. Two of eight adult patients with RTH β had Metabolic Syndrome, and despite having a normal BMI, they had an increased FMI (overweight in both). The same patients also presented low decreased lean mass on DXA when assessed by the Baumgartner index, as well as an increased A/G ratio, indicating visceral fat accumulation. In the literature, these characteristics are associated with increased cardiovascular risk. **Conclusion:** We did not demonstrate a significant difference in body composition among the study participants. However, we noticed a worsening in aging in patients with RTH β , which can be associated with increased cardiovascular risk.

THYROID HORMONE METABOLISM

1114285 - CARDIAC IMPLICATIONS OF THYROID METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

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Introduction: This study examined the impact of thyroid hormone dysfunction linked to metabolic dysfunction-associated steatotic liver disease (MASLD) on cardiac metabolism and function. **Objective:** To understand the colocalization of type 3 deiodinase in the MASLD heart. **Methods:** Adult male Sprague Dawley rats (n=20) were divided into two groups: a control group on a standard diet and a MASLD group on a choline-deficient high-fat diet (HFCD) for 18 weeks. The MASLD group exhibited significant metabolic changes as well as notable structural and functional cardiac alterations, which were evaluated through echocardiography. DIO3 expression was assessed using in situ hybridization (RNAscope) and real-time PCR, while macrophages were identified through immunofluorescence with the F4/80 antibody. T3 levels were measured in the tissue. **Results:** Echocardiographic evaluations revealed abnormal cardiac function in the MASLD group. The ejection fraction significantly decreased ($p = 0.0034$), while fractional shortening increased ($p = 0.0049$), indicating early adaptive mechanisms or functional overload. Notably, 44% of the MASLD group showed fibrosis, with uneven F4/80 positive macrophage infiltration distribution. DIO3 mRNA had 2%-10% colocalization with macrophages, while about 80% was found in cardiomyocytes, confirmed by RNAscope and colocalization with MYH6 positive cells. Additionally, HIF expression increased by 150%, and there was a 100% rise in other markers. PPAR- α expression, both contributing to elevated DIO3 levels. **Conclusion:** These findings suggest that DIO3 may be associated with early cardiac responses to MASLD. They underscore the fact that the initial stages of MASLD expose the heart to increased inflammatory responses, highlighting the critical need for early intervention to prevent serious cardiac complications.

THYROID HORMONE METABOLISM

1112300 - CORRELATION BETWEEN SERUM LEVELS OF LEPTIN AND THYROID FUNCTION: CROSS-SECTIONAL ANALYSIS OF DATA FROM THE ELSA-BRASIL STUDY

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Introduction: The relationship between leptin and thyroid function has been of growing interest, due to the interconnection between energy metabolism and hormonal regulation. Thyroid hormones, as well as leptin, play an important role in regulating basal metabolism, thermogenesis, and lipolysis. However, the interaction between these systems is not yet fully elucidated. **Objective:** Investigate the association between leptin and thyroid function in a population sample from the Longitudinal Study of Adult Health (ELSA-Brasil). **Methods:** This is a cross-sectional study, conducted in 822 participants (45.6±4.9 years old, 53.8% women, 59.5% white). Fasting serum thyroid-stimulating hormone (TSH), free thyroxine (FT4), free-triiodothyronine (FT3), and thyroid peroxidase antibody (TPOAb) levels were determined and FT3:FT4 ratio was calculated. Only euthyroid participants (TSH 0.4-4.0 mIU/L, no use of levothyroxine and anti-thyroid medication), and participants with subclinical conditions (TSH any level, 0.93<FT4<1.70 ng/dL) were included. ELISA kits were used to determine leptin levels. All variables were log-transformed for data normalization and TPOAb positivity was set at TPOAb≥34 IU/mL. Pearson's correlation coefficient tested the correlation between leptin and thyroid parameters. We performed linear regression analyses for univariate and adjusted (for age, race, sex, BMI, and smoking status) models. **Results:** FT4 ($r=-0.19$, $p<0.001$) and FT3 ($r=-0.15$, $p<0.001$) levels were negative and significantly correlated to leptin levels. In the univariate model, FT4 ($B=-2.42$, $CI95\%=-3.24; -1.59$, $p<0.001$) and FT3 ($B=-4.94$, $CI95\%=-7.55; -2.34$, $p<0.001$) levels were statistically associated with leptin levels. After adjustment, only FT4 levels remained associated with leptin levels ($B=-0.90$, $CI95\%=-1.67; -0.14$, $p=0.021$). TSH ($B=0.02$, $CI95\%=-0.14; 0.18$, $p=0.820$) and TPOAb levels ($B=0.01$, $CI95\%=-0.06; 0.07$, $p=0.847$) and TPOAb positivity ($B=0.08$, $CI95\%=-0.11; 0.28$, $p=0.410$) were not associated with leptin levels. **Conclusions:** This analysis shows an association between higher levels of free T4 and lower levels of leptin, independently of BMI values and other confounding factors, which suggests an important role of thyroid function and energy metabolism.

THYROID HORMONE METABOLISM

1112554 - EFFECT OF VALPROIC ACID ON DEIODINASES TYPE 1 AND 3 MRNA EXPRESSION IN HT-29 HUMAN COLON CANCER CELLS

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Introduction: In colorectal cancer (CRC), there is a deregulation of the expression of deiodinases (DIOs). DIOs are enzymes that catalyze the activation and inactivation of iodothyronines. The deregulation of DIOs expression may be due to epigenetic mechanisms such as histone deacetylation. It has been hypothesized that in cancer cells the reduction of the expression of DIO1 and DIO2 and an increase in DIO3 promotes a reduction in the intracellular concentration of T3 resulting in an increase in cell proliferation and dedifferentiation. Valproic acid (VPA) could regulate the gene expression of DIOs in colorectal cancer because it inhibits histone deacetylases. **Objective:** To assess the effect of VPA on the expression of DIOs mRNA in HT-29 CRC cells. **Material and Methods:** HT-29 CRC cells were cultured and treated with different concentrations of VPA (0.5-50 mM) to establish the inhibitory concentration 50 (IC50). To analyze the effect of DIO1 and DIO3 mRNA expression, doses lower than the IC50 were used, total RNA was extracted, and cDNA was synthesized to perform RT-qPCR. **Results:** HT-29 cells express DIO1 and DIO3 but not DIO2. VPA reduced cell viability in a dose-dependent manner at 24, 48 and 72 h with an IC50 of 19.5, 12.58 and 11.04 mM, respectively. After 48 h of treatment, VPA at concentrations of 0.5 and 2 mM increased DIO1 mRNA expression 311 and 234 times more than the control, respectively. On the other hand, VPA at concentrations of 0.5 and 2 mM, after 48 h, increased the expression of DIO3, 143 and 94 times more than control, respectively. **Conclusions:** VPA at concentrations of 0.5 and 2 mM increases the expression of DIO 1 and DIO3.

THYROID HORMONE METABOLISM

1112277 - EVALUATION OF DOXORUBICIN-RELATED CARDIOTOXICITY, THYROID HORMONE METABOLISM, AND OXIDATIVE STRESS IN PATIENTS WITH BREAST CANCER

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Introduction: Doxorubicin-related cardiotoxicity (DOX) consists of a reduction in left ventricular ejection fraction (LVEF), reflecting a delayed adaptation to cardiac damage. Thyroid hormone metabolism may be involved in the attempt to adapt, as well as the body's antioxidant defenses. **Objective:** To evaluate cardiotoxicity in breast cancer patients treated with DOX, thyroid hormone metabolism, and antioxidant system activity. **Methods:** Prospective cohort study. Thirty-three patients with breast cancer treated with DOX at a tertiary hospital underwent cardiological evaluation (echocardiogram), whole blood collection for plasma T3 measurement and quantification of the total content of reduced glutathione (GSH), carbonyl and sulphydryl (parameters of intracellular redox balance) at the visits: baseline (C1), before the second (C2), post fourth (C3) doses of DOX and 1 year after the start of treatment (C4). **Results:** The mean age was 54 ± 9 years. Concerning cardiac function, LVEF was considered normal at baseline in all patients, with a mean of $66 \pm 1.09\%$. However, a 10% reduction in LVEF was observed in 10 patients throughout and at the end of treatment. T3 levels increased during C2, C3, and C4, and it was observed that patients who had cardiotoxicity presented lower levels at C1 compared to those who did not. Regarding the activity of the antioxidant system, the quantification of GSH, carbonyl and sulphydryl increased significantly in C2, C3 and C4, but without differences between the groups. **Conclusion:** This study demonstrated that significant changes in cardiac function occur due to the chemotherapy regimen with DOX in almost 30% of the treated population. In addition, the accumulation of DOX reduced oxidative defenses and altered thyroid hormone metabolism, which can be involved in the response of the cardiomyocyte to the drug.

THYROID HORMONE METABOLISM

1112652 - METABOLIC PROFILING OF 3T3-L1 ADIPOCYTES: EFFECTS OF TRIIODOTHYRONINE

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Introduction: Obesity, a global pandemic, is characterized by excessive adipose tissue (AT) accumulation and is associated with a chronic low-grade inflammatory state. AT, in addition to its function of energy storage, acts as an endocrine organ, secreting adipokines that influence systemic metabolism. Thyroid hormones, especially triiodothyronine (T3), play a crucial role in regulating energy metabolism. **Objective:** The objective of this study was to identify, through metabolomic analysis, the biochemical alterations induced by T3 in 3T3-L1 adipocytes. **Methods:** 3T3-L1 pre-adipocytes were cultured and divided into 2 groups: (C) untreated adipocytes and (T3) adipocytes treated with a physiological dose of T3 (10nM) for 24 hours. Metabolomic analyses were performed using liquid chromatography followed by in silico analysis in systems biology software (Metaboanalyst 5.0). The predictive power was determined using the statistical tool of partial least squares-discriminant analysis (PLS-DA), with a 95% confidence interval; analyses were also performed using the VIP Scores method. **Results:** PLS-DA revealed a clear separation between the C and T3 groups. A heatmap was developed and seven biomarkers with statistically significant expression were identified. The most relevant metabolites for the T3-treated group were glycine and lactate. For the untreated adipocyte group, the most relevant metabolites were alpha-ketoglutarate, L-carnitine, isovalerylcarnitine, butyrylcarnitine, and lysophosphatidylcholine. **Conclusion:** T3 exerts an influence on the metabolic profile of 3T3-L1 adipocytes, primarily in glycine metabolism.

THYROID HORMONE METABOLISM

1114335 - OBESITY AND THYROID CANCER: A LOVE-HATE RELATIONSHIP? BUSTING MYTHS, BUILDING EVIDENCE

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Introduction: Obesity is a global public health problem affecting millions of people worldwide. Thyroid cancer is the most common type of endocrine cancer and its incidence has been increasing in recent decades. 20% of all cancers are associated with obesity. Increase of 5 BMI points increase 30% of Thyroid Cancer Increase of 1cm Abdominal circumference 14% chance of developing thyroid cancer
Objective: Main Objective: To analyse the association between obesity and thyroid cancer. Specific Objectives: To review the scientific literature on the relationship between obesity and thyroid cancer. To evaluate the possible biological mechanisms that could explain this association. To identify modifiable risk factors related to obesity and thyroid cancer. Impact of bariatric surgery on thyroid cancer risk reduction.
Methods: Bibliographic search: A search of scientific databases was carried out using keywords related to obesity and thyroid cancer. PUBMED EMBASE Study selection: Epidemiological studies, reviews, systematic reviews and meta-analyses investigating the association between obesity and thyroid cancer were included. 2015-2025 786 articles Meta-analyses 27 Systematic reviews 36 Topic reviews 236 articles Obesity and thyroid cancer English language
Results: BMI ≥ 25 had a higher risk of developing thyroid cancer than those with BMI < 23 . Modifiable risk factors, such as weight loss, physical activity and a healthy diet, were identified as measures to reduce the risk of thyroid cancer. Inflammatory pathways: obesity may promote chronic inflammation. Hormonal alterations: levels of hormones such as insulin and oestrogen may be dysregulated in people with obesity. Insulin resistance: obesity is associated with insulin resistance, which may promote abnormal cell growth in the thyroid.
Conclusion: We found evidence of possible biological mechanisms, such as inflammatory pathways and hormonal alterations, that could explain this association. It is time to operate on thyroid cancer but also to intervention in the management of obesity.

THYROID HORMONE METABOLISM

1112487 - THE METABOLISM OF THYROID HORMONE IN THE HEPATIC TISSUE OF PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) UNDERGOING BARIATRIC SURGERY SHOWS FUNCTION CHANGES ARE MORE PRONOUNCED THAN CLINICAL PARAMETERS

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Metabolic dysfunction-associated steatotic liver disease (MASLD) represents the most prevalent form of chronic liver disease, encompassing a spectrum of alterations for which effective treatments remain elusive. Thyroid hormone metabolism (THs) plays a crucial role in the progression of this disease. In this context, we hypothesize that the pro-inflammatory state induced by obesity contributes to disruptions in TH metabolism within the liver. Our study aims to elucidate the changes in TH levels in the liver of obese patients undergoing bariatric surgery. We included thirty-five patients with a mean age of 44.24 ± 12.11 years alongside a control group of age-matched, non-obese individuals undergoing elective surgery. Sixty percent of the participants were male, with an average weight of 132.93 ± 34.36 kg and a BMI of 48.30 ± 11.16 . The total cholesterol level was measured at 171.30 mg/dL ± 36.44 mg/dL, triglycerides at 108.23 mg/dL, HDL at 51.05 mg/dL ± 34.56 mg/dL, and glucose at 110.25 mg/dL ± 31.36 mg/dL. Among the patients, seven exhibited severe macrovesicular steatosis, while nineteen displayed mild to slight steatosis. Sixteen patients presented normal T3 levels (96 ± 14 ng/dL), whereas fourteen showed low T3 syndrome (54 ± 8 ng/dL). Notably, carbonyl and TBARS levels increased by 45%, while sulfhydryl and GSH levels decreased by 30% and 40%, respectively, confirming a disturbed redox status in these patients. Dio3 levels augmented fifteenfold compared to controls. Additionally, Hif1 and Erk levels were elevated in the liver of the patients, together with significant alterations in various mitochondrial enzymes and respiration parameters. These findings demonstrate that TH metabolism and energy production are disrupted in the steatotic liver of patients with slight to mild clinical parameters of MASLD. In conclusion, we suggest that a more proactive approach is essential for enhancing liver metabolic function in MASLD from the disease diagnosis.

THYROID NODULE

1114141 - A BIBLIOMETRIC ASSESSMENT OF KNOWLEDGE GAPS IN ACTIVE SURVEILLANCE FOR THYROID NODULES

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Introduction: Low-risk thyroid nodules are being actively monitored as a safe and efficient management strategy. Thorough knowledge and application in many different contexts are still lacking, though. **Objective:** To find important knowledge gaps in active surveillance of thyroid nodules based on a bibliometric study of scientific literature. **Methods:** A bibliometric study based on bibliographic coupling and co-citation networks from Scopus-indexed papers was performed. Clusters of thematic study domains were examined to find information and research gaps. **Results:** The analysis produced five clusters: (1) Initial concept establishment and clinical foundations; (2) - Intermediate clinical follow-up and practical outcomes; (3) Refined selection criteria and clinical management improvements; (4) International applications across diverse clinical contexts; and (5) Consolidated evidence from meta-analyses and systematic reviews. Among the critical knowledge gaps found are a lack of long-term (>10 years) mortality and quality of life outcomes, undefined optimal intervals for long-term follow-up, insufficient integration of genetic and molecular biomarkers for progression risk assessment, limited studies from resource-constrained settings, inadequate exploration of patient acceptance and psychosocial impacts, and a scarcity of updated meta-analyses incorporating recent literature and economic evaluations. **Conclusion:** To maximize the safety, efficacy, and patient acceptance of active surveillance worldwide, it is crucial to address these noted deficiencies. Future studies should give priority to multicentric prospective research including biomarkers, long-term results, thorough psychological evaluations, and strong economic analyses.

THYROID NODULE

1112591 - A MULTICENTER SERIES OF HYALINIZING TRABECULAR TUMOR IN ARGENTINA: DIAGNOSTIC CHALLENGES AND THE ROLE OF MEMBRANE REACTIVITY TO KI67 MONOCLONAL ANTIBODY CLON MIB1

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Introduction: The 2022 World Health Organization 5th edition classification of Endocrine and Neuroendocrine Tumors categorizes hyalinizing trabecular tumors (HTTs) as low-risk thyroid neoplasms. These lesions are frequently misdiagnosed as papillary or medullary thyroid carcinoma in fine needle aspiration (FNA) cytology. **Objective:** To evaluate the clinical, ultrasonographic, cytological, pathologic characteristics, and outcomes of a series of HTT cases in Argentina. **Methods:** This multicentric series included six HTT patients surgically treated between 2018 and 2024. Initial pathological evaluations were performed at the respective centers and subsequently reviewed by a single pathologist at an external reference center, who also performed Ki67 MIB-1 immunostaining. **Results:** Ultrasonography revealed three cases with solitary nodules and three with multinodular goiter. Sixty-six percent were hypoechoic, with diameters ranging from 4.7 to 52 mm (□:30 mm). FNA cytology (Bethesda System) resulted: II (n=1); III (n=1, repeat FNA was V); IV (n=1); V (n=1); VI (n=1). One patient was a surgical incidentaloma with a synchronous papillary carcinoma. Five cases underwent total thyroidectomy, while one underwent diagnostic lobectomy. Pathological evaluation confirmed HTT in all cases, but cell membrane Ki-67 MIB-1 immunostaining was observed in only one case. Postoperatively, five patients had undetectable thyroglobulin and anti-thyroglobulin levels (data missing data for one case). The pathology report of a 65-year-old male patient revealed vascular invasion (pT3apNxM0). This patient demonstrated an incomplete structural response, requiring local reintervention, which confirmed soft tissue and musculoskeletal infiltration by the same tumor. **Conclusions:** HTT presents variable clinical and ultrasonographic patterns and cytological diagnosis is challenging. Although cell membrane ki67 MIB-1 immunostaining is a desirable pathological criterion, only one patient in our series exhibited this finding. HTTs are generally low-risk tumors, albeit occasional cases may demonstrate aggressive behavior, as seen in one patient with carcinoma-like progression.

THYROID NODULE

1112221 - ANALYSIS OF THE COMPLEMENTARY ROLE OF CELL BLOCK IN THE EVALUATION OF THYROID NODULES UNDERGOING TO FINE-NEEDLE ASPIRATION BIOPSY

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Cytological evaluation of thyroid nodules, performed on selected nodules according to size and ultrasound malignancy assessment, can accurately classify most nodules; however, unsatisfactory (Bethesda I) or indeterminate (Bethesda III/IV) samples correspond to approximately 5%-10% and approximately 20%, respectively. Using the cell block in addition to cytology aims to reduce inadequate samples and assist in classifying indeterminate cases. In this retrospective study, we included patients over 18 years old with thyroid nodules who underwent fine-needle aspiration biopsy under ultrasonographic guidance (FNA-US) between January 2023 and January 2024 in a tertiary, university-based hospital to evaluate the complementary role of the cell block. Two hundred six patients treated by the public health system were included, with 257 nodules evaluated by FNA-US. We found a female predominance (85.9%) and an average age of 59 years old. The cytological classification of the nodules followed the Bethesda System, with 74.3% of cases being benign, 10.9% unsatisfactory, 10.9% indeterminate, and 3.9% malignant. The cell block technique was performed on 221 nodules. The combination of cytology and cell block significantly reduced the rate of unsatisfactory results (from 10.9% to 7.4%, $p=0.004$) and enabled the reclassification of 11 nodules with unsatisfactory or indeterminate cytology. Of the 21 nodules submitted to histological evaluation, cytology was 100% in agreement with malignant cases, but there were 2 cases (1.05%) of malignancy among the nodules initially classified as benign. The main contribution of cell block analysis to cytology in the present study was to significantly reduce the rate of unsatisfactory specimens. Therefore, cell block preparation can change patient management, such as avoiding repeated punctures or unnecessary surgeries, by allowing the reclassification of cases with unsatisfactory or indeterminate cytology, contributing to more accurate therapeutic decisions.

THYROID NODULE

1112414 - ANAPLASTIC THYROID CARCINOMA COEXISTING WITH PAPILLARY CARCINOMA - A CASE REPORT

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Anaplastic thyroid carcinoma is a rare (1,5% to 2%) and aggressive tumor, which mainly affects women over 60 years of age. It is believed that this tumor arises because of the loss of differentiation in well-differentiated thyroid carcinomas. The differential diagnosis of anaplastic carcinoma comprises medullary and poorly differentiated carcinomas, as well as sarcomas, squamous cell carcinoma, lymphomas and chronic fibrosing thyroiditis. MCR, 92 years old, referred for cervical ultrasound, due to an apparent nodulation in the right cervical region. She referred partial thyroidectomy 22 years ago, due to follicular thyroid carcinoma. On physical examination, there was a voluminous nodulation in the cervical region, with a stony consistency, and rounded contours. A cervical ultrasound was performed, which showed a hypoechoic nodular formation in the right thyroid fossa, with a solid pattern, imprecise limits, and a grossly heterogeneous texture; measured 4,0 x 3,0 x 3,2 cm, and had peripheral and central vascularization (CHAMMAS IV - TI-RADS 4). FNA (Fine Needle Aspiration) was performed, and the cytopathological diagnosis was 'Anaplastic carcinoma arising in papilliferous thyroid carcinoma', Bethesda category VI. Immunohistochemical analysis showed a change in the cell differentiation pattern during the course of the disease. The coexistence of a well-differentiated component and anaplastic carcinoma suggests dedifferentiation of a pre-existing, well-differentiated thyroid cancer through a multiphysics process of carcinogenesis. Most patients present with symptoms of extension of the carcinoma, such as dyspnea, dysphagia and cough. The median survival rate of these patients is five months, and almost 50% of cases have distant metastasis at the time of diagnosis.

THYROID NODULE

1112339 - BETHESDA NODULES CATEGORY I: THE REALITY OF FACING THIS CYTOLOGY RESULT IN A PRIVATE CLINIC IN ARGENTINA

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Introduction: The recommended approach for Bethesda I (BI) thyroid nodules involves repeating fine-needle aspiration (FNA) under ultrasound (US) guidance. Their therapeutic approach remains controversial, as does the reported malignancy rate. **Objective:** 1) To establish the prevalence of nodules with BI cytology and their risk of malignancy (ROM) 2) To identify US and cytological features associated with malignancy. **Methods:** Retrospective observational study. Patients > 18 years were included with FNA done between Jan 2020 - Jul 2024, followed at least one year. The final diagnosis was determined with histology (in case of surgery) and ROM was analyzed based on BI cytology (divided in three subgroups: blood, insufficient thyrocytes and cyst content) and US features (ATA 2015 and ACR-TIRADS 2017). **Results:** In this period, 1008 FNA were analyzed. The prevalence of BI thyroid nodules was < 1% (n=85); 77 women (90,6%), median age 54 years (18-78). Surgery was performed on 12 patients (12.9%) and histology confirmed malignancy in 6 cases. Of the 85 nodules BI, 53% (n=45) corresponded to intermediate-to-high ATA ultrasound risk, and 49.4% (n=42) were categorized as ACR-TIRADS IV-V. The majority of malignant nodules were associated with high risk US, although no significant correlation was found between US characteristics and ROM ($p = 0.26$). Respect to cytology, 70% (n=60) presented predominance of blood. Cytological results indicated that blood was not statistically significant compared to other subgroups ($p = 0.21$) and did not present an independent ROM (OR: 0.4; 95% CI: 0.026-6.176; $p = 0.5$). FNA was repeated in 43 patients, 8 of whom required surgery. **Conclusion:** According to our findings, there was no association between US and cytological characteristics and ROM, suggesting that an individualized approach is recommended for BI nodules.

THYROID NODULE

1113491 - CASE REPORT: RADIOFREQUENCY ABLATION AS A GAME-CHANGER IN NON-INVASIVE TREATMENT FOR BENIGN THYROID NODULES

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Case Presentation: A 67-year-old female patient with a history of hypothyroidism was referred to the Head and Neck Endocrinology department for evaluation of a thyroid nodule. Ultrasound imaging revealed a thyroid nodule measuring 1.6 cm in length, 1.1 cm in height, and 3.2 cm in transverse diameter, with a volume of 2.94 cc. A fine-needle aspiration biopsy (FNAB) was performed, and the cytology was classified as Bethesda II, indicating a benign lesion. Given the benign nature of the nodule, the patient was deemed appropriate for treatment with radiofrequency ablation (RFA). RFA was performed as a minimally invasive procedure under local anesthesia. Post-ablation, the patient was monitored closely with ultrasound evaluations. At the 7-month follow-up, the nodule had decreased significantly in size to 0.7 x 0.5 x 1.2 cm, with a volume of 0.21 cc. At the 12-month follow-up, no nodule was detectable on ultrasound, indicating complete resolution. Throughout the follow-up period, the patient's thyroid profile remained stable and within normal limits. **Discussion:** This case demonstrates the successful use of RFA as a treatment for benign thyroid nodules in a patient with hypothyroidism. The procedure resulted in a significant reduction in nodule size and complete resolution by 12 months, with no adverse effects on thyroid function. RFA is an effective, non-invasive treatment option for benign thyroid nodules, offering a favorable outcome for patients who are not candidates for surgery or prefer less invasive alternatives. **Final Comments:** This case emphasizes the clinical benefits of RFA in managing benign thyroid nodules, particularly for patients with underlying thyroid conditions, offering an excellent alternative to traditional surgical approaches.

THYROID NODULE

1112584 - CHARACTERIZATION OF FINE NEEDLE ASPIRATION BIOPSY OF THYROID NODULES SMALLER THAN 10MM IN A UNIVERSITY HEALTH CENTER ACCORDING TO ULTRASONOGRAPHIC RISK

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Introduction: The diagnosis of thyroid nodules is increasing among the general population, mainly due to the broad use of ultrasonography. Motivating more fine needle aspiration biopsies (FNAB) and, subsequently, an increased diagnosis of thyroid cancers. **Methods:** This is a retrospective study of all the FNAB, between January 2022 and September 2024 in a university health center, performed by an expert radiologist. Patients were referred from diverse Health centers. The inclusion criteria was Thyroid Nodule smaller than 10 mm. We evaluated ultrasonographic risk (USR) according to ATA guidelines and Bethesda classification. **Results:** From a total of 1553 FNA, 206 fulfilled the inclusion criteria. When classified according to Bethesda (B) System for Reporting Thyroid Cytopathology the rates were BI: 14.07%, BII 35.4%, BIII 16.99%, BIV 1.45%, and BV and BVI 31.6%. High USR had BV and BVI rates of 38.18% and 17.27% respectively, while low USR had a 3,7% probability of being a BV/VI, a 66,67% chance of being a BII and 22.03%, BIII. There was a significant association between intermediate-high and high USR and BV/VI when estimated by Chi-square test ($p < 0.01$), with an OR of 16.7 [6.33, 48.18] and a RR of 8.75 [3.14, 13.65] compared with low and intermediate risk. **Conclusion:** In our population, nodules smaller than 10 mm with a low USR had a 3.7% likelihood of being classified as BV/BVI. In contrast, high-risk nodules had a significantly higher probability of obtaining a BV/BVI result on FNAB. Additionally, we observed a BI rate of 14.07%, which may be attributed to the smaller size of the nodules. This highlights the importance of USR when deciding whether to perform FNAB on nodules smaller than 10 mm.

THYROID NODULE

1113832 - CLINICAL AND ECONOMIC IMPACT OF THE MIR-THYpe MOLECULAR TEST IN THE MANAGEMENT OF INDETERMINATE THYROID NODULES: REAL-WORLD EVIDENCE FROM A HOSPITAL-BASED STUDY

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Introduction: Indeterminate thyroid nodules (Bethesda III and IV) pose a significant clinical challenge, often leading to unnecessary surgeries, increased healthcare costs, and patient morbidity. The mir-THYpe molecular test was developed to improve risk stratification by combining microRNA profiling and mutation analysis. **Objective:** This study aimed to validate its clinical utility and cost-effectiveness in a real-world hospital setting. **Methods:** A prospective study was conducted involving 173 mir-THYpe tests performed at Hospital Samaritano (São Paulo, Brazil) from February 2024 to January 2025. Physicians completed structured questionnaires before and after receiving test results to assess changes in clinical decision-making. A cost-effectiveness analysis was performed, focusing on avoided surgical procedures and related healthcare costs. **Results:** In the mir-THYpe full cohort, 80% of cases showed a change in clinical management post-test, primarily reducing unnecessary surgeries. Of the 119 cases, over 50% would have undergone surgery without molecular testing. In the mir-THYpe pre-op group, 32% of cases had their surgical approach adjusted based on molecular results, guiding more personalized procedures. The economic analysis demonstrated that at a market price of R\$ 4,920.00 per test, the use of mir-THYpe resulted in an average net saving of R\$ 970.00 per patient tested, avoiding 37 invasive procedures. In the CBHPM scenario, the incremental cost was minimal, with an estimated budget impact of only R\$ 0.39/month per health plan beneficiary. Additionally, 100% of participating physicians reported high satisfaction with report clarity and technical support, while indicating areas for enhanced medical education regarding test applicability. **Conclusion:** The mir-THYpe molecular test demonstrated substantial clinical benefits by reducing unnecessary thyroid surgeries and guiding appropriate surgical decisions, while also proving to be cost-effective in real-world practice. These findings support its broader adoption as a valuable tool for optimizing the management of indeterminate thyroid nodules.

THYROID NODULE

1112426 - COMPREHENSIVE PROTEOMICS AND MACHINE LEARNING ANALYSIS TO DISTINGUISH FOLLICULAR ADENOMA AND FOLLICULAR THYROID CARCINOMA FROM INDETERMINATE THYROID NODULES

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Introduction: Preoperative diagnosis of follicular thyroid carcinoma (FTC) is challenging as it cannot be readily differentiated from follicular adenoma (FA) or benign follicular nodular disease (FND) based on sonographic or cytological features commonly utilized in real-world practice. **Methods:** This study utilized comprehensive proteomics and machine learning (ML) models to identify novel diagnostic biomarkers for classifying the three subtypes (FTC, FA, and FND). Bottom-up proteomics techniques were applied to quantify formalin-fixed paraffin-embedded (FFPE) thyroid tissues. A total of 202 FFPE tissues including 62 FNDs, 72 FAs, and 68 FTCs, were utilized for the proteomic analyses. **Results:** A total of 8,554 proteins were quantified by open spectrum-spectrum matches and approximately 9% of proteins (780 proteins) were differentially expressed in each group. Applying an ML model to the proteomics results in samples with preoperative indeterminate cytopathology (n=183) identified a combination of five proteins (CNDP2, DNAAF5, DYNC1H1, FARSF, and PDCD4), six proteins (DNAAF5, FAM149B1, RPS9, TAGLN2, UPF1, and UQCRC1), and seven proteins (ACTN4, DSTN, MACROH2A1, NUCB1, SPTAN1, TAGLN, and XRCC5) in the FND, FA, and FTC prediction models, respectively. The performance of the FND, FA, and FTC classifiers indicated that the median AUC values for the random forest were 0.832 (95% CI: 0.8240.839), 0.826 (95% CI: 0.8170.835), and 0.870 (95% CI: 0.8630.877), respectively. **Conclusion:** Quantitative proteome analysis of thyroid tissue and an ML model provided an optimized multi-protein panel that could distinguish FTC from benign subtypes. Our findings suggest that a proteomic approach can be applied to the differential diagnosis of FTC.

THYROID NODULE

1112479 - CORRELATION BETWEEN ATA 2015 ULTRASOUND SYSTEM AND BETHESDA SYSTEM FOR THYROID CYTOPATHOLOGY IN A TERTIARY CARE CENTER IN PARAGUAY

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Introduction: Thyroid nodules are frequent lesions, and ultrasound is the diagnostic method of choice to characterize them and stratify their risk of malignancy. **Objective:** To establish correlation between the ATA 2015 ultrasound classification of thyroid nodules and cytologic results by Bethesda, and to assess the sensitivity and specificity of the ATA classification for detection of nodules candidates for surgical treatment, in patients who underwent fine needle aspiration biopsy (FNAB) from January to November 2024, in a referral center. **Methods:** Prospective, observational, analytical design. A negative cytologic result (-) was considered for Bethesda II and III nodules and a positive result (+) for Bethesda IV, V and VI nodules, since these require surgical treatment, in order to assess the sensitivity and specificity of the ATA classification. Nodules of low and very low suspicion were considered negative (-) and those of intermediate and high suspicion positive (+). **Results:** Total of 73 patients. Mean age 54 ± 11.61 years, predominantly female, 94.52%. 41% of the nodules with ≥ 2 cm in their largest diameter. 18% and 30% were of very low and low suspicion respectively; 19% of intermediate suspicion and 33% of high suspicion. 16% were Bethesda IV, V and VI of which 92% were of intermediate and high suspicion. 51% Bethesda II, of which 29.72% were of very low suspicion and 43.34% of low suspicion. We found a sensitivity and specificity of 91.67% and 63.83% respectively, as well as a negative predictive value of 96.77% and a positive predictive value of 39.29%. **Conclusion:** Nodules with low and very low ultrasound suspicion by ATA, corresponded significantly with those with benign cytology, so the use of ATA criteria may be useful to limit the indications for FNAB in these cases. Keywords: thyroid nodule; ultrasound; fine needle aspiration biopsy.

THYROID NODULE

1112661 - CORRELATION BETWEEN NON-INVASIVE MARKERS OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AND MALIGNANCY RISK IN THYROID NODULES

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Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) affects approximately 25% of the global population. Recent evidence suggests a potential relationship between metabolic alterations and thyroid neoplasms, where insulin resistance and chronic inflammation associated with MASLD might influence thyroid cell proliferation and nodule malignancy risk. **Objective:** To determine the correlation between clinical, biochemical, and imaging non-invasive markers of MASLD and malignancy risk categories in thyroid nodules according to the Bethesda classification system. **Methods:** This preliminary analysis of an ongoing prospective cross-sectional study was conducted at La Raza National Medical Center in Mexico City, analyzing the first 39 patients with thyroid nodules who underwent vibration-controlled transient elastography (VCTE). Patients were divided into Likely MASLD (n=14) and Unlikely MASLD (n=25) groups. Statistical analysis included Shapiro-Wilk test for normality distribution, independent t-tests for parametric data, Mann-Whitney U test for non-parametric data, and MANOVA for body composition variables. Pearson or Spearman correlations were performed as appropriate. Binary logistic regression was used to determine adjusted odds ratios for risk factors. Post-hoc power analysis was conducted with Cohen's d effect size calculation. **Results:** Significant differences were found between Likely and Unlikely MASLD groups in BMI (32.8 ± 5.26 vs 26.4 ± 4.51 kg/m², $p < 0.001$), body fat percentage ($49.9 \pm 12.5\%$ vs $37.5 \pm 9.41\%$, $p < 0.001$), and CAP values (306 vs 236 dB/m, $p < 0.001$). Multivariate analysis revealed significant associations between MASLD markers and higher Bethesda risk categories. Key risk factors included elevated BMI (OR=2.8, 95%CI=1.4-5.6, $p=0.004$), increased visceral fat (OR=2.1, 95%CI=1.2-3.7, $p=0.009$), and high CAP values (OR=3.2, 95%CI=1.6-6.4, $p < 0.001$). **Conclusion:** In this preliminary analysis, non-invasive MASLD markers showed significant correlation with higher malignancy risk categories in thyroid nodules according to the Bethesda classification. The study achieved 78% power to detect medium effect sizes ($\alpha=0.05$). While these initial findings suggest potential utility in risk stratification, validation in the complete planned cohort is ongoing.

THYROID NODULE

1112235 - EFFICACY OF USING MUSIC THERAPY DURING THYROID FINE NEEDLE ASPIRATION BIOPSY IN REDUCING THE PERCEPTION OF PAIN AND ANXIETY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Thyroid Fine Needle Aspiration Biopsy (FNAB) is a commonly performed procedure following the detection of a thyroid nodule. However, despite generally being well-tolerated, this invasive technique may cause discomfort, including pain and anxiety. **Objective:** We conducted a meta-analysis to assess whether the use of music during thyroid fine needle aspiration biopsy reduces the perception of pain and anxiety compared to no music intervention in patients undergoing this procedure. **Methods:** This study conducted a systematic review and meta-analysis to evaluate the efficacy of music therapy in reducing pain and anxiety during thyroid fine needle aspiration biopsy procedures. The analysis utilized data from randomized controlled trials identified through searches of the PubMed, Embase, and Cochrane databases. Statistical analysis was performed using RevMan 5.4 software. **Results:** We included 3 randomized controlled trials with 702 patients, of whom 344 (49.1%) underwent music therapy during thyroid FNAB. Music therapy significantly reduced pain perception compared to the control group (MD -0.70; 95% CI -0.93 to -0.46; $p < 0.00001$; $I^2=99\%$; figure 1). Regarding anxiety, there was a trend favoring music therapy, but the results did not reach statistical significance (MD -1.33; 95% CI -2.85 to 0.20; $p=0.09$; $I^2=80\%$; figure 2). **Conclusion:** Our findings suggest that music therapy during thyroid FNAB significantly reduces pain perception compared to no intervention. However, its effect on anxiety warrants further investigation, given the lack of statistically significant results and the presence of heterogeneity across studies.

THYROID NODULE

1112401 - FINE-NEEDLE ASPIRATION WASH FOR CERVICAL LESIONS: A FOCUS ON PTH AND THYROGLOBULIN

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Introduction: Fine-needle aspiration wash (FNAW) thyroglobulin (Tg) and cytology are widely used for diagnosing cervical lesions. However, distinguishing thyroid from parathyroid and non-thyroid lesions presents a diagnostic challenge. The inclusion of parathyroid hormone (PTH) analysis in FNAW offers a complementary approach to enhance diagnostic accuracy. **Objective:** 1. To evaluate whether Tg-FNAW can be positive in parathyroid lesions 2. To evaluate the added diagnostic value of PTH measurement in FNAW for cervical lesions. 3. To determine the utility and cutoff point of different PTH-FNAW measurement platforms. **Methods:** A retrospective study was conducted on 207 cervical lesion aspirations performed between August 2010 and November 2024. FNAW samples were analyzed for Tg, PTH, and anti-thyroglobulin antibodies alongside cytology. PTH levels were measured using three platforms: Immulite 1000 (Siemens), Liaison (Diasorin), and Cobas c411 (Roche). Diagnostic performance was assessed using ROC curves. **Results:** Tg-FNAW was highly sensitive for thyroid origin lesions (100%) but was dosable in 14/30 parathyroid lesions. The 3 methods used showed similar and excellent performance for the diagnosis of parathyroid tissue, improving diagnostic accuracy (AUC 0.991.0, $p < 0.01$). PTH levels >90 pg/mL on the 3 platforms employed, were consistent with parathyroid tissue, even in cases with positive Tg or inconclusive cytology results. Negative Tg and PTH findings, combined with cytology, effectively identified diagnoses such as granulomas, and non-thyroid metastases (N=46). **Conclusion:** PTH measurement in FNAW is a valuable addition to Tg and cytology, enhancing the diagnostic precision for cervical lesions, with a cutoff value >90 pg/mL in all 3 platforms. This multimodal approach ensures accurate differentiation of thyroid, parathyroid, and non-thyroid lesions, supporting informed clinical decisions in complex cases.

THYROID NODULE

1112412 - FOCAL NODULAR THYROIDITIS WITH HYPERVASCULARIZATION: UNCOMMON PRESENTATIONS REGARDLESS OF CLINICAL PRESENTATION OR GLANDULAR PARENCHYMAL CHANGES

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Introduction: Thyroiditis exhibits diverse ultrasonographic features, often including diffuse hypoechogenicity and inflammation. However, focal thyroiditis presenting as hypervascularized nodules is less common and may be mistaken for malignancy. This case series highlights three instances of focal nodular thyroiditis with hypervascularized nodules, emphasizing the importance of accurate diagnosis to prevent unnecessary interventions. **Objective:** To describe and analyze the ultrasonographic and cytological characteristics of three cases of focal thyroiditis with hypervascularized nodules, aiming to improve diagnostic accuracy and reduce unnecessary treatments. **Methods:** Three patients with thyroid nodules classified as ACR TI-RADS 4 underwent fine needle aspiration (FNA) biopsy for evaluation. Ultrasonographic findings, including nodule size, composition, echogenicity, shape, margin, vascularization patterns, and glandular parenchymal changes, were assessed. Cytological results confirmed the diagnosis in each case. **Results:** Case 1: A 35-year-old male presented with a 1.0 x 0.83 x 0.59 cm solid, hypoechoic, hypervascularized nodule in a gland with mildly heterogeneous echotexture. Cytology confirmed benign lymphocytic thyroiditis. Case 2: A 43-year-old male with no family history of thyroid disease had a 2.7 x 1.2 x 1.46 cm hypoechoic nodule with lobulated margins and central vascularization, in a gland with mildly heterogeneous echotexture. Cytology confirmed thyroiditis. Case 3: A 61-year-old female with chronic thyroiditis and elevated PTH levels presented with a 1.7 x 1.67 x 1.6 cm (updated to 1.9 x 1.9 x 1.7 cm in March 2024) mixed nodule with lobulated margins, in the lower third of the right lobe, within grossly heterogeneous glandular echotexture. Cytology confirmed thyroiditis. **Conclusion:** Focal thyroiditis with hypervascularized nodules can mimic malignancy on ultrasound, particularly in ACR TI-RADS 4 nodules. Accurate recognition of preserved thyroid parenchyma and careful cytological assessment are essential to distinguish benign conditions from malignancy, minimizing unnecessary interventions.

THYROID NODULE

1112427 - GRAVES' DISEASE FOLLOWING MICROWAVE ABLATION OF A THYROID NODULE: A CASE REPORT

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Case Presentation: A 45-year-old male patient presented with a 60.8 mL nodule in the left thyroid lobe and local compressive symptoms. Cytology was compatible with a colloid nodule, with normal thyroid function and negative antibodies. The patient underwent microwave ablation (MWA). Three months after the procedure, there was an 83% reduction in nodule volume, with normal thyroid function. At follow-up, one year and three months later, the patient developed weight loss, palpitations, and exophthalmos. Positive TRAB confirmed the diagnosis of Graves Disease (GD). Scintigraphy showed hyperfunctioning thyroid parenchyma with a hypofunctioning nodule. Due to new nodule growth, partial thyroidectomy was performed, and histopathology confirmed a colloid nodule. **Discussion:** Patients undergoing nodule ablation may develop thyroiditis a few weeks after the procedure. However, in this case, in addition to thyrotoxicosis symptoms, the presence of positive TRAB and exophthalmos confirmed the diagnosis of GD. In a series of 34 cases of microwave ablation, only one patient developed GD three months after the procedure. Episodes of hyperthyroidism after MWA of thyroid nodules are rare and generally transient, occurring in approximately 1.4% of cases. There are reports of two cases of GD following radiofrequency ablation, one after 14 weeks and another after 8 weeks. In the present case, with microwave ablation, the presentation was more delayed, occurring 60 weeks after the procedure. One hypothesis is that the local reaction induced by the technique exposed thyroid antigens, triggering an immune response that led to the development of the disease. **Final Comments:** The pathophysiological mechanism linking GD to microwave ablation is not well established. As this is a relatively recent technique, there are few reports of rare complications such as this. Nonetheless, it is clear that monitoring thyroid function before and after the procedure is essential, as medium- to long-term follow-up of these patients.

THYROID NODULE

1112408 - IMPACT OF ON-SITE CYTOLOGICAL EVALUATION ON BETHESDA CLASSIFICATION OUTCOME IN A PRIVATE CENTER VERSUS IN A PUBLIC CENTER

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Introduction: The evaluation of thyroid nodules has three main pillars: clinical, ultrasound and cytological. However, between 6.4-33.6% of cytological samples are unsatisfactory; for this reason, Rapid on-site evaluation (ROSE) has recently been chosen to improve it. **Objective:** Determine the impact on Bethesda classification by incorporating ROSE of thyroid nodules samples evaluated in a public and a private center. **Methods:** Analytical, cross-sectional and retrospective study. The databases of thyroid nodules cytology in a public center (2016-2018) without ROSE, and in a private center (2021-2024) with ROSE were analyzed. The ultrasound classification of suspected malignancy was based on ATA 2016 and ACR-TIRADS systems. A fine needle aspiration guided by ultrasound was performed in all cases by a unique operator. STATA 18 version was used. Descriptive analyses were performed with Chi2/Fishers Exact Test for proportions and Students T or Mann-Whitney U for means according to their normality. Bivariate and multivariate analysis was performed by Logistic Regression. **Results:** 308 nodules without ROSE, and 427 nodules with ROSE were analyzed. Females predominated in both databases with a higher proportion of males in the private center (6.82% vs 16.39%, $p < 0.01$). No significant difference in age. There were significant differences in the number of punctures and place of birth. Bethesda category 1, 3, 5 was decreased; and Bethesda 2 was increase with ROSE ($p < 0.01$). Bivariate analysis showed that ROSE (RR -7.25 $p < 0.001$ 95% CI [-3.34; -1.92]) and performing a single puncture (RR -4.44 $p < 0.001$ 95% CI [-6.46; -2.50]) are protective against the risk of Bethesda 1 cytology; this was confirmed by the multivariate analysis. ROSE was associated with a lower risk of Bethesda 3 cytology (RR -4.52 $p < 0.001$ 95% CI [0.01;0.15]). **Conclusions:** The use of ROSE decreases the risk of Bethesda 1, 3 and 5 cytology, and increases Bethesda 2.

THYROID NODULE

1112519 - IMPLEMENTATION OF SENDIMUST (SENDIMADS ULTRASOUND STRUCTURED REPORT FOR THYROID NODULES). A FREE MULTILANGUAGE WINDOWS-BASED DESKTOP APPLICATION TO GENERATE COMPLETE STRUCTURED THYROID ULTRASOUND REPORTS

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Introduction: Ultrasound characterization is often incompletely described in the reports, making it difficult to assess criteria for biopsy and to evaluate nodule growth during follow-up. **Objective:** To develop a desktop tool to generate completely structured thyroid ultrasound reports aiming to improve reports quality, homogenize terminology, facilitate follow-up and decision-making, and reduce reporting time. **Methods:** A Windows-based desktop application, SENDIMUST, was programmed with Python language and several libraries to implement the graphic interface, the internal management of information, the representation of images and the generation of the structured report. Predefined selection menus describe characteristics of the thyroid gland, nodules, and cervical lymph nodes. Fields necessary for thyroid nodule risk assessment are mandatory. Shape and risk category of several systems are automatically calculated. Uploading previous reports prepopulates fields with the latest entry; and allows calculating growth rates from historic measurements. A pictogram displays nodules scaled and colored according to risk category in the appropriate location. No personal data is collected. The report is automatically copied to the clipboard in txt format. To evaluate the impact of SENDIMUST on reporting time, 7 thyroid ultrasound experts recorded the time spent issuing ultrasound reports of patients with at least 1 thyroid nodule in duplicate: manually and with SENDIMUST. A mixed-effects model was used to compare time between methods adjusting for number of nodules. **Results:** 128 ultrasounds were analyzed. The median time spent reporting thyroid ultrasounds was 110 seconds (IQR 79-150) manually; and 93 seconds (IQR 67-136) with SENDIMUST. After adjusting for the number of nodules and considering paired data and variability between each reporting physician, reporting time with SENDIMUST was 19 seconds faster (95% CI, 12-27). **Conclusion:** SENDIMUST reduced reporting time while ensuring complete and standardized reports. Larger time savings are expected for reporting follow-up ultrasounds

THYROID NODULE

1112273 - MANAGEMENT OF PATIENTS WITH AUTONOMOUSLY FUNCTIONING THYROID NODULES AND NORMAL TSH AND FT4 BLOOD LEVEL

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1 - Polyclinic Lacic

Objective: The purpose of this study was to evaluate the results of radionuclide therapy with iodine-131 (I-131) in patients (pts) with autonomously functioning thyroid nodules (AFTNs) and a normal TSH and FT4 blood level. **Methods:** In this study 131 cytological benign AFTNs in 116 pts (100 female and 16 male) with normal TSH and FT4 level have been treated with a fixed I-131 doses (370 MBq). Clinical exam, ultrasonography with color Doppler (US), fine needle aspiration biopsy (FNAB), TSH, FT4, FT3, anti-TPO, anti-Tg, anti-TSH receptor and thyroid scan (scintigraphy) have been performed in all pts before and 6 months after I-131 therapy. **Results:** The median age of the pts was 61 (range 35 - 90) years. AFTNs were located more frequently in the right thyroid lobe (73 nodules) than in the left lobe (58 nodules). In 19 pts a solitary AFTN has been found on ultrasonography and the other 97 patients had AFTNs in multinodular goiter. 15 pts had two AFTNs. On post I-131 therapy thyroid scan in 80 AFTNs complete therapy effect has been observed, but in 51 AFTNs a scintigraphically partial effect has been noted. Statistical analysis showed a significant reduction in the thyroid ($p=2,8179E-24$) and AFTNs ($p=4,0351E-06$) volume after I-131 therapy. TSH value significantly increased ($p=3,0081E-05$) and FT4 value significantly decreased ($p=3,1438E-05$) after I-131 therapy. FT3 ($p=0,3757$), anti-TPO ($p=0,7615$) and anti-Tg ($p=0,1412$) and anti-TSH receptor ($p=0,1182$) values did not change significantly. **Conclusion:** This study shows that radionuclide therapy with I-131 in pts with AFTN and normal TSH and FT4 blood level is a very effective modality. The effect of the I-131 therapy on AFTNs can be evaluated with a thyroid scan 6 months after I-131 therapy.

THYROID NODULE

1114261 - MERGING TIRADS AND THE AMERICAN THYROID ASSOCIATION (ATA) 2015 CLASSIFICATION FOR THYROID NODULES – A TOOL TO IMPROVE THE RISK OF MALIGNANCY ASSESSMENT FOR NON-CLASSIFIABLE NODULES WITH INDETERMINATE CYTOLOGY

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Introduction: Although the published ATA ultrasound classification nodule guidelines (2015) has been widely used, there remains a subset of nodules that do not fit into any of its defined categories. Most non-classifiable (NC-ATA) nodules include those with sonographic suspicious features (SSF) that are either iso- or hyperechoic, as well as mixed cystic-solid nodules. A recent meta-analysis reported a prevalence of NC-ATA nodules of 7.8%, with an overall risk of malignancy (RoM) of 20.3%, making it a clinically relevant subset. **Objective:** This cohort study aimed to assess the RoM in cytologically indeterminate NC-ATA nodules with confirmed outcomes and to merge the ATA 2015 and TIRADS classifications to better stratify these nodules. **Methods:** This was a cohort study of indeterminate thyroid nodules with confirmed outcome. Malignancy was confirmed exclusively by surgery, while benign outcomes were determined via histopathology (n=122), benign fine-needle aspiration biopsy (n=14) or scintigraphy-confirmed autonomy (n=3). **Results:** Preliminary results indicate that among 216 indeterminate nodules, 26 (12%) were NC-ATA, with a malignancy rate of 26.9%. These nodules were predominantly solid (81%) and either iso- or hyperechoic (81%). Among iso- or hyperechoic nodules, the most frequent SSFs were non-ovoid shape (65%) and microcalcifications (41%), while suspicious margins and macrocalcifications were each found in 18% of cases. Notably, iso- or hyperechoic nodules with only one SSF were not associated with malignancy, whereas among those with two SSFs, 57% were malignant. In the overall cohort, the malignancy prevalence according to the ATA 2015 classification and the proposed merged classification was as follows: low-risk (27% [n=25] vs. 30% [n=35]), intermediate-risk (44% [n=21] vs. 40.7% [n=24]), and high-risk (67% [n=32] vs. 63.4% [n=26]). Both analyses demonstrated statistical significance when low-risk nodules were used as the reference group (p<0.01). **Conclusion:** Integrating the ATA 2015 and TIRADS classifications may enhance risk stratification for NC-ATA indeterminate nodules, improving clinical decision-making and patient management

THYROID NODULE

1112179 - PARATHYROID ADENOMA: RADIOLOGIC FEATURES AND CORRELATION STUDY WITH 99mTc-SESTAMIBI SPECT FINDINGS

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Objective: Our study was intended to describe the typical radiologic features of parathyroid adenoma and correlation study with 99mTc-sestamibi SPECT findings. **Methods:** A review of a surgical database and electronic medical records from 2018 to 2023 identified the cases of 17 patients who underwent preoperative cervical sonography for primary hyperparathyroidism with subsequent resection of pathologically proven parathyroid adenoma. Two radiologists retrospectively evaluated the preoperative ultrasound images and assessed for morphologic characteristics, size, location, and color Doppler vascularity. 99mTc-sestamibi SPECT findings, surgical and pathologic reports were reviewed. **Results:** Most of the parathyroid adenomas (15/17, 86%) were deep or inferolateral to the adjacent thyroid. An echogenic border separating the adenoma from the overlying thyroid was identified in all cases. 14 cases were solid (82%), one case was solid and cystic, and two cases were cystic (11%) in sonographic morphology. Color Doppler examination of 14 patients showed feeding vessels with internal color flow to the solid components in 7 patients (50%). All patients underwent preoperative 99mTc-sestamibi SPECT, and the adenoma was definitively localized in 9 patients (52%) and equivocally localized in 6 patients (34%). One case of ectopic mediastinal parathyroid adenoma was identified by 99mTc-sestamibi SPECT and subsequently confirmed by chest computed tomography. **Conclusion:** Awareness of typical radiologic features (location, morphologic characteristics, color Doppler findings) may aid radiologists in preoperative localization of parathyroid adenoma. And 99mTc-sestamibi SPECT is also helpful to the diagnosis of this tumor.

THYROID NODULE

1112389 - PERIPHERAL DISCONTINUOUS HYPERECHOIC FOCI IN THYROID NODULES: A NEW ULTRASONOGRAPHIC PATTERN SUGGESTIVE OF PAPILLARY CARCINOMA

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Introduction: Most ultrasound-based risk stratification systems for thyroid nodules recognize several types of echogenic foci, including punctate echogenic foci (microcalcifications), coarse internal calcifications, and peripheral (rim) calcifications, with differing associations with malignancy. **Objective:** We have identified a new, previously undescribed pattern of peripheral discontinuous small echogenic foci that is highly associated with papillary thyroid cancer. **Methods:** In this multicenter, retrospective, observational case series, we gathered ultrasound images of thyroid nodules with peripheral discontinuous small echogenic foci from patients in Brazil, the United States, Italy, and Romania. Cases were included based solely on the presence of this pattern, regardless of nodule echogenicity or shape. Each nodule underwent assessment by a multidisciplinary team of experienced radiologists, endocrinologists, head and neck surgeons, and cytopathologists. Final diagnoses were confirmed by cytopathological and histopathological analysis. **Results:** 12 nodules met the inclusion criteria. All were confirmed to be papillary carcinoma by histopathological examination. These findings are consistent with the initial three-case series presented at the 2024 annual meeting of the American Thyroid Association 2024 by (L.D.R.) et al. **Conclusion:** This case series suggests that a peripheral arrangement of discontinuous small hyperechoic foci is strongly associated with papillary carcinoma. Further studies with larger sample sizes are warranted to verify the implications of this ultrasonographic finding and possibly inform future changes to risk stratification systems for thyroid nodules.

THYROID NODULE

1114058 - PREDICTING CERVICAL LYMPH NODE METASTASIS IN PAPILLARY THYROID CARCINOMA USING CAPSULE DISRUPTION LENGTH MEASURED BY 3D-US

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Introduction: Thyroid cancer (TC), particularly Papillary Thyroid Carcinoma (PTC), is a prevalent endocrine malignancy with a propensity for lymph node metastasis (LNM) at initial diagnosis, impacting patient prognosis. Extrathyroidal extension (ETE) is a key factor in preoperative LNM prediction. The criteria for ultrasound diagnosis of ETE remain controversial and quantitative indicator of ETE is lacking. **Objective:** The aim is to determine if the length of capsule disruption (LCD) on three-dimensional ultrasound (3D-US) can predict cervical LNM in PTC patients. **Methods:** A prospective cohort of 168 patients from Peking Union Medical College Hospital was examined by 3D-US. LCD was measured using the omniview mode of 3D-US. Statistical analyses included Chi-square tests, T tests, Mann-Whitney tests, ROC curve analysis and logistic regression analysis. **Results:** Of the 126 patients included, 71 had LNM. Younger age, male gender, larger malignant nodules, LCD, echogenic foci and thyroid capsule invasion were significantly associated with LNM. LCD ≥ 0.42 cm increases LNM risk by 4.097 ($p < 0.001$). A nomogram was constructed incorporating gender, age, maximum diameter of the largest malignant nodule (MDLM), and LCD to estimate the risk of LNM. The accuracy and AUC of the nomogram were 73.0% and 0.795(0.718-0.873). **Conclusion:** LCD on 3D-US is a significant predictor of cervical LNM in PTC patients. This study's nomogram, based on easily measurable parameters, can help in preoperative assessment of LNM risk, potentially guiding surgical management.

THYROID NODULE

1112201 - PRELIMINARY RESULTS OF A PROSPECTIVE STUDY ON THE EFFICACY AND SAFETY OF SINGLE-SESSION RADIOFREQUENCY ABLATION IN TREATING BENIGN THYROID NODULES

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Objective: This study aimed to assess the safety and effectiveness of radiofrequency ablation (RFA) for benign thyroid nodules and identify independent factors affecting nodule volume reduction rates at one and six months post-treatment. **Materials and Methods:** Conducted at a single medical center, this prospective study included 80 benign thyroid nodules in 68 patients undergoing RFA. The procedures employed two key techniques: the trans-isthmic and moving-shot approaches. Clinical and ultrasound evaluations were performed at one and six months after treatment. The primary outcomes measured were the volume reduction ratio (VRR) at these intervals, while secondary outcomes included therapeutic success rates and complication rates. Multiple linear regression analysis was applied to pinpoint independent factors influencing VRR. **Results:** The study followed 68 patients with 80 nodules over one and six months. The average VRR was 41.00% at one month and 69.65% at six months, with an 82.9% therapeutic success rate at the six-month mark. Symptom and cosmetic scores showed significant improvement after one month, while thyroid function remained stable. Three cases of minor complications (temporary voice changes) were noted. Regression analysis indicated that both the internal composition and initial volume of nodules were significantly associated with VRR at the one-month follow-up. **Conclusion:** RFA was shown to be a safe and effective treatment for benign thyroid nodules, offering an alternative therapeutic option with promising outcomes.

THYROID NODULE

1112355 - PREVALENCE AND DIAGNOSTIC IMPLICATIONS OF BRAF, RAS MUTATIONS, AND RET/PTC REARRANGEMENTS IN THYROID NODULES: A STUDY IN A BRAZILIAN PUBLIC HEALTH POPULATION

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Introduction: A simplified molecular profile, including BRAF and RAS gene mutations and RET/PTC rearrangements, has been proposed for pre-surgical evaluation of thyroid nodules. However, its applicability may vary across different populations. **Objective:** The objective of this study was to assess the prevalence of BRAF and RAS gene mutations and RET/PTC rearrangements in a cohort of Brazilian patients with thyroid nodules evaluated by FNAB within the public health system. **Methods:** Point mutations in BRAF and RAS genes were detected through DNA analysis using Sanger sequencing. The rearrangements RET/PTC1 and RET/PTC3 were detected in RNA samples with reverse transcriptase-polymerase chain reaction. **Results:** A total of 233 thyroid nodules in 221 patients (86.9% female; mean age, 55.5 ± 14.0 years) were evaluated. High-quality DNA and RNA were obtained from 201 nodules. Twenty-eight mutations were identified (13.9% of the samples), including 11 BRAF-like (10 BRAF V600E and 1 RET/PTC1 fusion) and 17 RAS-like (9 HRAS codon 61, 5 NRAS codon 61, and 3 KRAS codons 12/13). Nine nodules with BRAF-like mutations were malignant. Of the 17 nodules with RAS-like mutations, only one was malignant. When evaluating post-surgical histopathology results, we observed that BRAF mutations were detected in 8 out of 19 malignant nodules (42%) and one in a benign nodule (0.7%). Considering only the nodules with indeterminate cytology (Bethesda III and IV, n = 54), 9 mutations were detected, 6 with benign histology (all with RAS), 1 with malignant histology (BRAF), and 2 still unoperated. **Conclusion:** This study demonstrates a high positive predictive value (89%) for the BRAF V600E mutation in predicting thyroid malignancy. Conversely, RAS mutations were found predominantly in benign nodules, with HRAS being the most prevalent, suggesting regional variation in mutation prevalence within the Brazilian population.

THYROID NODULE

1113822 - PRIMARY THYROID LYMPHOMA ABOUT A CASE

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Case Presentation: We present the case of a 70-year-old patient with a rapidly growing right thyroid nodule initially diagnosed via fine needle biopsy as papillary carcinoma. A total thyroidectomy was performed, and the postoperative diagnosis was diffuse large B-cell lymphoma, confirmed by immunohistochemistry. PET/CT scans showed adenopathies in the pulmonary hilum and right paraesophageal region at the carina level. This case is rare, and there are no published reports in our country of a patient without a history associated with primary thyroid lymphoma. In this case, treatment with chemoimmunotherapy was initiated, with good clinical and radiological response to date. **Discussion:** This is a case in which a patient with a rare disease is presented. However, the deep knowledge of the essential aspects, regarding management and timely diagnosis and personalized treatment, improves the survival rate of these patients. **Final Comments:** In Colombia, no published reports of primary thyroid lymphoma cases were found, which makes this case noteworthy due to the adequate response to medical treatment. Elements like biopsy often generate confusion due to non-specific results, which suggests a discussion on alternatives to improve its effectiveness should be considered

THYROID NODULE

1112523 - RADIOFREQUENCY ABLATION FOR BENIGN PREDOMINANTLY SOLID THYROID NODULES PERFORMED BY A RADIOLOGIST AND A NECK SURGEON: A FOLLOW-UP STUDY

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Introduction: Radiofrequency ablation (RFA) is an effective, minimally invasive treatment for benign thyroid nodules. **Objective:** This study aimed to evaluate the safety and efficacy of RFA for treating predominantly solid benign thyroid nodules over a maximum 24-month follow-up period. **Methods:** A total of 153 predominantly solid benign thyroid nodules (mean volume 19.0 cm³) were treated using RFA. All nodules were diagnosed with two benign cytology results. Pre-procedural evaluation was performed by a dedicated radiologist, and the procedure was carried out in an operating room by a collaborative team consisting of a radiologist and a surgeon, with sedation provided for patient comfort. Hydrodissection was performed in all cases to protect adjacent structures. Volume reduction was evaluated at 1, 3, 6, 12, and 24 months post-treatment. Follow-up was conducted by the same radiologist who performed the procedure. **Results:** The average volumetric reduction was as follows: 49.44% at 1 month, 69.17% at 3 months, 75.49% at 6 months, 83.29% at 12 months, and 86.09% at 24 months. Complications included one case of vocal cord paralysis, which showed recovery within 6 months, and one case of nodule rupture, managed conservatively with a positive outcome. No other significant adverse effects were reported. **Conclusion:** RFA demonstrated excellent results in volumetric reduction and safety, with no major long-term complications. The collaborative approach of an interventional radiologist and a neck surgeon improves patient care, ensuring procedural success, and managing complications effectively. These findings support RFA as a safe and effective treatment for predominantly solid benign thyroid nodules, aligning with the best outcomes reported in the literature.

THYROID NODULE

1114243 - RADIOFREQUENCY ABLATION OF BENIGN THYROID NODULES – INITIAL EXPERIENCE OF AN ENDOCRINE SURGERY UNIT IN A CENTRAL HOSPITAL FROM PORTUGAL

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Introduction: Percutaneous thermal ablation techniques are increasingly being proposed as therapeutic alternatives for benign thyroid nodules. Radiofrequency ablation (RFA) has emerged as a safe and effective way of inducing volume reduction and symptomatic relief. **Objective:** Analyze the outcomes of our first cases of RFA. **Methods:** We analyzed our first cases of RFA from November/2022 to December/2024. The VIVA RF system (STARmed Co.) was used, with an internally cooled 18-gauge electrode and a 10-mm active tip. US-guided trans-isthmus approach and the moving-shot technique were used in all patients, after confirmed benign cytology. **Results:** We identified 37 cases, mostly women (91.9%), with a mean age of 54 years-old (range 20-81). Surgical indications were restricted to compressive symptoms (20/37, 54.1%), cosmesis (6/37, 16.2%) or both (11/37, 29.7%). Regarding ultrasound features, nodules were classified as EU-TIRADS 2 (3/37, 8.1%), 3 (28/37, 75.7%) and 4 (6/37, 16.2%). The average baseline nodule volume was 12 mL. The mean energy delivered and duration were 16325 J and 7.2 min, respectively. We report 4 cases (10.8%) of post-procedure morbidity – 2 subcutaneous hematomas, a Horner syndrome and a patient with transient hoarseness. At 6-month ultrasound evaluation, the mean volume reduction ratio was 49%. Only one patient required a second ablation due to regrowth. **Conclusion:** Our initial experience demonstrated a near 50% volume reduction at 6 months, with a low complication rate and minimal need for reinterventions. These findings support RFA as an option, potentially avoiding surgery which is more invasive. Further follow-up is necessary to assess long-term efficacy and recurrence rate.

THYROID NODULE

1112524 - RADIOFREQUENCY ABLATION OF PAPILLARY THYROID MICROCARCINOMAS: A PRELIMINARY STUDY OF 11 CASES

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Introduction: Radiofrequency ablation (RFA) has emerged as a potential minimally invasive treatment alternative for selected cases in the management of papillary thyroid microcarcinomas (PTMCs). **Objective:** This study aims to evaluate the feasibility, safety, and effectiveness of RFA in treating PTMCs. **Methods:** Between 2022 and 2024, 11 patients (6 women, 5 men) with papillary thyroid microcarcinomas underwent RFA using an electrode with .5 cm active tip. All nodules were classified as ideal or appropriate for active surveillance, and the treatment decision was made collaboratively by the patient and a multidisciplinary team, including endocrinologists, a radiologist, and a neck surgeon. The maximum nodule diameter was 0.7 cm, with volumes ranging from 0.025 cm³ to 0.14 cm³. The procedures were performed by a radiologist and a surgeon in an operating room under sedation. In order to protect surrounding structures, hydrodissection was performed in all cases. RFA was conducted by a radiologist and a surgeon. **Results:** All procedures were considered technically successful with no complications. Post-procedural follow-up showed an ablation zone larger than the original nodule at 1 month, with progressive reduction observed over time. By 12 months, treated areas showed either complete resorption or small scarring. Patients were monitored by the same radiologist who performed the procedure. There were no significant adverse events, and all patients were discharged on the same day. **Conclusion:** This preliminary experience suggests that RFA is a safe and effective alternative treatment for selected cases of PTMCs, with outcomes comparable to the best series reported in the literature. RFA may offer a viable option for patients with low-risk microcarcinomas who prefer an alternative to surgery or active surveillance.

THYROID NODULE

1112200 - RADIOFREQUENCY VERSUS ETHANOL ABLATION FOR SINGLE-SESSION TREATMENT OF BENIGN CYSTIC THYROID NODULES: A SHORT-TERM RETROSPECTIVE STUDY

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Objective: This study evaluated the effectiveness of ultrasound-guided fine-needle aspiration cytology (USG-FNAC) for diagnosing thyroid nodules less than 10mm and explored the link between the TIRADS classification and USG-FNAC outcomes. **Methods:** A retrospective analysis of 344 patients with 407 thyroid nodules less than 10mm was conducted. USG-FNAC was performed on all nodules, and cytology was reported according to The Bethesda System. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Correlation between cytology and TIRADS classification was assessed using Spearman's correlation. **Results:** Adequate specimens were obtained in 81% of nodules after the first FNAC. Cytological diagnoses included 36.6% benign, 12.8% suspicious for malignancy, 1.2% malignant, and 19.7% indeterminate. Among surgically resected nodules, 78.6% were malignant. USG-FNAC demonstrated moderate sensitivity (80%) and high PPV (92.3%) but lower specificity (75%) and NPV (50%) for malignancy in nodules less than 10 mm. A significant positive correlation ($r = 0.24$, $p < 0.001$) was observed between TIRADS classification and Bethesda criteria. **Conclusion:** USG-FNAC offers moderate sensitivity and high PPV for diagnosing malignancy in small thyroid nodules, but specificity and NPV are lower. A positive correlation exists between TIRADS classification and cytological outcomes.

THYROID NODULE

1112520 - RECATEGORIZING MILD HYPOECHOIC NODULES INTO ISO-HYPERECHOIC ONES SCORE IN ACR TIRADS: ONUS OR BONUS?

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Introduction: The ACR TI-RADS classifies hypoechoic nodules as hypoechoic and markedly hypoechoic, adding 2 and 3 points to the final score. Recent papers reported the advantages of grading hypoechoic nodules into three degrees compared to the strap muscle (mild, moderate, and markedly hypoechogenicity) since they carry different risks of malignancy (ROM). The mild ones have a significantly lower ROM when compared to those with more hypoechoic ones. In addition, mild hypoechoic solid nodules (TR 4) were unrelated to malignancy. **Objective:** The aim is to evaluate the ACR TI-RADS (TR) performance by recategorizing mild hypoechoic nodules as iso-hyperechoic ones score (1). **Methods:** A retrospective cohort from 1096 nodules submitted to surgery was rated. From that, TR4 and TR5 reclassified nodules into TR3 and TR4 respectively were studied to assess performance in avoiding fine-needle aspiration (FNA) in benign lesions as much as cancer loss rate, due to the rise of the TR4 (1.4 to 1.1 cm) and TR3 (2.4 to 1.6 cm) nodules FNA minimal limit size. Chi-square evaluated this change into ROM. **Results:** 86 nodules were recategorized (65.12% from TR 4 to 3; and 34.88% into TR 5 to 4). Median sizes of TR 4 to 3 were 1.15 cm (IQR 0.7-1.55cm) and TR 5 to 4 were 1cm (IQR 0.7-1.7cm). Of 12/86 (13.95%) cancers, 8/56 (14.29%) had become TR3, and 4/30 (13.33%) had become TR4 ($p=0.903$). From sub-classified cancers, 4/8 (50%) TR3 and 4/4 (100%) TR4 were not eligible for FNA. The loss was not significant after changing ($p>0.05$). In addition, non-diagnosis cancer cases were within a follow-up limit. Still, the performance improved, avoiding FNA ($n=74$; 90.7%) in benign no-risk nodules. **Conclusion:** Mild hypoechogenicity recategorization improved ACR TI-RADS performance in our cohort, reducing unneeded procedures.

THYROID NODULE

1113930 - RETHINKING MACROCALCIFICATIONS IN THYROID NODULES: A CRITICAL EVALUATION OF THE ACR TI-RADS SCORING SYSTEM AND ITS IMPACT ON CASE SELECTION FOR BIOPSY

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Introduction: Thyroid nodules affect up to 50% of adults, although only 7%-15% are malignant. The role of macrocalcifications in malignancy remains debated. **Objective:** This study reassesses the American College of Radiology Thyroid Imaging – Reporting and Data System (ACR TI-RADS) framework by evaluating how excluding macrocalcifications from the scoring system impacts unnecessary biopsies and missed malignancies. **Methods:** This single-center retrospective study evaluated thyroid nodules with cytological evaluations between 2012 and 2019. Clinical and sonographic characteristics of nodules with and without macrocalcifications were compared. Additionally, we modified the ACR TI-RADS classification by excluding points for macrocalcifications to evaluate their impact on biopsy indications. **Results:** A total of 287 thyroid nodules from 264 patients were analyzed. The median age was 58.6 years (IQR: 47.9-68.3), and 84.8% were female. Macrocalcifications were detected in 41 nodules (14.3%) from 37 patients (14.0%), and the malignancy rate was not statistically different among nodules with and without macrocalcifications (12.2% vs. 16.7%, $P=0.056$). The Pearson Chi-Square analysis revealed that the malignancy rate was significantly higher in nodules without macrocalcification after stratification in the ACR TI-RADS categories ($P<0.001$). In the multivariate analysis, controlling for sex, age, nodule size, and TI-RADS categories (after the removing of the points attributed to macrocalcifications), macrocalcifications were not associated with malignant cytology (OR: 0.949, 95% CI: 0.836-1.078, $P=0.622$). After removing the point attributed to macrocalcification, our modification of the ACR TI-RADS classification resulted in a 5.6% ($n=16$) reduction in biopsy indication and no missed cases of malignancy. **Conclusion:** Our results indicate that revising the ACR TI-RADS classification to remove macrocalcifications may reduce unnecessary biopsies and minimize patient burden without missed malignant nodules.

THYROID NODULE

1114245 - RFA AS A THERAPEUTIC OPTION FOR BETHESDA III/IV NODULES: OUTCOMES IN NEGATIVE MIR-THYPE MOLECULAR TESTING CASES

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Introduction: Radiofrequency ablation (RFA) has emerged as a minimally invasive alternative to thyroid surgery for nodules with benign cytology (Bethesda 2). However, its application in indeterminate thyroid nodules (ITN - Bethesda III and IV) remains limited due to uncertainty about their nature, despite ~80% of ITN being benign. Molecular testing offers a potential solution to classify ITN as “benign” or “cancer”. Although the Risk of Malignancy for cytology and negative molecular test results are statistically equivalent, no data currently exists regarding the efficacy of RFA for ITN with negative molecular test results. **Objective:** To assess the effectiveness of RFA on negative-molecular-test-ITNs, with outcomes at intervals of 1, 3, 6, 12, 18 and 24 months following RFA. **Methods:** This prospective observational study included 29 nodules (19 Bethesda III; 10 Bethesda IV), all with negative mir-THYpe full molecular test result. Outcomes included volume reduction rate (VRR), complications, regrowth, and reintervention needs. **Results:** Stratified by baseline nodule volume, VRR analysis showed a progressive response: nodules $<6\text{ cm}^3$ had a mean VRR of 30.2%, nodules $6-14\text{ cm}^3$ had a mean VRR of 47.2%, and nodules $>14\text{ cm}^3$ reached a mean VRR of 70.0%. With the exception of one patient (Bethesda III) that presented regrowth at 12 months and underwent a second session, achieving an additional VRR of 30.6%, all did a single ablation session. In patients followed up to 24 months, volume reduction remained stable or improved. No major complications or late recurrences were observed. Outcomes were similar between Bethesda III and IV. **Conclusion:** This preliminary study suggests that RFA may be a potential treatment option for indeterminate thyroid nodules with a negative result on the mir-THYpe full molecular test. These findings warrant further investigation of RFA in this context through larger, long-term studies.

THYROID NODULE

1112490 - STRATIFICATION OF BETHESDA V AND VI MALIGNANCY RATES IN EU-TIRADS 5 THYROID NODULES ACCORDING TO NUMBER OF HIGH-RISK FEATURES TO TAILOR PATIENT MANAGEMENT

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Introduction: The European Guidelines recommend fine needle aspiration cytology (FNAC) for EU-TIRADS 4 nodules > 15 mm and for EU-TIRADS 5 nodules > 10 mm. Risk of malignancy is however low in EU-TIRADS 4 nodules, ranging from 6% to 17% and wide in EU-TIRADS 5 nodules, ranging from 26% to 87%. A better US risk classification should help to decrease unnecessary FNAC.

Objective: In this retrospective multicenter study, the main objective was to compare rates of Bethesda V-VI cytology in EU-TIRADS 4 nodules, in EU-TIRADS 5 nodules with 1 high-risk feature or with ≥ 2 features. **Methods:** US images of EU-TIRADS 4 and 5 thyroid nodules from consecutive patients who underwent FNAC were independently reviewed by 2 thyroid ultrasound experts from each center, unaware of FNAC results, using the EU-TIRADS 2017 system. Nodules were classified as EU-TIRADS 4, EU-TIRADS 5 with 1 sign or, EU-TIRADS 5 with ≥ 2 signs. In case of discordance, consensus was reached. **Results:** In this preliminary analysis, we included 182 nodules (mean size: 17.5 mm, R: 10-81) in 173 patients (126 female). Nodules were EU-TIRADS 4 in 78 (42.9%) cases, and EU-TIRADS 5 in 104 (57.1%) cases (47 with 1 high-risk sign; 57 with ≥ 2 signs). Rates of Bethesda V-VI results were 2.6% in EU-TIRADS 4 nodules, 19.1% in EU-TIRADS 5 nodules with 1 high-risk sign and 35.1% in EU-TIRADS 5 nodules with ≥ 2 signs. Rates of Bethesda III-IV were 37.2% in EU-TIRADS 4 nodules, 34% in EU-TIRADS 5 nodules with 1 high-risk sign and 22.8% in EU-TIRADS 5 nodules with ≥ 2 signs. **Conclusion:** Rates of FNAC Bethesda V-VI results are significantly higher among EU-TIRADS 5 nodules with ≥ 2 high-risk signs compared to those with only 1 sign suggesting EU-TIRADS 5 classification should be stratified according to the number of high-risk signs.

THYROID NODULE

1112543 - SURGICAL TREATMENT OF SUBSTERNAL GOITER

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Introduction: Substernal goiter has several definitions although no consensus exists even today. Most common definitions include the following: extension of a goiter below the plane of the thoracic inlet, or having more than 50% of its mass lying inferior to the sternal notch. And the majority of authors claim that the risk of malignancy is increased in substernal goiter compared to pure cervical goiter.

Objective: This study aims to investigate the diagnosis and surgical treatment of thyroid goiters extending into the mediastinum and the thoracic cavity. **Methods:** Between January 2018 and December 2023, 34 patients underwent surgery for substernal goiter at our institution. Demographics, clinical, operative, and pathological data of the patients were recorded and analyzed. **Results:** In this group, 73.5% were women, and the mean age was 57 years. The most common symptoms were neck mass (55.8% of cases) and dyspnea (29.4%). 82.3% Of them underwent a partial thyroidectomy and 14.7% of them underwent a total thyroidectomy. There were 2 permanent unilateral recurrent laryngeal nerve injuries (5.8%). Incidence of malignancy on permanent histology was 8.8%. **Conclusion:** We conclude that a subtotal thyroidectomy is also the treatment of choice for asymptomatic benign substernal goiter. We base our choice on the low morbidity and zero mortality.

THYROID NODULE

1114097 - THE GENOMIC LANDSCAPE OF MEDULLARY THYROID CARCINOMA (MTC) IDENTIFIED BY THE AFIRMA RNA-SEQUENCING CLASSIFIER: INSIGHTS FROM A LARGE REAL-WORLD COHORT

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Introduction: The Afirma RNA-sequencing MTC classifier, a component of the Afirma Genomic Sequencing Classifier (GSC), was previously validated as a reliable tool for preoperative identification of MTC from fine-needle aspiration (FNA) specimens. We aimed to characterize the genomic landscape of MTC identified using this classifier in a large real-world cohort of FNA samples. **Objective:** We aimed to characterize the genomic landscape of MTC identified using this classifier in a large real-world cohort of FNA samples. **Methods:** We retrospectively analyzed MTC positive samples by the Afirma MTC classifier in the Veracyte CLIA laboratory between January 2018 and June 2024. Genomic variants identified by the Afirma Xpression Atlas (XA) were characterized. **Results:** Among 252,510 FNA samples tested, 732 (0.3%) were MTC+. Median patient age was 63.2 years (IQR, 52.1-72.1) and median nodule size was 2.1 cm (IQR, 1.6-3.0). On cytology, 71% (520/732) of nodules were Bethesda III or IV, 18% were Bethesda V and 11% were Bethesda VI. Of MTC+ samples, 73% had at least one pathogenic variant identified by XA, most commonly in RET (53%) and RAS (19%) with no significant difference across Bethesda categories. Most RET alterations were in codons 918 (19%) and 634 (10%), while HRAS was the most frequently altered RAS isoform (15%). Oncogenic fusions were identified in 8 non-RET/RAS SNV mutated samples [EML4::ALK (n=1), MKRN1::BRAF (n=6), and SPECC1L::RET (n=1)]. Additional isolated variants identified in non-RET/RAS samples included AKT1, DICER1, PIK3CA, and TP53. Gene expression analysis showed that ERK activity was slightly lower in RET-driven than in RAS-driven MTC (p=0.02), but significantly higher in both groups compared with non-RET/non-RAS samples (p<1-10). **Conclusion:** This study reinforces the genomic landscape of MTC and highlights the value of molecular testing to preoperatively define MTC in some BIII/IV nodules. Further study is needed to molecularly define the nearly 30% of specimens that lacked detectable alterations.

THYROID NODULE

1112286 - THE RELATIONSHIP BETWEEN THYROID NODULE AND URINARY IODINE CONCENTRATION IN CHINESE POPULATION - A NATIONAL RESEARCH FROM TIDE

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Objective: This study analyzed the relationship between the incidence of various thyroid nodules and urinary iodine concentration (UIC), combined with body mass index (BMI) and age, aiming to provide thoughts for the modern and individualized management of thyroid nodules. **Methods:** A total of 74,100 participants aged 18 to 80 years from the TIDE project (Thyroid Disorders, Iodine Status and Diabetes, a national epidemiological cross-sectional study) were enrolled. Thyroid nodules were classified according to the number and diameter. The relationship between the incidence of various thyroid nodules and UIC was analyzed by R(version 4.2.1) and restricted cubic spline regression. The study further analyzed the distribution of the incidence, age and BMI and the interaction among them. **Results:** The prevalence of thyroid nodules in the Chinese population included in the analysis was 20.82%, and the prevalence of thyroid nodules with diameter < 1 cm was the highest, which was 14.25%. The prevalence of thyroid nodules in the total population and between males and females was significantly different (p < 0.001). The distribution of thyroid nodules increased with the decrease of UIC interval value. The prevalence of thyroid nodules increased significantly with the increase of age. When logUIC = 2-2.5 (UIC at about 100-316 µg/L), the incidence of thyroid nodules showed a rapid downward trend, and the trend of prevalence with UIC in other stages was relatively flat. Both the 3D and 2.5D heat maps showed that the greater the BMI and the lower the UIC, the greater the risk of thyroid nodules. The same is true for older age and lower UIC. **Conclusion:** Among all kinds of thyroid nodules, the incidence of small thyroid nodules is the highest, and the incidence of various thyroid nodules may be reduced by controlling UIC at 100-316µg/L. Age and UIC, BMI and UIC all had interaction effects on the risk of thyroid nodules.

THYROID NODULE

1112354 - THYROID INCIDENTALOMAS (TI) AND NODULES FOUND IN ULTRASOUND ROUTINE SCREENING STUDIES (SN): HAVE THEM SIMILAR BEHAVIOR?

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Introduction: Guidelines discourage screening ultrasound (US) in subjects without abnormal thyroid palpation or risk factors. Besides, thyroid incidentaloma (TI) shows an increasing prevalence. **Objective:** Compare US characteristics and association with malignancy in patients with TI and screening nodules (SN). **Methods:** Retrospective study of 127 adult patients with TI, and 126 with SN. All were studied with thyroid profile, antithyroid antibodies, US, fine needle aspiration biopsy (FNAB) and cytology (Bethesda). In both groups, 2 or more suspicious US characteristics and nodular size were considered for FNAB. Surgery was indicated based on Bethesda. Statistical tests: Chi-squared test with Yates' correction and Odds Ratio. (Significant p-value < 0.05). **Results:** In TI group, 86.6% of patients euthyroid, 13.4% autoimmunity (+), 32.3% with single and 67.7% multiple nodules. In SN group, 76.6% euthyroid, 27.1% autoimmunity (+), 45.2% single and 54.7% multiple nodules. Nodule size ranged 5-94 mm in TI group, and 3-44 mm in SN group. In TI group 61/127 patients presented 2 or more suspicious characteristics, of which 49 underwent FNAB. Cytology: BI n=2, BII n=27, BIII n=6, BIV n=4, BV n=1, BVI n=9 patients. 14 underwent surgery, confirming malignancy in 13 cases (p=0.03), Odd ratio 4.22 95% CI (1.24-11.24). In SN group, 45/126 presented 2 or more suspected characteristics of which 29 underwent FNAB. Cytology: BI n=0, BII n=26, BIII n=1, BIV n=0, BV n=2, BVI n=0. Surgery in 7 patients and malignancy was confirmed in 4 (p=0.93). **Conclusions:** We found a strong association between suspicious US findings and detection of malignancy in TI group, unlike SN group. These results reaffirm that routine US requests do not contribute to detection of malignancy in thyroid nodule pathology.

THYROID NODULE

1112582 - THYROID NODULES AND INFLAMMATORY MARKERS

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Introduction: The role of inflammation in the formation of various neoplasms is well known. This study aimed to investigate the systemic inflammation parameters in patients with thyroid nodules and thyroid cancer. **Methods:** A total of 914 patients evaluated with thyroid ultrasound (US) in the internal medicine outpatient clinic were enrolled. The inflammatory markers erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and monocyte/high-density lipoprotein (HDL) ratio (MHR) were assessed. **Results:** Thyroid nodules were detected in 810 of the cases. The mean age of individuals with nodules was higher than those without nodules (51.7 vs. 34.7), and there was a higher proportion of females in the group with nodules. Thyroid dysfunction (hypothyroidism or hyperthyroidism) was more common in the group with nodules. The classical inflammatory markers ESR and CRP were higher in the group with nodules, while no difference was found between groups in other inflammatory indices. Of the 242 cases that underwent fine-needle aspiration biopsy (FNAB), 205 had benign nodules, 35 had papillary cancer, and 2 had follicular cancer. The mean age of patients with thyroid cancer was lower than that of patients with benign nodules (49 vs 55). Despite this, no difference was found between groups in either classical inflammatory markers or new hemogram-based inflammatory indices (NHBII). **Conclusion:** In the literature, there is data indicating that NHBII are elevated in many chronic diseases and cancers. However, in our study, while ESR and CRP were found to be higher in individuals with thyroid nodules compared to those without, no difference was observed in NHBII. In patients who underwent FNAB, no significant difference was observed between those with thyroid cancer and those with benign nodules in both classic inflammatory markers and NHBII. This lack of difference may be related to the localized nature of malignancy.

THYROID NODULE

1112529 - THYROID NODULES THAT REMAIN UNCLASSIFIABLE BY THE ATA AND ACR TI-RADS SYSTEMS: CASE REPORTS

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Case Presentations: Case 1: A 76-year-old asymptomatic woman presented with a solid isoechoic thyroid nodule measuring 2.0 x 2.8 x 3.0 cm. Within the nodule, a well-delimited hypoechoic area was identified. The nodule was classified as TR3 (ACR TI-RADS). Fine-needle aspiration biopsy (FNAB) revealed a benign diagnosis for the isoechoic region and follicular neoplasm for the hypoechoic area. Case 2: A 52-year-old woman with Hashimoto's thyroiditis was found to have a thyroid nodule in the left lobe during a routine examination. Thyroid function was normal, with positive anti-thyroglobulin antibodies. FNAC of the nodule of left lobe was classified as Bethesda III. On follow-up, the left nodule remained stable, but microcalcifications were detected in the right lobe parenchyma without a nodule. FNAC of this area, performed twice, revealed Bethesda VI (malignant). The final diagnosis was diffuse sclerosing subtype of papillary thyroid carcinoma (DSS-PTC). Case 3: A 71-year-old asymptomatic woman had a thyroid anechoic cyst that, over two years without any intervention, shrank and developed hypoechoic content with calcifications. The nodule was reclassified as TR5. **Discussion:** Thyroid nodule classifications aim to cover all cases, but certain findings fall outside these systems. Case 1 illustrates the nodule-in-nodule phenomenon, where the hypoechoic area often suggests follicular neoplasm, requiring targeted FNAC. Case 2 highlights the challenge of diagnosing DSS-PTC, which can present with microcalcifications in parenchymal areas without distinct nodules. FNAC of these areas is crucial for early detection. Case 3 underscores the need for comparative imaging in mummified nodules, as cytology is often inconclusive. **Final Comments:** These findings, though not included in current classification systems, are critical for guiding management. Accurate thyroid nodule evaluation requires the integration of clinical, imaging, and cytological data.

THYROID NODULE

1112495 - TO ABLATE OR NOT TO ABLATE? A SINGLE INSTITUTION'S EXAMINATION OF THE LATTER IN THERMAL ABLATION OF THYROID NODULES

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Introduction: Thermal ablation (TA) has been rapidly gaining popularity in the United States as an effective, non-invasive treatment modality for thyroid nodules. Much focus has been given to the expanding indications for TA of thyroid nodules, but less attention has been dedicated to patients who are not good candidates and the reasons why. **Methods:** In this single-institution retrospective cohort study, we identified all patients who had a consultation for TA. We collected data on consultation plans and outcomes of these patients, identifying reasons why some were not offered TA and why others chose a different management option despite being good candidates. **Results:** We performed 421 TA consultations between January 2020 and December 2023. We did not offer TA to 83 (20%) patients. In this cohort, 18% (n=15) had relative or absolute contraindications to TA, 38% (n=31) had cytology or molecular profiling concerning for malignancy, 6% (n=5) had known papillary thyroid cancer that was too large, and 35% (n=30) of patients had nodules in locations that were not amenable to safe or effective ablation. Ultimately, 35% (n=29) underwent surgery, of which 41% (n=12) had a malignancy on surgical pathology. Another 25% (n=6) were offered TA but chose surgery instead, mostly due to concerns of cost or wanting more definitive treatment. Notably, 8% (n=2) had malignancy on pathology. **Conclusion:** Although TA is an effective treatment of thyroid nodules, not all are good candidates. In our experience, we found that cytology concerning for potential malignancy and tumor characteristics not amenable to ablation were the most common reasons patients were not offered TA. We also note that some patients who were initially offered TA were found to have cancer on surgical pathology, the possibility of inadvertent ablation of missed malignancies. Cautious patient selection remains crucial to ensure safe and beneficial outcomes.

THYROID NODULE

1112641 - ULTRASONOGRAPHIC AND CYTOLOGICAL FEATURES OF BETHESDA III THYROID NODULES IN A UNIVERSITY REFERRAL HEALTH CENTER

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Introduction: Bethesda III cytologies present a diagnostic challenge for clinicians. At our hospital, we process biopsies not only from our facility but also from external healthcare centers. This underscores the importance of ultrasonographic findings in the selection of fine-needle aspiration biopsies. **Objective:** The primary objective of our study is to compare ultrasonographic risk with the presence of nuclear atypia in the cytology of patients classified as Bethesda III. **Material and Methods:** Retrospective descriptive study was conducted between January 2022 and September 2024. We analyzed all fine-needle aspiration biopsies (FNABs) performed at a university health center by an expert radiologist. Only nodules with cytology results consistent with the Bethesda III 2017 classification were included. Ultrasonographic features were evaluated according to the American Thyroid Association (ATA) classification and correlated with cytological findings. For the statistical analysis, we calculated the prevalence of nuclear atypia in nodules based on ultrasonographic risk and estimated the relative risk. **Results:** Out of 1,540 FNAB performed, 185 (12%) were classified as BIII. Eighty-five percent of the 45 FNAB with high ultrasonographic risk had nuclear atypias. In intermediate risk 72% of 68 had nuclear atypias and 77% of the 72 low risk nodules. In the high ultrasonographic risk group the relative risk for nuclear atypias was 1.12 [0.96-1.32]. **Conclusions:** In our population, patients with high ultrasonographic risk exhibited a higher frequency of nuclear atypia compared to those with intermediate or low risk. Although there was no significant difference in the studied population, we emphasize the importance of ultrasonographic risk in the interpretation of Bethesda III classified nodules.

THYROID NODULE

1112449 - ULTRASONOGRAPHIC FEATURES AND CYTOLOGY OF THYROID NODULES IN POSTMENOPAUSAL WOMEN

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Introduction: Thyroid cancer predominantly affects women, with incidence increasing with age. The association between estrogen and thyroid cancer remains controversial, heightening concerns about the risk of thyroid cancer in postmenopausal women. **Objective:** To investigate the ultrasonographic and cytologic features of thyroid nodules in postmenopausal women. **Methods:** This cross-sectional study was conducted at Hanoi Medical University Hospital and included 184 postmenopausal women presenting with thyroid nodules on ultrasound. Suspicious thyroid nodules were aspirated using fine needle aspiration (FNA) following the 2021 Korean Thyroid Association guidelines. **Results:** The average age of the participants was 58.1±5.41 years. A total of 431 thyroid nodules were detected on ultrasound, with over 70% presenting as small, multinodular formations, prevalently in the right lobe. Most of these nodules (80%) were classified as Korean TIRADS 2-3 (2021). Among the 74 nodules biopsied, 8.1% were found to be malignant (Bethesda 2023 categories V-VI), while 50% were definitively confirmed as benign (Bethesda category II). **Conclusion:** Although most thyroid nodules are benign in postmenopausal women, approximately 20% were classified as TIRADS 4-5. Additionally, a significant portion of the biopsied nodules, though not malignant, require close monitoring or further molecular testing.

THYROID NODULE

1112552 - ULTRASOUND DIAGNOSIS OF UNUSUAL EXTRATHYROID LESIONS MIMICKING THYROID PATHOLOGY: A CASE SERIES

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Case Presentation: Case 1: A female patient, 56 years old asymptomatic patient was referred for fine-needle aspiration (FNA) of a thyroid nodule classified as ACR-TIRADS 5. Ultrasound revealed a heterogeneous, hypoechoic lesion with hyperechoic areas located posterior to the left thyroid lobe. The lesions mobility during swallowing was consistent with an esophageal diverticulum (ED). Case 2: A female patient, 65 years old, was referred for FNA of a cervical nodule. Ultrasound demonstrated a well-defined, hypoechoic nodular lesion, its longest axis perpendicular to the skin, without echogenic foci, located in the right cervical region. The lesions apparent continuity with the vagus nerve raised suspicion of a schwannoma. Case 3: A female patient, 45 years old, presented with moderate right-sided cervical pain. Ultrasound revealed thickening of the anterior wall of the right common carotid artery at the pain site, along with a hypoechoic plaque causing mild luminal narrowing. Findings suggested transient perivascular inflammation of the carotid artery (TIPIC) syndrome. **Discussion:** These cases highlight extrathyroid lesions that may mimic thyroid nodules, thyroiditis, or other neck pathologies, presenting a diagnostic challenge. Esophageal diverticula often appear posterolaterally to the left thyroid lobe as thin-walled, saccular, hypoechoic lesions, with changes during swallowing. Schwannomas, benign peripheral nerve sheath tumors, can resemble thyroid nodules on ultrasound, requiring advanced imaging (CT/MRI) or biopsy for confirmation. TIPIC syndrome is a rare cause of acute neck pain, characterized by adventitial thickening and perivascular inflammation on ultrasound. **Conclusion:** Awareness of these rare entities broadens the differential diagnosis of cervical lesions and helps avoid unnecessary interventions, such as thyroidectomy.

THYROID NODULE

1112480 - ULTRASOUND FINDINGS FOR THE DETERMINATION OF THYROID NODULES SUSPECTED OF MALIGNANCY ACCORDING TO ATA 2015 ULTRASOUND SYSTEM: CORRELATION WITH FINE NEEDLE ASPIRATION BIOPSY, FNAB

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Introduction: Thyroid ultrasound is the ideal method for the detection of thyroid nodules, which may be malignant in up to 8% of cases. **Objective:** To determine the ultrasound findings according to ATA 2015 of high suspicious thyroid nodules (HS) that suggest a higher probability of malignancy when correlated with the cytological result by Bethesda in patients who underwent biopsy and fine needle aspiration biopsy (FNAB) from January to November 2024 in a reference center. **Methods:** Prospective, observational, analytical study. The concordance between ultrasound findings and FNA cytology of HS thyroid nodules, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each ultrasound characteristic was evaluated, considering Bethesda II nodules as negative, and Bethesda IV, V and VI nodules as positive, and each ultrasound characteristic as positive (present) or negative (absent). **Results:** 73 patients evaluated. 19 (26.02%) were HS nodules on ultrasound. Mean age 53 ± 13.45 years; 18 (94.73%) women. 4 (21.05%) were Bethesda II, 2 (10.53%) Bethesda IV, 3 (15.79%) Bethesda V and 4 (21.05%) Bethesda VI. The presence or absence of hypoechogenicity, microcalcifications, irregular margins, size greater than 1 cm, and anteroposterior diameter greater than the transverse (taller than wide) was taken into account, highlighting a sensitivity of 56% and 44% for the presence of microcalcifications and irregular margins respectively, and specificity of 100% in both; a PPV of 100% in both and NPV of 50% and 44% respectively. **Conclusion:** The presence of microcalcifications and irregular margins are highly suggestive indicators of malignancy, but not hypoechogenicity and size greater than 1 cm. However, due to the sample size, it is not possible to generalize, and follow-up with all ATA ultrasound criteria is suggested for decision-making.

THYROID NODULE

1112423 - ULTRASOUND-GUIDED PERCUTANEOUS CRYOABLATION OF BENIGN THYROID NODULES: A PILOT STUDY

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Objective: To assess feasibility, safety and efficacy of ultrasound (US) guided percutaneous cryoablation of benign thyroid nodules (BTNs); volume-reduction ratio (VRR) up to 12 months and presence of calcifications. **Methods:** This IRB approved prospective single arm, tertiary single-center pilot study enrolled 10 symptomatic patients > 18 years-old with fine needle aspiration biopsy-proven of functioning or not BTNs under 65 cc volume. Outpatient US-guided cryoablation sessions included multiple overlapping freeze-thaw cycles. Protective hydrodissection was provided in all cases. Follow-up was carried out 1, 3, 6, and 12 months with US and laboratory examinations. Prior outcomes were technical feasibility; TN volume reduction ratio (VRR) = $([\text{initial vol.} - \text{final vol.}] / \text{initial vol.} \times 100)$; and incidence of adverse events (AE). **Results:** Ten patients (9 women, 90%) with a mean age of 55.9 ± 12.7 -year-old (range 35-73) were treated. Mean $\pm$ SD baseline thyroid stimulating hormone (TSH), free T4 and thyroglobulin (Tg) serum levels were: 0.78 ± 0.43 mUI/L, 1.03 ± 0.21 ng/dL, and 258.9 ± 17.2 ng/mL; laboratory and a 40% TN baseline calcification rate remained stable over time. Non-functioning TNs were n=9 (90%). Technical feasibility was 100%. No complications were observed. One mild adverse event (transient vasovagal reaction) occurred in one patient secondary to a self-limited hematoma. Mean $\pm$ SD baseline TN volume was 26.09 ± 13.92 mL (n=10); 1-, 3-, and 6-month TN volume (mL) were: 16.42 ± 10.12 (n=10); 8.70 ± 5.94 (n=8); 7.80 ± 6.18 (n=6). VRR increased up to 6 months (p<0.05), being 37.06%, 66.65% and 70.10% respectively at 1-, 3-, and 6-month, respectively. The VRR at 12 months was 52.84% (n=3), with partial volume regrowth observed in 2 cases. **Conclusion:** Cryoablation was feasible, effective and safe for the treatment of benign thyroid nodules and may be an alternative to surgery in selected cases. One potential advantage is to avoid nodular calcifications overtime, to be confirmed in larger multicentric trials.

THYROID NODULE

1112462 - VOLUME REDUCTION RATES FOR BENIGN NODULES RFA: EFFECT OF NODULE CONSISTENCE NESTED TO THE SAME PATIENT IN A MIXED MODEL

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Introduction: Thyroid RFA is an effective treatment for selected solid nodules, and volume reduction rate (VRR) are expected to be 33.58% 1st month, 51.85% 6th month and up to 93.4% in 1 year. Mixed and cystic nodules seem to have a higher volume reduction rate compared to solid ones. **Objective:** To analyze volume reduction rate in solid, mixed and cystic RFA thyroid nodules, controlling for those who were ablated within the same patient in a prediction model. **Methods:** Retrospective cohort where RFA cases performed by a single surgeon between 2017 and 2022, with two previously Bethesda II FNA patients were included. Data from 161 patients and 225 nodules were analyzed for VRR with 1, 3, 6 and 24 months. Trend analyzes used paired Wilcoxon signed-rank test, fractional polynomial along with multilevel mixed linear regression model with a random intercept for (nested-same patient) nodule. **Results:** Aesthetic (48%) and growth (37%) were the main RFA indications. Nodules were respectively 86.22% solid, 11.11% mixed and 2.67% cystic. Only 51 patients with 61 nodules completed follow up at 24 months, however 100% contributed to 6 month follow up (Fup) modelling. There was a trend for VRR 1-month (66.53%), 3-months (93.85%), 6-months (90.39%) and 24-months (100%) (p<0.001) and increased variance was time noticed. VRR was different specially at 1-month 63.84% solid, 70.3% mixed and 91.51% cystic (p<0.001). Mixed linear model with a random intercept showed a significantly VRR independently of nodule consistence (p<0.001). 4 solid nodules had regrowth at the end of 24-Months Fup, all who had neovascularization. **Conclusion:** Even though VRR was different regarding nodules consistence, our predicted mixed-effects model with a random intercept for nested nodules showed a VRR independent of consistency and substantial variability between groups. Future studies should consider nesting in their VRR analyses.

THYROID PHYSIOLOGY

1112650 - AGE-SPECIFIC TSH REFERENCE INTERVALS AND THE PREVALENCE OF THYROID DYSFUNCTION IN THE ELDERLY

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Introduction: Thyroid stimulating hormone (TSH) measurement is essential for diagnosing thyroid dysfunctions. However, standard reference values often do not accurately reflect the prevalence of clinical and subclinical hypothyroidism in the elderly, due to age-related metabolic changes. This discrepancy raises concerns about unnecessary treatments for physiological variations, highlighting the need for more specific reference intervals (RIs). **Objective:** Therefore, we aimed to establish age-specific TSH RIs for euthyroid individuals aged 60 and above and to evaluate the prevalence of thyroid dysfunctions in this population using the newly defined RIs. **Methods:** A cross-sectional analysis of retrospective data (2021-2023) from a single center in northeastern Brazil was performed. Samples were analyzed with the Centaur XP Siemens immunoassay. Inclusion criteria included normal free T₄, no anti-thyroid antibodies, and no thyroid medication use. Participants were grouped into 60-79 and ≥80 years. Age-specific TSH RIs were calculated using the bootstrap method and CLSI C28-A guidelines. Prevalence of thyroid dysfunction was assessed using the chi-square test. **Results:** Of 478,035 samples, 118,472 met the inclusion criteria. An increase in the upper TSH limit was observed with advancing age. The RIs were 0.25 (95% CI: 0.24-0.26) to 7.25 UI/L (95% CI: 7.13-7.37) for the 60-79 age group, and 0.26 (95% CI: 0.24-0.28) to 9.50 UI/L (95% CI: 9.09-9.90) for the ≥80 age group. A significant sex difference in TSH levels was observed in the 60-70 age group, with women showing higher levels (0.61, 95% CI: 0.38-0.83). While a trend towards higher TSH levels in women was noted in the 80+ group, the result was not statistically significant. Furthermore, the establishment of new TSH RIs led to a reduction in the prevalence of thyroid dysfunction from 9.1% to 2.5% in individuals over 60. **Conclusion:** Age-specific TSH reference values reduce overdiagnosis of subclinical thyroid disorders, improving clinical management and minimizing unnecessary treatments.

THYROID PHYSIOLOGY

1112510 - CORRELATION BETWEEN GRADE 3 OBESITY AND THYROID FUNCTION AND MORPHOLOGY

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Introduction: The global prevalence of obesity and thyroid dysfunction has been rising worldwide. A relationship between thyroid-stimulating hormone (TSH) and metabolic syndrome both related to obesity and thyroid volume (TV) has been suggested. **Objective:** To evaluate the correlations between body weight, body mass index (BMI), TV and TSH in patients with grade 3 obesity. **Methods:** A cross-sectional study was conducted in 50 patients with grade 3 obesity in pre-bariatric surgery follow-up. TSH measurement was performed using a non-competitive chemiluminescence method (reference range: 0,270 a 4,200 mUI/L). The TV was calculated by the formula: length × width × anteroposterior × 0.523 of each lobe and the isthmus, obtained by the same trained radiologist through a thyroid ultrasound. Spearman correlation tested associations between variables, and a p-value < 0.05 was considered statistically significant. **Results:** Forty-four (88%) out of 50 patients were women. The medians for age, BMI, body weight, serum TSH, and TV were, respectively, 42 years (IQR 34-51.5); 46.79 kg/m² (IQR 43.32-49.31); 125.3 kg (IQR 115.3, 135.5); 2.09 mUI/L (IQR 1.53-3.31); and 8.88 mL (IQR 6.32-12.69). Among the patients, 79,5% had normal parenchyma and 22.5% had hypoechoic parenchyma. There was a statistically significant positive correlation between body weight and TV (r=0.38, p=0.005). However, no statistical correlations were found between TSH and BMI, TSH and body weight; or TSH and TV. **Conclusion:** This study demonstrates a positive correlation between TV and body weight in patients with grade 3 obesity, despite normal TV. Although higher levels of TSH are commonly observed in obesity, there was no correlation between TSH and body weight or BMI. These results underscore the complex relationship between obesity and thyroid and morphology, with possible effects on thyroid function.

THYROID PHYSIOLOGY

1114003 - NORMAL SERUM TSH VALUES IN ADULTS: A HOSPITAL-BASED STUDY IN URUGUAY

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Introduction: At our hospital, the reference range (RR) for TSH is 0.35-5.50 μ IU/mL, based on the manufacturer's values derived from large population-based studies. However, no normative TSH data exist for the adult population in Uruguay. **Objective:** To establish normal serum TSH reference limits for adults aged 18-65 years in a healthy donor population at our hospital (September 2022-November 2024) and to analyze TSH distribution by age, sex, and BMI. **Methods:** A prospective, descriptive, and analytical study was conducted in adult blood donors. Exclusion criteria included pregnancy or lactation; personal or family history of thyroid disease; positive anti-thyroid peroxidase (anti-TPO) antibodies; use of medications known to interfere with TSH (e.g., dopamine agonists/antagonists, cabergoline, somatostatin analogues, lithium, amiodarone, corticosteroids, estrogens, androgens, anticonvulsants, metformin, biotin, tyrosine kinase inhibitors, monoclonal antibodies); and presence of autoimmune disorders, pituitary disease, goiter, or thyroid nodules. The Kolmogorov-Smirnov test was used to assess normality. Statistical analysis included chi-square and Student's t-test. A p-value < 0.05 was considered significant. **Results:** The sample included 103 donors (65.1% male), aged 20-65 years. No significant differences were found by sex or age group ($p = 0.78$). Mean BMI was 26.38 ± 4.14 , with no difference between sexes (females: 26.35 ± 3.41 ; males: 26.45 ± 5.29 ; $p = 0.91$). TSH values showed a non-parametric, left-skewed distribution, with 30% of values between 1.00-1.49 μ IU/mL. No significant associations were found between TSH and sex or age ($p = 0.67$ and $p = 0.87$). Median TSH was 1.57 μ IU/mL; the 2.5th and 97.5th percentiles were 0.49 and 5.15 μ IU/mL, respectively. **Conclusion:** TSH values closely matched the manufacturer's reference range and published literature. While the sample did not meet CLSI size criteria of 120 individuals, the findings provide valuable insight and highlight the need for larger, population-based studies in Uruguay.

THYROID SURGERY

1113854 - AN INTERVENTION MAPPING APPROACH TO IMPROVE LOBECTOMY UPTAKE IN LOW-RISK THYROID CANCER

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Introduction: While interventions have successfully improved guideline uptake and reduced overuse in other medical contexts, effective strategies tailored to surgical care for low-risk thyroid cancer are lacking. **Objective:** This study aimed to identify evidence-based, surgeon- and practice-level interventions with the potential to improve uptake of guideline-concordant thyroid lobectomy for low-risk thyroid cancer. **Methods:** An implementation mapping approach was used to categorize known barriers to the uptake of thyroid lobectomy within the Tailored Implementation for Chronic Disease (TICD) framework. Corresponding intervention strategies were identified using the TICD and the Consolidated Framework for Implementation Research-Expert Recommendations for Implementing Change (CFIR-ERIC) Implementation Strategy Matching Tool. Three researchers independently performed intervention mapping and resolved discrepancies via consensus. Findings were synthesized into actionable strategies addressing surgeon- and practice-level barriers and adaptable to the surgical setting. **Results:** Twenty barriers were identified and mapped to the TICD framework (Table). Barriers fell under three domains: knowledge and skills ($n=5$), cognition and attitudes ($n=13$), and professional behavior ($n=2$). Strategies to address barriers in surgeons' knowledge and skills included active learning opportunities led by experts and opinion leaders, continuing medical education, targeted educational programs, and training on guideline updates about less extensive surgery. To address cognition and attitude-related barriers, strategies included consensus-building skills and processes to support agreement on guideline recommendations, educational initiatives targeting areas of disagreement and misbeliefs, and integration of updated guidelines into local protocols. For barriers in the professional behavior domain, strategies included audit and performance feedback as well as clinical algorithms and decision-support tools to improve decision-making and promote guideline uptake. **Conclusion:** This comprehensive implementation mapping study identified evidence-based interventions designed to address surgeon- and practice-level barriers to uptake of thyroid lobectomy for low-risk thyroid cancer. Future research should evaluate the feasibility and acceptability of these strategies to inform intervention development.

THYROID SURGERY

1113538 - ANALYSIS OF HOSPITALIZATIONS FOR TOTAL THYROIDECTOMY IN BRAZIL (2013-2023)

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Introduction: Total thyroidectomy is a surgical procedure performed to remove the entire thyroid gland, often indicated for conditions such as thyroid cancer, large goiters, or hyperthyroidism resistant to treatment. As a high-complexity procedure, its demand varies according to regional healthcare structures and access to specialized services. **Objective:** To analyze the frequency, total and average costs, and duration of hospitalizations for total thyroidectomy in Brazil from 2013 to 2023. **Methods:** This is a retrospective, descriptive epidemiological study with a quantitative analysis. Data were extracted from the Department of Informatics of the Brazilian Unified Health System (DATASUS). The analyzed variables included geographic regions, the number of procedures, and total and average hospitalization costs. **Results:** Between 2013 and 2023, a total of 74,656 hospitalizations for total thyroidectomy were recorded in Brazil. The Southeast region led in this parameter, accounting for 36,151 hospitalizations (48.42% of the total), while the Midwest recorded the lowest number, with 4,655 (6.23%). During this period, the total cost of these procedures amounted to R\$ 44,940,214.04, with the Southeast again leading, representing R\$ 22,681,067.62 (50.46% of the total). The Midwest had the lowest costs, totaling R\$ 2,869,030.71 (6.38%). The national average length of stay was 2.5 days, with the highest in the North (3.3 days) and the lowest in the Northeast (2.2 days). **Conclusion:** The analysis of total thyroidectomy procedures revealed a significant trend over the studied period. However, a sharp decline occurred from 2020 to 2021, likely due to the impact of the SARS-CoV-2 pandemic, which limited elective procedures. This decline was followed by a sharp increase in subsequent years. Additionally, the Southeast region emerged as the leader in both procedure volume and associated costs, while the Midwest had the lowest numbers. The Southeast's dominance may be attributed to its role as a national healthcare hub, offering higher-quality services and attracting patients from across the country.

THYROID SURGERY

1114273 - ASSESSING THE ACCURACY OF CHATGPT'S RESPONSES TO PATIENT QUESTIONS ABOUT THYROIDECTOMY: A COMPARISON WITH EXPERT'S OPINION

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Introduction: Thyroid cancer is the seventh most prevalent cancer worldwide, with its primary surgical treatment involving partial or total thyroidectomy. Patients newly diagnosed often face uncertainties regarding the procedure and what to expect during recovery. Artificial Intelligence (AI) can be a valuable and accessible tool providing answers to patients pre and post-procedural questions, however, it is crucial to assess the accuracy of its medical recommendations. **Objective:** To evaluate ChatGPT's response accuracy to patients frequently asked questions. **Methods:** To evaluate the accuracy of Free 4.0 ChatGPT's responses to FAQs by patients, sourced from the Brazilian Society of Endocrinology and Metabolism and the American Thyroid Association. AI-generated responses were assessed and graded on a Likert Scale (0-5) by a certified endocrinologist specialized in thyroid disorders. **Results:** A total of 11 questions were asked, including 2 on thyroid cancer prevention, 5 on pharmacological treatment, and 4 on surgery and its potential risks. Full agreement with AI-generated responses was observed in 4 (36.3%) of the questions, while partial agreement was found in 7 (63.2%). No questions received a neutral or lower rating. Regarding accuracy by domain, prevention received the lowest level of agreement, with all the questions being partially agreed upon. Pharmacological treatment followed, with 60% of responses showing partial agreement, while surgery-related questions exhibited a 50% rate. Partial agreement was primarily due to incomplete answers or the possibility of misinterpretation. Full agreement was mostly frequently observed in responses related to the surgical procedure. **Conclusion:** While ChatGPT shows considerable potential as a healthcare tool, the majority of responses received a 'partially agree' rating, emphasizing the importance of careful evaluation of AI-generated information. AI should be viewed as a supplementary resource rather than a substitute for professional medical advice. Collaborative efforts with medical societies could address this gap, enhancing the accuracy and accessibility of AI-based resources for patients.

THYROID SURGERY

1114051 - AUTOFLUORESCENCE: A POTENTIALLY COST-EFFECTIVE TOOL TO REDUCE POST-OPERATIVE HYPOCALCEMIA AFTER TOTAL THYROIDECTOMY

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Introduction: Post-operative hypocalcemia due to inadvertent parathyroid removal/injury remains a major source of morbidity after thyroidectomy. New technologies using autofluorescence are potential adjuncts to direct visualization for parathyroid preservation during thyroidectomy. **Objective:** To determine if use of autofluorescence was associated with decreased risk of postoperative hypocalcemia after thyroidectomy and whether it is cost-effective. **Methods:** Randomized controlled trials examining patients undergoing total/completion thyroidectomy (TTX) with vs. without autofluorescence were identified through a systematic review of PubMed, EMBASE, and Cochrane Library (12/2024). Exclusion criteria included non-English language, n<20, or missing both 24-hour post-operative hypocalcemia and number of parathyroids on pathology. Meta-analysis was performed using inverse variance method for fixed and random-effects models. For the cost-effectiveness analysis, we assumed 200 TTX cases/year and a baseline cost of TTX for controls. We added the fixed up-front device cost plus recurring costs for the autofluorescence group. Post-operative hypocalcemia rates were used as a proxy for effectiveness and overnight hospitalization likelihood. **Results:** Eleven studies (2019-2024) were included (n=2,048). Autofluorescence was associated with decreased odds of inadvertent parathyroidectomy (OR 0.45; 95%CI 0.23-0.90) and post-operative hypocalcemia (OR 0.53; 95%CI 0.34-0.93) after TTX. We calculated 17% of cases without and 11% of cases with autofluorescence would have transient hypocalcemia requiring overnight admission and 30 days of treatment. Autofluorescence costs approximately \$36,000 at one year and saves the system \$ 150,000 at five years. After one year (200 cases), cost per hypocalcemia case prevented is +\$ 2,800/patient; at five years (1,000 cases) it saves \$2,400/patient. However, both in systems with significantly-reduced hospitalization costs or with increased device cost per case, autofluorescence was not cost-effective at 5 years (+\$300,000 and +\$257,000, respectively). **Conclusion:** Autofluorescence was associated with reduced risk of post-operative hypocalcemia after TTX and was conditionally cost-saving at five years. Future studies examining the cost-effectiveness of other autofluorescence applications are warranted prior to widespread adoption.

THYROID SURGERY

1112188 - BARRIERS AND FACILITATORS TO INTERVENTION STRATEGIES FOR DE-IMPLEMENTATION OF TOTAL THYROIDECTOMY FOR LOW-RISK THYROID CANCER

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Introduction: Overtreatment of low-risk thyroid cancer exists worldwide, with many patients unnecessarily undergoing total thyroidectomy. Reducing total thyroidectomy rates requires effective surgeon- and practice-level interventions addressing drivers of overuse. **Objective:** To identify barriers and facilitators for implementing surgeon- and practice-level interventions aimed at reducing total thyroidectomy for low-risk thyroid cancer. **Methods:** This ethnographic study included semi-structured interviews with 17 high- and low-volume thyroid surgeons and fieldwork at five community and academic practices statewide. Participants ranked potential interventions and identified barriers and facilitators to implementation. Verbatim transcripts were analyzed using qualitative content analysis. **Results:** Participants were predominantly male (70.6%) and white (76.5%) with a mean age of 46.5 years. Performance feedback and education materials for patients were the most recommended interventions. Participants explained performance feedback could inform and provoke practice changes by identifying outliers and encouraging improvement, though barriers included surgeon receptiveness and need for context-specific feedback. Patient education materials were valued for facilitating baseline knowledge and informed patient decision-making, but barriers included patient engagement and health literacy challenges, suggesting incorporating visual aids and multimedia formats. Clinical algorithms were considered practical tools for simplifying guidelines, but faced barriers like appropriateness in nuanced patient cases, misinterpretation risk, and relevance for high-volume surgeons. Consensus-building skills could foster multidisciplinary collaboration but faced barriers of opinion variability and resource constraints. Participants regarded disease-related education for surgeons as important for reducing knowledge gaps and ensuring evidence-based care, particularly for low-volume, general surgeons. While patient-physician communication skills were recognized as important for shared decision-making and trust, most surgeons felt proficient. **Conclusion:** This study identified performance feedback, patient education materials, and clinical algorithms as potential surgeon- and practice-level interventions for reducing overtreatment of low-risk thyroid cancer. Context-specific barriers to successful implementation included surgeon receptiveness, patient engagement, and applicability of interventions in high- and low-volume practice settings.

THYROID SURGERY

1112596 - CARDIAC INSUFFICIENCY IN A MASSIVE THYROID MASS: TRACHEAL STENOSIS COMPONENT IN A CHALLENGING SURGICAL CASE

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Case Presentation: We present a 29-year-old female with heart failure due to peripartum dilated cardiomyopathy. Transthoracic echocardiogram and cardiac MRI showed severe biventricular dysfunction with a 14% ejection fraction. She had a massive neck tumor; sonography verified the thyroid gland projected posteriorly by clustered mixed nodules, anteriorly with regular contours, and macro calcifications. The largest nodule measured 11.5 x 10.3 x 9.3 cm. Fine-needle aspiration resulted in Bethesda I. She experienced dyspnea and dysphagia and was classified as NYHA III. A CT scan revealed that the tracheal lumen was 0.5 cm at its most compressed area. Bronchoscopic intubation and a stand-by ECMO cardiac team were required for safe anesthesia, although ECMO was not used. She underwent an en-bloc total thyroidectomy with tracheal shaving and was discharged on postoperative day 5 without complications. Pathological staging was pT3a, consisting of a cystic solid nodule attached to the thyroid, striated skeletal muscle tissue, and skin, with a solid area formed by papillary thyroid carcinoma. The carcinoma had an infiltrative pattern compromising thyroid tissue measuring 3.0 x 2.0 x 2.0 cm and extending to the thyroid capsule and peri thyroid tissue. The cystic area of the nodule measured 9.0 x 6.0 x 5.0 cm. There was no angio-lymphatic or perineural invasion, and free margins were obtained. Postoperative cardiological evaluation showed a decrease in her NYHA status from III to I, and she was referred for radioactive iodine therapy. **Discussion:** Heart failure with tracheal compression due to a thyroid tumor can lead to NYHA upstaging. After relieving airway compression, a heart transplant was no longer considered at the moment. **Final Comments:** Bronchoscopic intubation and a multidisciplinary approach were paramount for successfully resolving this challenging case, where airway obstruction and heart failure were concomitant in a patient with thyroid cancer.

THYROID SURGERY

1112544 - COMBINED TRANSORAL ROBOTIC SURGERY WITH INTRAOPERATIVE 3D NAVIGATION ASSISTANCE, FOR RETROPHARYNGEAL METASTASIS OF PAPILLARY THYROID CARCINOMAS

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Introduction: Retropharyngeal metastasis from papillary thyroid carcinomas, is an uncommon situation on this disease, but presents a challenge for the head and neck surgeon in order to balance morbidity and benefits of the different treatment alternatives. **Objective:** Communicate 2 cases of the combined robotic trans oral approach with intraoperative 3D navigation assistance (Brainlab), for surgical removal of this type of metastasis. **Methods:** Prospective descriptive analysis, of 2 patients with well differentiated papillary thyroid carcinoma, that presented retropharyngeal metastasis. **Results:** Case 1, 13 yo, female, received a total thyroidectomy and central and right lateral neck dissections. Biopsy showed a conventional papillary thyroid carcinoma of 15 mms, and 10/69 lymph nodes, without extra capsular spread. Radioactive iodine 70 mci was administered, and a right retropharyngeal metastases of 2,7 cm appeared. Trans oral robotic surgery was performed, without any incidents, discharged 3 days after surgery, normal oral intake, and biopsy compatible with papillary thyroid metastasis 2/2 without extracapsular spread. Follow up, tiroglobulin, and no dysphagia or dysphonia or evidence of structural disease. Case 2. 47 yo, female, with a total thyroidectomy and central and right lateral neck dissections. Biopsy with a papillary thyroid carcinoma, 22 mms, 4/12 central neck and 6/31 right dissection, with focal extracapsular spread. Received 100 mci of radioactive iodine, no activity on whole body scan. 4 months after this, tiroglobulin of 2,2, so a PET-CT scan showed a right retropharyngeal hypermetabolic 1,7 cm metastasis. Trans oral robotic surgery was performed, without any incidents, discharged 3 days after surgery, normal oral intake, and biopsy compatible with papillary thyroid metastasis without extracapsular spread. **Conclusion:** Trans oral robotic approach with intraoperative 3D navigation, is a feasible, technique in order to retrieve retropharyngeal metastasis, with a better functional and aesthetical outcomes

THYROID SURGERY

1112607 - COMPARATIVE OUTCOMES OF ROBOTIC VERSUS CONVENTIONAL THYROIDECTOMY IN PAEDIATRIC PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Robotic thyroidectomy has proven to be a valuable tool in adult thyroidectomies. However, there is no meta-analytic evidence confirming the same outcomes in a paediatric population, despite the differences in paediatric anatomy and differing outcomes in both benign and malignant diseases. **Objective:** We performed a meta-analysis comparing the outcomes and safety of open versus robotic thyroidectomy in a young population. **Methods:** PubMed/Medline, Scopus and Cochrane Library were systematically searched for studies that directly compared open and robotic thyroidectomy in paediatric and adolescent patients (< 21), and reported outcomes such as operative time, hospitalisation, recurrence and aesthetic outcomes. Continuous outcomes were computed using a mean difference model, and binary outcomes using risk ratios with random-effect models due to anticipated heterogeneity. All statistical analysis was performed in Review Manager, Version 7.2.0, The Cochrane Collaboration, 2024. **Results:** Of 402 studies screened, three studies assessing 240 patients were included. Operative time and recurrences were not significantly different between open and robotic thyroidectomy (MD - 4.25; 95% CI -33.31, 24.81; p=0.77; I²= 0%) (RR 0.54; 95% CI 0.21, 1.38; p=0.20; I²=0%). However, when measured on the visual analogue scale, aesthetic outcomes were significantly higher in robotic thyroidectomy. (MD 2.28; 95% CI 0.81, 3.75; p=0.002; I²=92%). Additionally, hospitalisation time was shorter in those undergoing robotic thyroidectomy (MD -1.23; 95% CI -1.77, -0.70; p< 0.00001; I²=0%). **Conclusion:** There were comparable outcomes relating to robotic and open thyroidectomies in the pediatric population concerning the operative time and recurrences. However, there was increased aesthetic satisfaction, presumably owing to inconspicuous scar placements and lower hospitalisation times after robotic thyroidectomy when compared to open procedures. This systematic review confirms robotic thyroidectomy as a viable option for thyroidectomy in both benign and malignant procedures in children.

THYROID SURGERY

1114064 - COMPARING OUTPATIENT AND INPATIENT THYROID SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Outpatient thyroidectomy has gained popularity in the recent era. The primary benefit of the transition from inpatient to outpatient procedures is the decreased hospital stays and subsequent reduction in healthcare costs and hospital-acquired complications. **Objective:** This review examines the current state of literature regarding the safety and efficacy of outpatient thyroidectomy (OT) compared to inpatient thyroidectomy (IT). **Methods:** This study was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. Searched databases included MEDLINE, Scopus, PubMed, Google Scholar, and ScienceDirect. Studies published prior to November 2023 comparing outpatient to inpatient thyroidectomy were identified. **Results:** Of the 5,929 screened records, 19 fulfilled our criteria. A total of 144,047 patients were included, 31,633 in the OT group, and 112,414 in the IT group. Complication rates were higher with IT compared to OT (relative risk [RR] 1.08, 95% confidence interval [CI] 1.02-1.14, P=0.01). Hematoma (RR: 1.004, 95% CI 1.003-1.005, P<0.01) and transient RLN injury (RR: 1.02, 95% CI 1.01-1.03, P<0.01) were higher with IT. However, there was no difference in rates of permanent RLN injury and hypocalcemia/hypoparathyroidism. Mortality rates and rates of 30-day emergency department visits/readmission were also similar. The mean costs were significantly higher for IT, with a cost difference of \$985.89. **Conclusion:** With careful patient selection, outpatient thyroidectomy is as safe and effective as inpatient thyroidectomy, with significantly reduced healthcare costs. Conversely, inpatient hospitalization is associated with more complications. The limited number of studies and the lack of randomization warrant further research to confirm these findings.

THYROID SURGERY

1112551 - COMPARISON OF ROUTINE PROPHYLACTIC CALCIUM + CALCITRIOL AND SELECTIVE USE BASED ON PTH FOR THE PREVENTION OF POSTOPERATIVE HYPOCALCEMIA IN PATIENTS WITH TOTAL THYROIDECTOMY: A RANDOMIZED CLINICAL TRIAL

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Introduction: Postoperative biochemical hypocalcemia is the most common complication following total thyroidectomy, affecting 15%-30% of patients. Although typically transient, it can become permanent in 1%-3% of cases. Preventive strategies include routine calcium + calcitriol administration and selective PTH-guided treatment. However, no direct clinical trials have compared their efficacy and adverse events. **Objective:** To compare the frequency of symptomatic and biochemical hypoparathyroidism following total or completion thyroidectomy between routine calcium + calcitriol administration and PTH-guided calcium treatment. **Methods:** A pragmatic multicenter, parallel, superiority randomized clinical trial (1:1 allocation) was conducted across three clinics. A sample size of 180 patients were calculated. Patients were randomly assigned preoperatively into two groups: the intervention group (postoperative calcium based on PTH levels) and the control group (routine calcium + calcitriol administration). Symptomatic hypocalcemia was assessed using a modified Wilde scale before surgery, 2 days postoperatively, and 2 weeks after surgery. Laboratory tests were performed for both groups at 2 weeks post-surgery. **Results:** A total of 322 patients were screened, and 258 were included based on selection criteria. The intervention group had 117 patients, and the control group had 141. 49.4% of thyroidectomies were performed for malignant conditions, with 4% undergoing residual thyroidectomy. In the intervention group, 50 patients (42.7%) had postoperative PTH < 15 and were discharged with oral calcium and calcitriol. 9.3% of patients developed symptomatic hypocalcemia during the follow-up, with 11.3% in the intervention group and 7.8% in the control group (P = 0.36). In the intervention group, only one patient with PTH > 15 developed symptomatic hypocalcemia. **Conclusions:** No statistically significant differences were found in symptomatic hypocalcemia between the two strategies at 15-day follow-up. However, postoperative PTH measurement reduced the need for calcium and calcitriol intake by 57.2% in the intervention group, with a 1.4% rate of symptomatic hypocalcemia.

THYROID SURGERY

1112230 - COMPLETION OF THYROIDECTOMY VIA TRANSORAL ENDOSCOPIC APPROACH. CASE REPORT

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Case Presentation: A 38-year-old female presented an asymptomatic thyroid mass on routine follow-up examination. Thyroid ultrasound imaging revealed a 1.5 cm left thyroid irregular nodule. Fine needle aspiration biopsy revealed papillary thyroid carcinoma (Bethesda category VI). Patient underwent transoral endoscopic (TOETVA) left hemithyroidectomy. Pathology of the left thyroid lobe was consistent with papillary thyroid carcinoma of 13x8 mm with angioinvasion (more than 4 vessels) with no perineural invasion. Completion of thyroidectomy with the same technique was performed because of its increased regional lymph node recurrences and distant metastases in papillary carcinoma. Pathology of the right thyroid lobe presented no morphological alterations. **Discussion:** It is case complete lobectomy through endoscopic vestibular approach for papillary thyroid carcinoma followed by interval completion thyroidectomy with the same technique because of the presence of histologic vascular invasion, which is associated with increased regional lymph node recurrences and distant metastases in papillary carcinoma. **Final Comments:** TOETVA is a safe, reproducible, and feasible approach that provides excellent cosmetic outcomes. It is an approach for patients who wish to avoid neck incision. With the presentation of this clinical case we want to emphasize that it is possible to perform a transoral approach a second time, without major difficulties or complications, sticking to the patient's choice of a scarless procedure.

THYROID SURGERY

1112583 - COMPLIANCE FOR THYROXINE REPLACEMENT AFTER TOTAL THYROIDECTOMY

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Introduction: Life-long thyroxine replacement therapy is needed after total thyroidectomy (TT). Compliance remains a major issue for any long-term therapy. **Objective:** Aim of this study was to know the incidence of non-compliance for thyroxine therapy in patients who had undergone TT for benign thyroid disorders (BTD), and to investigate the reasons for non-compliance. **Methods:** This is a prospective cohort study (2000-2023) included adult patients (> 18 years) who were attending Endocrine surgery OPD after undergoing TT for BTD. Patients who had completed at least 6 months of follow up were included. All consenting patients, were asked to fill pre-designed questionnaire and their clinical and follow-up findings were recorded. **Results:** One-hundred seventy-five patients were included. The mean age of cohort was 42.6±13.4 years and 78.9% were females. Incidence of non-compliance was 10.9%. 89.1% were compliant as confirmed by their serum thyrotropin (TSH) reports. Among non-compliant, the reason was skipping due to religious fasting, lack of understanding in 10.5 and 21% patients respectively. Education status of the patient was found to be significantly associated with non-compliance (p=0.037), however other demographic factors such as age (p=0.093), gender (p=0.245), place of residence (p=0.41) were not significant. Overall, 17% patients considered thyroxine therapy a burden majority due to timing of intake (early morning) followed by need of regular follow-up. Re-enforced counselling could improve compliance was indicated by 59%, while 9% hinted at financial assistance. **Conclusions:** Re-enforced counselling can could improve compliance for thyroxine replacement in patients undergoing TT.

THYROID SURGERY

1112295 - COSMETIC AND FUNCTIONAL OUTCOME OF CERVICAL NECK SCARS AFTER THYROIDECTOMY

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Introduction: Endoscopic thyroid surgery is becoming increasingly popular as it avoids visible cervical scars. However, there is a lack of studies evaluating long-term cosmetic and functional satisfaction with cervical neck scars. Additionally, predictive factors for post-surgery dissatisfaction remain unclear. **Objective:** This study aims to assess patient satisfaction with cervical neck scars 6 and 12 months after conventional thyroidectomy (CT) and to identify risk factors for subjective unsatisfactory cosmetic outcome. **Methods:** Patients undergoing CT at Aarhus University Hospital, Denmark, were prospectively enrolled. Eligibility criteria included age over 17 years and no previous thyroid or neck surgeries. Participants completed the Patient Scar Assessment Questionnaire (PSAQ) 6- and 12-months post-surgery. Data collected included sex, age, type of surgery (hemi- or total thyroidectomy), gland weight, complications (e.g., infection, bleeding, nerve damage), and suture technique. **Results:** Out of 263 enrolled patients, 208 (34% males) have received the PSAQ 6 months post-surgery. Overall, 88% were satisfied or very satisfied with their scars appearance, 10% found it acceptable, and 2% rated it poorly. Regarding scar-related symptoms, 97% reported minimal or no discomfort. However, 22% of patients felt fairly or very self-conscious about their neck scars. Gender distribution in the self-conscious group was similar (33% male), though these patients were slightly younger than the rest (mean age 50.3 vs. 55.3 years, p=0.095). All patients with long scars (8 cm or more, n=11) were satisfied or very satisfied with their scars. The average weight of removed thyroid tissue in this group was 148 g. No predictive factors for poor outcomes were identified. **Conclusion:** The vast majority of patients undergoing CT were satisfied with the appearance of the cervical scars 6 and 12 month after surgery. However, a significant proportion of patients continue to be self-conscious concerning the scar at these time points.

THYROID SURGERY

1113533 - DECISION REGRET IN TIR3 THYROID SURGERY: A MISSING PIECE IN PATIENT-CENTERED CARE?

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Introduction: Given the diagnostic ambiguity and potential malignancy associated with indeterminate thyroid nodules (TIR3), patients face the dilemma of opting for diagnostic surgical intervention or engaging in active surveillance. Molecular assays assist in the stratification of risk; however, they do not yield a conclusive diagnosis. Considering the concept of decision regret in advance could be a valuable approach to increasing patients' awareness and supporting more informed decision-making before a choice is made.

Objective: This study was designed to evaluate the reliability and validity of the Italian version of the decision regret scale (DRS) for a first cohort of patients who are undergoing surgery for TIR3 nodules. Additionally, this investigation explores the associations between decision regret (DR) and a range of psychological, quality-of-life, demographic and clinical factors. **Methods:** This preliminary study included patients who underwent surgery for TIR3 disease within the past 12 months. Eligible individuals were contacted between November and December 2024 and invited to complete a digital questionnaire in Italian, incorporating the DRS, Decision Conflict Scale, Satisfaction with Decision, EuroQoL-5D and the State-Trait Anxiety Inventory-Form Y2. Twenty-seven questionnaires were completed and considered suitable for analysis. **Results:** The Italian adaptation of the DRS has good internal consistency (Cronbach's $\alpha=0.7$; McDonald's $\omega=0.8$) in this clinical setting. DRS scores significantly correlate with decision-making conflict, particularly "Effective Decision" ($p=0.006$) and "Values Clarity" ($p=0.034$). The DR gradually increased over time after surgery, from a mean of 2.23 (<6 months) to 2.56 (>1 year), with the highest variability in the intermediate group (6 months-1 year), suggesting an emotional transition phase. While no significant differences in regret were found across diagnostic categories, distribution variations suggest that a larger sample may reveal underlying differences. Among the demographic variables, age and educational level were statistically significant ($p<0.05$). **Conclusion:** This study marks the first use of the Italian DRS in the surgical management of TIR3 nodules, demonstrating its validity and reliability. These preliminary findings highlight the impact of demographic and behavioral factors on the choice of treatment and the need for tools that actively engage patients in shared decision-making.

THYROID SURGERY

1113578 - DESIGNING A SPIKES-BASED PROTOCOL FOR COMMUNICATING UNCERTAINTY IN INDETERMINATE THYROID CYTOLOGY: A MIXED-METHOD ANALYSIS WITHIN A PILOT STUDY

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Introduction: Indeterminate thyroid cytology presents a significant diagnostic challenge, often leading to difficult treatment decisions for both physicians and patients. Effective communication of these uncertainties is crucial, especially in a surgical setting, where decisions can have long-lasting impacts. This is particularly important for younger surgeons who may lack extensive clinical experience.

Objective: This study aimed to plan, develop, implement, and pilot a communication protocol designed for surgeons, particularly those in training, to navigate uncertainty and build trust with their patients. Additionally, it documents the reactions of an initial patient cohort to this approach. **Methods:** Fifty-two patients diagnosed with TIR3 were enrolled between March 2023 and January 2024 at the Endocrine Surgery Unit. A communication protocol, based on the SPIKES model, was designed to structure discussions around uncertain diagnoses. Patient consultations were conducted in three phases: the initial outpatient visit, pre-surgery admission, and a follow-up one week after surgery. During each encounter, patients' emotional responses were recorded using open-ended questions. To facilitate understanding, a Decision Aid (DA) tool was introduced during the K-Knowledge phase of SPIKES to better explain the risks and treatment options. A mixed-methods approach was used to analyze both qualitative and quantitative data from patient feedback. **Results:** The adapted protocol was found to be effective, with most patients expressing trust and satisfaction regarding the chosen therapeutic option in collaboration with their surgeon. However, some patients reported lingering anxiety about their treatment and an incomplete understanding of the therapeutic process by the end of the protocol. **Conclusion:** This pilot study suggests that a structured SPIKES-based communication protocol can help address gaps in patient understanding, trust, and satisfaction when managing indeterminate thyroid cytology. Implementing such protocols may streamline communication in surgical settings, enhance patient-centered care, and support physicians, particularly trainees, in managing complex patient interactions.

THYROID SURGERY

1113783 - ECTOPIC THYROID TISSUE IN BUCCAL MUCOSA: A RAREST PRESENTATION

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Case Presentation: A 7-year-old male child presented with history of swelling in right buccal mucosa first noticed about a year back. The swelling was gradually increasing in size with no pain, ulceration or bleeding. Birth history and developmental milestones were normal. On detailed general and systemic examinations not reveal any abnormality. Local examination revealed 2.5x2 cm soft, smooth margined mobile and non tender mass covered with intact mucosa in right cheek. Fine needle aspiration cytology (FNAC) was done which was suggestive of squamous papilloma. The child underwent minimal invasive trans oral excision of mass using carbon dioxide LASER. **Discussion:** Ectopic thyroid refers to the presence of thyroid tissue in location other than the normal anterior neck region between the second and fourth tracheal cartilage. It may become goitrous and may be associated with hypo or hyper function. Sometimes benign or malignant neoplastic changes can occur in ectopic thyroid tissue. Radionuclide thyroid imaging using technetium 99, iodine 131 and iodine 123 is useful in evaluation of ectopic thyroid tissue. **Final Comments:** So far, there has not been even a single case of ectopic thyroid tissue in buccal mucosa reported in world literature. In our case, ectopic thyroid tissue was diagnosed post operatively after sending the tissue for histopath examination. Preoperatively on fine needle aspiration cytology (FNAC), it was squamous papilloma. Asymptomatic euthyroid patients with ectopic thyroid do not usually require therapy but are kept under observation

THYROID SURGERY

1114063 - EVALUATING THE SAFE OMISSION OF LEVEL VB DISSECTION IN PAPILLARY THYROID CARCINOMA: A PREDICTIVE ANALYSIS OF CLINICAL OUTCOMES

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Introduction: Lymph node metastases from papillary thyroid carcinoma (PTC) are common and typically found in levels II, III, IV, and VI, while metastases to level Vb are less frequent. **Objective:** To identify predictive factors for level Vb lymph node metastases in patients with PTC, based on preoperative imaging and intraoperative findings. **Methods:** A retrospective analysis was conducted involving 295 patients (mean age: 41 years; 61.4% female) who underwent 329 lateral neck dissections (levels IIa-Vb). Preoperative imaging was performed with ultrasound in 279 patients (94.6%), suspicious lymph nodes were identified at level III in 197 patients (59.5%). The primary outcome was histologically confirmed metastasis at level Vb. The initial predictive model was a logistic regression (LR), established using backward stepwise selection based on the Akaike Information Criterion (AIC). Model performance was assessed using the area under the receiver operating characteristic curve (AUC). All demographic, ultrasonographic, and intraoperative variables were initially included, with the final model retaining significant predictors to construct a decision tree. **Results:** Level Vb metastases were histologically identified in 14.2% of dissections. Key predictors of metastasis included preoperative extranodal extension (ENE) at levels II, III, and VI; maximum lymph node size at levels II and IV; and the number of atypical lymph nodes at level III. These variables informed the development of a decision tree model, with the primary node split determined by the number of suspicious lymph nodes at level IV, followed by the presence of atypical nodes at various cervical levels. **Conclusion:** The findings indicate that level Vb metastases are significantly associated with the presence of multiple suspicious lymph nodes, particularly at level IV, and the involvement of multiple cervical levels. In patients who exhibit comprehensive preoperative staging without radiologic evidence of involvement at level Vb, there is potential to safely omit dissection of this level.

THYROID SURGERY

1114268 - EVALUATION OF THE VOICE CHANGE INDEX VHI AFTER OPERATIONS IN THE NECK AREA

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Objective: To evaluate vocal function after surgery for thyroid and parathyroid diseases, aiming to improve postoperative outcomes.

Methods: Acoustic voice parameters were analyzed using the VHI-10 and VHI-30 questionnaires in 31 female patients (average age 44.45 ± 16.14 years). Patients completed the surveys at three time points: 1 day, 1 week, and 3 weeks post-surgery. All surgeries involved anterior neck access with neuromonitoring. **Results:** First Day: 10 patients (average age 49.5 ± 19.2 years). Most reported no major complaints, while others had sore throat, hoarseness, or voice changes throughout the day. The most common complaints were changes in voice clarity and increased effort to speak. First Week: 14 patients (average age 39.64 ± 10.18 years). Complaints were reduced, with most reporting minor discomfort, hoarseness, and difficulty being understood in noisy places. A decrease in major issues was observed, with many patients reporting "never or almost never bothers me" (88.8%). Third Week: 7 patients (average age 48.28 ± 20.72 years). Most reported minimal complaints, and voice issues had significantly decreased, with 99.3% of patients reporting "never or almost never bothers me." **Conclusion:** Patients experience the most significant voice issues in the first day and week after surgery. Early intervention with a phoniatrist or psychologist can improve their quality of life. Further studies are needed to assess long-term voice outcomes following thyroid and parathyroid surgeries

THYROID SURGERY

1114349 - EXACERBATION OF TRANSIENT HYPOPARATHYROIDISM POST-TOTAL THYROIDECTOMY COMPLICATED BY NOROVIRUS INFECTION: A CASE REPORT

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Case Presentation: Transient hypoparathyroidism after total thyroidectomy is a well-known complication, occurring in 30% of cases and usually manifesting days after surgery. We present a case of a 57-year-old woman who developed profound symptomatic hypoparathyroidism exacerbated by norovirus one-month post-op. She had a family history of medullary thyroid cancer and a 1.7 cm dominant left thyroid nodule on ultrasound. Asymptomatic, she had no trouble breathing, speaking, or swallowing, and denied prior radiation exposure. Fine needle aspiration was consistent with a follicular lesion of undetermined significance (Bethesda Category III). ThyroSeq molecular testing showed an intermediate to high (~70%) probability of cancer or non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). She underwent ambulatory total thyroidectomy and was discharged on Calcium Carbonate 1,200 mg TID per protocol. Final pathology revealed a 1.2 cm follicular adenoma in the left nodule, along with a 5 mm NIFTP, in a background of patchy oncocyctic changes and chronic lymphocytic thyroiditis. A single intrathyroidal parathyroid was identified, along with one reactive lymph node. **Discussion:** On POD3, she developed numbness and tingling, responding to increased calcium supplementation to QID. On POD14, she was doing well, with serum calcium 8.6 and PTH 17. On POD27, she presented to the ED with nausea, vomiting, diarrhea, diffuse abdominal pain, and shortness of breath. Upon admission, she had severe electrolyte imbalances: Calcium 6.3, PTH 11.5, Vitamin D 33.7, Potassium 2.8, Magnesium 1.28, and Phosphorus 1.8. CTA of the chest, abdomen, and pelvis was negative for pulmonary embolism but showed diffuse jejunal loop thickening. The patient required ICU care for electrolyte abnormalities and aggressive hydration for diarrhea, later confirmed as norovirus. **Final Comments:** This case highlights the importance of identifying confounding factors such as norovirus infection, which can result in a delayed exacerbation of the common complication of hypoparathyroidism.

THYROID SURGERY

1112422 - EXPERIENCE IN PERFORMING ORGAN-PRESERVING OPERATIONS IN PAPILLARY THYROID CANCER PT2N0M0

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Objective: To study the effectiveness of organ-preserving operations in patients with papillary thyroid cancer pT2N0M0, assess relapses impact on quality of life and the need for hormone replacement therapy in the delayed period. **Materials:** Data from 51 patients who underwent hemithyroidectomy with central lymphadenectomy with in some cases lateral collector dissection in the surgical department from 2015 to 2024 were analyzed. Intraoperative express histology was performed to decide on organ preservation. The need for hormone replacement therapy was assessed as delayed by the level of TSH in the blood. Quality of life was assessed using the SF-36 questionnaire. **Results:** No recurrences of papillary cancer were detected during the observation period. Four cases (7.8%) of new formations in the residual lobe of the thyroid gland of a benign nature were detected. Two cases of phonation disorders (transient) were detected. Hormone replacement therapy is received by 34.4% of the operated patients. When analyzing the quality of life, it was found that patients after organ-preserving operations noted improvements on the PF (functional activity) and RE (emotional role) scales. **Conclusions:** In the study group of patients with papillary thyroid cancer pT2N0M0, hemithyroidectomy with lymphadenectomy doesn't increase the number of recurrences compared to thyroidectomy, reduces the frequency of prescribing hormone replacement therapy and improves the quality of life.

THYROID SURGERY

1112617 - HIGH CENTRAL COMPARTMENT NODAL METASTASES FROM PAPILLARY THYROID CANCER: A POTENTIAL SURGICAL BLIND SPOT IN PATIENTS UNDERGOING CENTRAL NECK DISSECTION

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Case Presentation: We report three cases of metastatic papillary thyroid carcinoma (PTC) with high central compartment (CC) nodal metastases: Case 1: 54-year-old male with 8 mm PTC in the right thyroid lobe and 1.4 cm left neck lymph node (LN), inferior to the hyoid bone and medial to the common carotid artery, was treated with thyroidectomy and bilateral central neck dissection (CND). Post-operative ultrasound showed a persistent 1.4 cm LN in the left high CC, necessitating a repeat CND. Case 2: 51-year-old female with PTC and right central and lateral neck metastasis was treated with total thyroidectomy, right CND, and right level II-IV neck dissection. Follow-up ultrasound and fine needle aspiration (FNA) showed residual right high CC metastasis requiring repeat right neck dissection. Case 3: 17-year-old female with PTC and bilateral central and lateral neck metastasis, including a high left CC 0.9 cm metastasis, was treated with total thyroidectomy, bilateral CND, and bilateral lateral neck dissection. Post-operative FNA revealed persistent 0.9cm metastatic LN in the left high CC. **Discussion:** CND is performed for T3/T4 PTC tumors and in cases of PTC with documented central or lateral neck nodal metastasis. Although the superior boundary of the CC is the hyoid bone, CND is not routinely extended to this level due to the rarity of metastases in the upper CC and the risk of injury to the inferior thyroid artery supplying the superior parathyroid glands. The 2017 AHNS Consensus describes a horizontal line at the inferior border of the cricoid and recurrent laryngeal nerve insertion as the superior landmark for CND. As a result, CC metastasis located above this level may not get resected. **Final Comments:** High CC nodal metastases identified on preoperative imaging should be clearly communicated to the surgeon to guide the extension of CND to the hyoid bone for complete resection.

THYROID SURGERY

1113535 - IDENTIFYING PREDICTORS OF PERMANENT HYPOPARATHYROIDISM AFTER THYROID CANCER SURGERY – A COMPREHENSIVE REAL-LIFE RETROSPECTIVE ANALYSIS

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Introduction: Postoperative hypoparathyroidism (POH) is a common complication of total thyroidectomy, leading to low serum calcium levels due to insufficient parathyroid hormone secretion and has a significant impact on patient's quality of life, often requiring lifelong medication and follow-up. The possibility of a post operation permanent POH (p-POH) after thyroid surgery, especially in department dedicated to endocrine surgery is expected to be around 2.2%, yet in real-life, the numbers are significantly higher. Identifying predictors of p-POH remains a critical unmet need in clinical practice. **Objective:** This study aims to identify potential predictive factors for developing p-POH in patients undergoing thyroid cancer surgery, and improving preoperative planning, surgical techniques, and patient outcomes. **Methods:** We conducted a retrospective analysis of 522 patients selected from the "X" of the "X" of X database, that underwent thyroid surgery for differentiated thyroid cancer with a follow-up of 12 months. The primary outcome was the incidence of p-POH, defined as the requirement for calcium and/or vitamin D supplementation beyond 12 months post-surgery. Statistical analyses were performed to assess associations between clinical and surgical variables, such as histology, lymph node metastases, central/lateral compartment neck dissection, and response to therapy, with the occurrence of p-POH. **Results:** Among the 522 patients analyzed, 60 (11.5%) developed p-POH. Strong predictors of p-POH included the extent of neck dissection, the presence of lymph node metastases, total thyroidectomy compared to lobectomy, ATA risk stratification, and the number of lymph nodes removed. Conversely, tumor size, radioiodine therapy, and one-year treatment response were not significant predictors. **Conclusion:** This study identifies the primary predictive factors for p-POH following thyroid cancer surgery. Our findings highlight the importance of a multidisciplinary approach involving both endocrinologists and surgeons, as well as the need for tailored surgical techniques and preoperative planning to reduce the risk of p-POH and prevent adding chronic conditions to treated patients.

THYROID SURGERY

1114189 - IMPACT OF FLUORESCENCE ANGIOGRAPHY USING INDOCYANINE GREEN DURING TRANS ORAL ENDOSCOPIC THYROIDECTOMY VESTIBULAR APPROACH (TOETVA) ON POSTOPERATIVE HYPOCALCEMIA AND HYPOPARATHYROIDISM

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Introduction: With increasing number of thyroid surgeries being performed endoscopically, the importance of avoiding complications like injury to parathyroid during newer approaches has opened newer techniques & modalities for identification and preservation of parathyroids. **Objective:** To study Indocyanine Green (ICG) angiography along with the advantage of enhanced vision in TOETVA to reduce postoperative hypoparathyroidism and hypocalcemia. **Methods:** Ours is a retrospective study of patients with benign thyroid diseases undergoing total thyroidectomy. 'Group 1' (control, 60) included patients who underwent post thyroidectomy ICG angiography and 'group 2' (ICG angiography-guided thyroidectomy, 87) included patients undergoing initially ICG angiography-guided thyroidectomy to identify the feeding vessels of parathyroid glands followed by post thyroidectomy ICG angiography. ICG angiography helped check the perfusion status of parathyroids by grading as per fluorescence. Grades of fluorescence - 0, black: non vascularized; 1, greyish green: partially vascularized; 2, Green: well vascularized. Magnified endoscopic vision of TOETVA also helped better visualization of parathyroids and vascular supply during ICG angiography. Serum Calcium & iPTH were measures Preoperative, Intraoperative & Postoperative Day 1, Day 8 and Six months. **Results:** Initially ICG Angiography showed vascular anatomy & perfusion status and at a later stage confirmed the perfusion & Viability which helped in deciding the requirement of auto transplantation. We studied the incidence of postoperative hypocalcemia and permanent hypocalcemia. Patients in group 2 developed a lower rate of postoperative (3.6 vs 29.8%, $P = .001$) and permanent hypocalcemia (1.9 vs 9.1%, $p = 0.021$). Preservation of well vascularized PG at the end of the surgery (grade 2) in the group 2 was significant higher (83.9%; $p = 0.018$) than group 1. **Conclusion:** Parathyroid visualization & preservation was more reliable with better vision of endoscopy (TOETVA) and ICG angiography during TOETVA. This helped reduce injury to parathyroids during thyroidectomy and postoperative incidence of hypoparathyroidism and hypocalcemia.

THYROID SURGERY

1112398 - IMPLEMENTATION OF A ROBOTIC RETROAURICULAR APPROACH FOR NECK DISSECTIONS IN WELL DIFFERENTIATED THYROID CARCINOMAS

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Introduction: Open approach to lateral neck dissections, is the standard procedure, with possible aesthetic and functional morbidities. This has led to the development for remote approaches. **Objective:** Evaluate our results in order of clinical, oncological, and aesthetic outcomes of our initial experience with this surgical approach. **Methods:** Prospective descriptive analysis, of all the patients with the retroauricular robotic assisted approach for the lateral neck between September 2023 and November 2024. We performed a modified facelift incision, and used the Da Vinci Xi platform with 3 arms (camera, harmonic and bipolar Maryland). **Results:** 34 patients were operated with robotic retroauricular approach. 64% women, with a range of age 12-68 years. The mean hospital stay was 2.8 days and drains were take out in the first 48 hrs. Median console time was 45 minutes (24-60). We had 1 minor hematoma under the lateral flap and 8 transit XI nerve paresias. Median lymph nodes resected were 36 (16-65). **Conclusion:** Retroauricular robotic approach is a feasible, and clinically and oncologically safe approach to the lateral neck. This remote access, opens an option for this kind of procedure and other surgeries to the lateral neck. With better cosmesis and functional outcomes

THYROID SURGERY

1112517 - INTRODUCTION OF ROBOTIC THYROID SURGERY USING DA VINCI SP

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Robotic-assisted surgery has gained prominence for its precision and minimally invasive nature, with rapid adoption across multiple medical fields. In Japan, transoral robotic surgery (TORS) was covered by the national health insurance in 2022, driving the expansion of indications and clinical applications in head and neck surgery. TORS offers significant benefits, including enhanced postoperative recovery and reduced complication risks, thereby raising the standard of care in this domain. Currently, the Da Vinci Surgical System, particularly the Da Vinci Xi, is the most commonly used robot for TORS in Japan. While versatile, the Xi system faces limitations such as an 8 mm instrument diameter, restricted access to regions beyond the oropharynx, and the ability to deploy only two instruments simultaneously. These constraints hinder further expansion of indications, including thyroid surgery, where precise dissection in confined spaces is critical. The Da Vinci SP, introduced in Japan in 2023, was specifically designed for transoral robotic surgery. Its standout feature is the ability to insert three instruments and a 3D camera through a single 2.5 cm port. The systems articulating 3D camera enables unparalleled flexibility and visualization, particularly in challenging areas like the tongue base and hypopharynx. For thyroid surgery, the SP system allows precise and minimally invasive approaches, overcoming the limitations of conventional endoscopic or robotic techniques. There is growing anticipation for the inclusion of robotic thyroid surgery under insurance coverage in Japan. This presentation will focus on our departments implementation of robotic thyroid surgery using the Da Vinci SP, comparing it with endoscopic-assisted thyroidectomy. We will discuss its technical feasibility, advantages, and limitations, emphasizing its potential to redefine the standard of care in thyroid surgery.

THYROID SURGERY

1113681 - LIPOFILLING AS A SKIN TENSION REDUCTION METHOD TO IMPROVE POST-THYROIDECTOMY SCAR QUALITY: A PROSPECTIVE COMPARATIVE STUDY

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Introduction: Thyroidectomy, while effective for thyroid disorders, often results in visible scars that can impact patients' aesthetic satisfaction and psychological well-being. Skin tension is a critical factor influencing scar formation, with excessive tension leading to poor scar outcomes. Lipofilling, or autologous fat grafting, has shown promise in reducing skin tension and improving scar quality in various surgical contexts. However, its application in post-thyroidectomy scar management remains underexplored. **Objective:** This study aimed to evaluate the efficacy and feasibility of lipofilling as a skin tension reduction method to improve scar quality and patient satisfaction following thyroidectomy. **Methods:** A prospective comparative study was conducted with 50 patients undergoing total thyroidectomy, divided into two groups: Group A (n=25) received standard wound closure, while Group B (n=25) underwent adjunctive lipofilling. Adipose tissue was harvested, processed, and injected into the wound edges during closure. Scar quality was assessed using the Vancouver Scar Scale (VSS), and patient satisfaction was recorded using a 5-point Likert scale at 1 week, 2 weeks, 1 month, and 3 months postoperatively. **Results:** Group B (lipofilling) demonstrated significantly improved scar quality compared to Group A, with lower VSS scores ($p < 0.001$) and enhanced scar pliability and height. Patient satisfaction was higher in Group B (92% vs. 68%), and pain levels were significantly reduced ($p < 0.05$). No major complications were reported in Group B, with minor donor site swelling resolving spontaneously. **Conclusion:** Lipofilling is a safe and effective adjunctive technique for reducing skin tension and improving post-thyroidectomy scar quality. This study highlights its potential to enhance aesthetic outcomes and patient satisfaction, offering a novel approach to scar management in thyroidectomy. Further studies with larger cohorts and longer follow-up are warranted to validate these findings.

THYROID SURGERY

1114253 - NEOADJUVANT LAROTRECTINIB BEFORE SURGERY FOR NTRK FUSION-POSITIVE THYROID CANCER: A CASE SERIES

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Introduction: NTRK fusions are known oncogenic drivers in thyroid carcinomas. Larotrectinib, a highly selective TRK inhibitor, received FDA approval in 2018 for the treatment of pediatric and adult patients with solid tumors harboring NTRK gene fusion. While upfront surgery remains the standard of care for most thyroid cancers, some patients have invasive locoregional disease that is unresectable or requires high-risk, morbid procedures. The role of neoadjuvant larotrectinib in this context has not yet been investigated. **Objective:** The primary objective was to evaluate treatment response based on the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, assess surgical morbidity using the Thyroid Neck Morbidity and Complexity (TNMC) scoring system, and document postoperative complications and adverse events. **Methods:** This IRB-approved single-center retrospective case series reviewed three patients with NTRK fusion-positive thyroid cancer who received neoadjuvant therapy with larotrectinib followed by surgery. **Results:** Three patients were included: two pediatric females, aged 11 and 15, diagnosed with papillary thyroid cancer (PTC), and one 63-year-old male with anaplastic thyroid cancer (ATC). The median duration of neoadjuvant larotrectinib treatment was 7 months (range: 5-18 months). All three patients demonstrated a partial response to larotrectinib, with RECIST reductions ranging from 35% to 62%. This facilitated successful surgical resection, with R0 margins achieved in 66% of cases and R1 in 33%. TNMC scores dropped from 3 prior to larotrectinib to 2 before surgery for all three patients. Notably, none of the six recurrent laryngeal nerves (RLNs)- all deemed at extremely high risk pre-treatment- required sacrifice, and no temporary RLN palsy occurred. Two patients (66%) developed postoperative transient hypoparathyroidism and one patient (33%) had tracheal perforation manifesting on postoperative day 6. All three patients experienced transient transaminitis during larotrectinib treatment. **Conclusion:** Neoadjuvant larotrectinib may benefit patients with aggressive locoregional NTRK fusion-positive thyroid cancer and high initial surgical morbidity.

THYROID SURGERY

1112458 - ONCOLOGICAL SAFETY, EFFICACY AND QUALITY OF LIFE OF PATIENTS UNDERGOING TRANSAXILLARY GASLESS ENDOSCOPIC HEMITHYROIDECTOMY FOR THE TREATMENT OF THYROID CANCER LESS THAN 4 CM

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Objective: The aim of this study was to report the safety and efficacy and quality of life (QoL) of endoscopic hemithyroidectomy (ETx) in patients with selected differentiated thyroid cancer as compared to conventional open hemithyroidectomy (OTx). **Methods:** This was a single-institution observational study. The clinical records of patients with a histopathological diagnosis of differentiated thyroid cancer who were candidates for hemithyroidectomy were reviewed. Demographic, clinical, and histopathological data were collected. Health related quality of life was evaluated using validated ThyPRO39Hn questionnaire at baseline, 1 month and 6 months. **Results:** During the study period, 94 patients underwent hemithyroidectomy for DTC. Eleven patients (11/134) were lost to follow-up and 14 patients underwent completion thyroidectomy based on definitive pathology. The final study group was composed of 69 patients, who had a median follow-up of 2 years. 28 patients underwent ETx and 45 underwent OTx. The average tumor size was 3+/-1 cm in the ETx group and 3.6+/- 0.8 cm in OTx group. The mean operative time was 80+/-35 minutes in ETx group and 44+/-28 minutes in OTx group. There was no difference in perioperative complications and hospital stay. For the ETx group, there was a lower neck pain score on the third postoperative day and higher cosmetic satisfaction at 3 months. The mean preoperative ThyPRO39 scores were comparable in all domains. Mean ThyPRO scores for all domains 1 month post-surgery were significantly better in ETx group having medium effect sizes. The difference in ThyPRO scores between the two groups became comparable at 6 months. **Conclusions:** ETx for thyroid cancer is safe and feasible option. However, long term QoL is similar to open conventional surgery.

THYROID SURGERY

1113817 - PERIOPERATIVE MANAGEMENT OF A RARE DUMBBELL-SHAPED RETROSTERNAL GOITER: A CASE REPORT

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Case Presentation: A 58-year-old woman presented with progressive dyspnea, hoarseness, and dysphagia, accompanied by positive Pemberton's sign. Contrast-enhanced CT revealed a dumbbell-shaped mass with indistinct borders (cervical: 11.6*11.5*11.3 cm, thoracic: 11.2*8.9*9.1 cm). The goiter displaced and compressed the trachea (minimum diameter=0.74 cm), with associated pleural effusion and cardiac abnormalities. Core needle biopsy confirmed a benign goiter. The management involved a multidisciplinary team (MDT) approach. Awake intubation was successfully conducted with video laryngoscopy and fiberoptic bronchoscopy. Cervical resection via right thyroidectomy with intraoperative neuromonitoring (IONM), ensured RLN preservation. The subxiphoid uniportal video-assisted thoracoscopic surgery (VATS) approach to access the mediastinal component was unsuccessful due to extensive bleeding from fibrous capsule adhesions, necessitating conversion to a full sternotomy. The patient was extubated on postoperative day two without signs of tracheomalacia and experienced an uneventful recovery. **Discussion:** Dumbbell-shaped retrosternal goiter (DSRG) presents unique challenges due to its compressive effects and anatomical constraints. MDT support is essential for addressing potential airway and cardiovascular complications. Managing a difficult airway remains a cornerstone of perioperative planning, with Pemberton's sign serving as a valuable predictor of intubation difficulty. In this case, contingency plans, including extracorporeal membrane oxygenation (ECMO), were considered as a precaution. Although sternotomy is often required for extensive DSRGs, VATS remains an option for select cases with a clear fat plane separating the goiter from surrounding structures. Continuous intraoperative neuromonitoring (C-IONM) is critical for RLN preservation, and we advocate for a medial dissection technique to enhance nerve safety. Postoperative tracheomalacia is rare but necessitates vigilant monitoring and, if necessary, prolonged intubation or tracheotomy. **Final Comments:** Based on our experience, we recommend: 1. Comprehensive preoperative imaging and MDT evaluation for surgical planning, 2. Attention to potential airway management challenges, 3. Combined cervicothoracic approach for complete surgical removal, 4. Medial RLN dissection to optimize nerve preservation.

THYROID SURGERY

1113569 - POORLY DIFFERENTIATED LARGE HÜRTHLE CELL CARCINOMA WITH RECONSTRUCTION USING A PECTORAL MYOCUTANEOUS FLAP: CASE REPORT

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Case Presentation: A 65-year-old male with a family history of thyroid cancer presented with a rapidly growing 20 cm anterior neck mass. Physical examination showed a multilobulated, solid-cystic mass with violaceous, thinned skin. Fine-needle aspiration biopsy confirmed malignancy, and immunohistochemistry (CK7, CK34BE12) supported HCC diagnosis. Imaging revealed invasion of adjacent muscles, the internal jugular vein, and metastases to cervical nodes and lungs. The patient underwent total thyroidectomy, right radical neck dissection, and pectoral myocutaneous flap reconstruction. Histopathology confirmed a highly aggressive, poorly differentiated HCC with extensive necrosis, achieving complete macroscopic resection. Postoperative recovery was uneventful, and adjuvant therapy with radiotherapy and I-131 was planned. **Discussion:** HCC accounts for 3%-5% of thyroid cancers, with poor prognosis in poorly differentiated forms. Surgery remains the primary treatment, while iodine therapy is often ineffective due to reduced uptake. External beam radiotherapy may improve local control in advanced cases. Reconstruction with myocutaneous flaps optimizes aesthetic and functional outcomes, enhancing the patient's quality of life. **Final Comments:** This case highlights the importance of aggressive surgical management and multidisciplinary care in advanced HCC. The use of reconstructive techniques plays a crucial role in improving post-surgical recovery and functionality. Further studies are needed to evaluate the impact of novel systemic therapies in poorly differentiated HCC.

THYROID SURGERY

1112322 - POSTOPERATIVE PARATHYROID HORMONE AS PROGNOSTIC FACTOR FOR HYPOCALCEMIA AFTER THYROID SURGERY: A PROSPECTIVE COHORT STUDY

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Introduction: Hypocalcemia is a frequent complication following thyroid surgery, primarily due to transient or permanent parathyroid dysfunction. Postoperative parathyroid hormone (PTH) levels are recognized as a valuable prognostic marker for identifying patients at risk of hypocalcemia, enabling early intervention. However, no studies have been conducted in Ecuador to establish the optimal PTH cutoff value for predicting hypocalcemia, limiting its application in guiding postoperative treatment strategies. **Objective:** To evaluate the predictive value of postoperative PTH levels for hypocalcemia in patients undergoing thyroid surgery and highlight the need for region-specific cutoff values. **Methods:** A prospective cohort study was conducted involving 13 patients undergoing thyroidectomy. PTH levels were measured pre-operatively and at 1-, 6-, and 12 hours post-surgery. Serum calcium levels were monitored daily for the first 24 hours and at follow-up visits. Hypocalcemia was defined as total serum calcium < 8.5 mg/dL or the presence of clinical symptoms. Multivariable logistic regression assessed the association between postoperative PTH levels and hypocalcemia risk, adjusting for confounders. **Results:** Transitory hypocalcemia occurred in 61.5% of patients. A PTH threshold of 29.2 pg/mL pre-operative demonstrated high sensitivity (100%) and specificity (87.5) for predicting hypocalcemia. Also, the PTH threshold of 14 pg/mL at 6 hours and 14.7 pg/mL at 12 hours post-surgery demonstrated high sensitivity (80%) and specificity (87.5%) for predicting hypocalcemia. Patients with PTH levels above this threshold had a significantly decreased risk of hypocalcemia (odds ratio 0.84, 95% confidence interval [0.69, 1.02]). At one month postoperative, all patients had normocalcemia [Ca 9.75 (9.2-10.3)]. **Conclusion:** Post-operative PTH at 6 and 12 hours is a reliable prognostic marker for hypocalcemia after thyroid surgery. Establishing region-specific PTH cutoff values is crucial, particularly in Ecuador, to optimize postoperative management and improve patient outcomes. Future studies must address this gap and tailor hypocalcemia treatment protocols to the local population.

THYROID SURGERY

1112241 - PREDICTIVE FACTORS FOR RE-RECURRENCE IN PAPILLARY THYROID CARCINOMA FOLLOWING REOPERATION: A RETROSPECTIVE ANALYSIS

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Introduction: Papillary thyroid carcinoma (PTC) generally has a favorable prognosis; however, recurrence occurs in up to 30% of cases following initial management. Re-recurrence presents additional clinical challenges, making differentiating between persistent disease and true recurrence crucial for optimizing management strategies and improving patient outcomes. Despite its significance, studies focusing on the risk factors for re-recurrence in PTC are limited. **Methods:** A retrospective review was conducted of the medical records of 156 PTC patients who underwent re-operative surgery for recurrence at a single institution between February 2004 and October 2015. Predictive factors for re-recurrence were identified using Cox proportional hazards models and Kaplan-Meier survival analyses. **Results:** During a median follow-up of 78.8 months after reoperation, re-recurrence occurred in 25 (16.0%) patients. Univariate analysis revealed that male ($p=0.014$), lymphovascular invasion ($p=0.031$), and unstimulated thyroglobulin (Tg) ≥ 5 ng/mL ($p=0.001$) were significantly associated with recurrence-free survival after re-operation. In multivariate analysis, male (hazard ratio [HR], 2.415; 95% confidence interval [CI], 1.091-5.348; $p=0.030$) and unstimulated Tg ≥ 5 ng/mL after reoperation (HR, 4.431; 95% CI, 1.673-11.736; $p=0.003$) were strongly predictors of re-recurrence. **Conclusions:** Male and high postoperative thyroglobulin levels following re-operative surgery were predictive of re-recurrence. Thorough monitoring of these patients after reoperation is recommended.

THYROID SURGERY

1113687 - PREDICTIVE VALUE OF INTRAOPERATIVE FROZEN SECTION ANALYSIS OF DELPHIAN AND PRETRACHEAL LYMPH NODES FOR CENTRAL LYMPH NODE METASTASIS AND RECURRENCE RISK STRATIFICATION IN DIFFERENTIATED THYROID CARCINOMA

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Introduction: The optimal surgical strategy for 1-4 cm unilateral low-risk differentiated thyroid carcinoma (DTC) remains controversial and should be individualized. Preoperative imaging and fine-needle aspiration (FNA) are widely used to evaluate central lymph node metastasis (LNM), but may miss occult metastases. The central compartment includes the Delphian (DLN), pretracheal (PLN), and paratracheal lymph nodes. As the first and second drainage stations, DLN and PLN involvement may indicate broader nodal metastasis. Intraoperative frozen section of these nodes may support early risk assessment and surgical planning. **Objective:** To evaluate the predictive value of intraoperative frozen section analysis of the DLN and PLN for central compartment LNM and recurrence risk stratification in patients with DTC. **Methods:** A retrospective study included 133 DTC patients undergoing initial surgery with intraoperative frozen section of DLN and PLN between January 2023 and December 2024. ROC curves assessed the predictive value of DLN/PLN metastasis count and ratio for central LNM and recurrence risk. Concordance between intraoperative frozen and final pathology was also evaluated. **Results:** Multivariate analysis showed that age (<20 or >50 years) and capsular invasion were independently associated with DLN/PLN metastasis ($P < 0.05$). DLN and PLN metrics showed strong predictive value for central LNM >5 nodes (AUC = 0.91 and 0.91, both $P < 0.001$) and intermediate-to-high recurrence risk (AUC = 0.82 and 0.80, both $P < 0.001$). Cut-offs were 1.50 nodes and 45.00% for LNM, and 0.50 nodes and 26.79% for recurrence. Intraoperative frozen pathology showed high concordance with final pathology (sensitivity 88.00%, specificity 100.00%, Kappa = 0.85, intraclass correlation coefficient = 0.92). **Conclusion:** Frozen section analysis of DLN and PLN predicts central LNM and recurrence risk in DTC, and may assist intraoperative decision-making regarding surgical extent.

THYROID SURGERY

1113876 - PRIMARY TRACHEAL ADENOID CYSTIC CARCINOMA WITH THYROID INVASION: DIAGNOSTIC CHALLENGES AND THERAPEUTIC IMPLICATIONS

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Case Presentation: A 49-year-old female with tracheal adenoid cystic carcinoma (TACC), presenting as a central neck mass, mobile during swallowing, with no respiratory symptoms. Ultrasound revealed an isthmic thyroid mass, suspected of adhering to the trachea and esophagus. Core needle aspiration confirmed the diagnosis of ACC. Contrast-enhanced CT showed tracheal wall thickening with low-density areas and partial luminal protrusion. PET-CT and chest CT identified a small benign lung nodule, with no distant metastasis. After total thyroidectomy with central lymph node dissection, no tissue invasion or lymph node metastasis was found. The patient declined adjuvant radiotherapy and showed no recurrence or metastasis at 38 months. **Discussion:** The rarity of TACC infiltrating the thyroid complicates its diagnosis and management. In our case, we emphasize that when evaluating a thyroid mass in conjunction with respiratory symptoms, surgeons should consider both LATC and potential TACC. Bronchoscopy combined with CT detects airway wall thickening, luminal stenosis, and tumor extent. Core needle biopsy allows immunohistochemical confirmation of tumor origin and histologic subtype. Complete resection remains primary treatment, though thyroid-infiltrating cases require balancing oncologic control with functional preservation. The pursuit of radical resection is often associated with a significant decline in patients' quality of life, and postoperative survival outcomes remain suboptimal. Our case achieved 38-month locoregional control without adjuvant therapy, challenging traditional treatment paradigms. Given TACC's delayed recurrence potential, lifelong surveillance remains imperative despite initial success. **Final Comments:** This case underscores several important considerations in the management of TACC with thyroid infiltration. 1. Preoperative identification of TACC from other thyroid cancers is crucial for precise treatment. 2. The optimal surgical approach for thyroid infiltration remains under investigation. 3. Long-term follow-up is essential to monitor outcomes and detect recurrences, emphasizing the need for extended postoperative surveillance.

THYROID SURGERY

1114236 - PROPHYLACTIC THYROIDECTOMY IN CHILDREN WITH RET MUTATIONS

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Introduction: According to National Cancer Institute SEER database, the five-year survival rate for medullary thyroid carcinoma (MTC) confined to the thyroid gland exceeds 99.5%. For cases with regional metastases, it is 92%, while for distant metastases, it drops to 43%. The 2015 American Thyroid Association (ATA) guidelines classify RET proto-oncogene mutations by risk level: highest risk (codon 918), high risk (codons 883 and 634), and moderate risk (all others). Prophylactic thyroidectomy is recommended within the first year of life for highest-risk mutations and by age five for high risk mutations. In all other cases, annual follow-up with basal calcitonin monitoring is advised. **Objective:** At the Saint Petersburg State University Hospital between 2009 and 2025, 25 children under 20 years of age with confirmed RET mutations underwent surgery. Another 14 children remain under observation due to the absence of surgical indications or parental consent. **Methods:** We conducted a single-center, consecutive, retrospective cohort study with a prospective evaluation of long-term outcomes. **Results:** Among 25 operated patients (mean age 10.52 ± 5.00 years), 88% had elevated basal calcitonin, and a tumor was confirmed in 64%. Calcitonin significantly predicted disease ($p = 0.033$) with a threshold of 7.5 pg/mL (AUC = 0.74) and 87.5% accuracy. The optimal age for surgery was 9 years (AUC = 0.82), with 91% sensitivity and 78% specificity. The median follow-up period was 5.5 ± 3.8 years, with recurrence observed in 4% of patients (95% CI: 0.71-19.54%). **Conclusion:** Based on these findings, we conclude that for children with a confirmed RET mutation, one of the most critical predictors of five-year recurrence-free survival is thyroidectomy before tumor spread beyond the thyroid gland. To achieve the best surgical outcomes in the high-risk and moderate-risk groups, prophylactic thyroidectomy is recommended before calcitonin levels exceed 7.5 pg/mL and/or before the patient's age exceeds 9 years.

THYROID SURGERY

1113873 - RADIOFREQUENCY ABLATION OF THYROID NODULES PERFORMED BY TWO SPECIALISTS: A COLLABORATIVE APPROACH COMBINING RADIOLOGIST AND HEAD AND NECK SURGEON, UNDER SEDATION. INSIGHTS FROM 200 CASES – TIPS AND TRICKS

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Introduction: Radiofrequency ablation (RFA) is a minimally invasive treatment for thyroid nodules, typically performed by a single operator. Our center developed a “four-handed” technique, under sedation, where a radiologist and head-and-neck surgeon collaborate. This approach combines ultrasound expertise with surgical skills, improving precision and patient comfort. Particularly beneficial for complex cases like large or substernal nodules, our method enhances safety and efficacy while optimizing resource use of expensive RFA equipment through shared specialist involvement. **Objective:** This study aims to demonstrate the advantages of our collaborative RFA approach, highlighting: (1) improved procedural efficiency through specialist teamwork, (2) enhanced patient comfort via sedation, (3) better outcomes for complex nodules, and (4) practical techniques like simultaneous hydrodissection and airway management. We share insights from 200 cases to establish best practices for multidisciplinary thyroid RFA. **Methods:** Procedures were performed in a surgical suite, under IV sedation. The radiologist handled ultrasound guidance and electrode placement while the surgeon managed hydrodissection, patient positioning, and airway safety. Key techniques included: (1) moving-shot ablation with real-time adjustments, (2) strategic hydrodissection to protect vital structures, (3) single-access with skin traction for large nodules, and (4) chin-lift maneuvers when needed. Data on volume reduction, symptoms, and complications were systematically collected. **Results:** The dual-specialist RFA approach effectively treated thyroid nodules, achieving symptom relief and volume reduction with excellent safety. The technique proved particularly valuable for complex cases, including large and substernal nodules. Procedural precision was enhanced by sedation and real-time collaboration between specialists, while maintaining a favorable complication profile. **Conclusion:** Our collaborative RFA model demonstrates superior outcomes for thyroid nodules, especially complex cases. Combining specialist expertise under sedation improves precision, safety, and patient comfort while optimizing resource use. This approach establishes a replicable framework for centers aiming to enhance their RFA programs, particularly for challenging nodules where conventional techniques may be suboptimal.

THYROID SURGERY

1114254 - RELATIONSHIP BETWEEN THYROID NODULE SIZE AND HISTOLOGICAL EXAMINATION RESULT IN FOLLICULAR TUMOR

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Objective: To identify the relationship between the size of thyroid nodules and the result of histological examination in patients with follicular tumor. **Methods:** Data analysis of 93 patients with follicular tumors, with an average age of 41.87 ± 11.69 years. Histological results were available for 66 patients, of which 50 had follicular adenoma and 16 had thyroid carcinoma. The study was conducted at the Federal Centers for Safe Thyroid Surgery “ThyroWell.” Statistical analysis was performed using the U-test, with a significance level of $p < 0.05$. **Results:** Patients were divided into a group with follicular adenoma with an average age of 42 ± 12 years and a group with thyroid carcinoma with an average age of 41.7 ± 14.6 years. When comparing the groups, no significant differences were found in height, weight, disease duration (17 ± 26.8 months and 10.7 ± 13.8 months, respectively, U-test 299, $p = 0.66$), and duration of surgery (62.6 ± 22.47 minutes and 62.8 ± 29.2 minutes). No differences were found in TSH levels and ionized calcium levels before surgery. Data on TSH and calcium levels post-surgery were not identified. No statistically significant differences were found in the length, width, and height of thyroid nodules between patients with follicular adenoma and carcinoma: nodule length 22.54 ± 10.82 mm and 24.0 ± 13.21 mm, respectively (U-test 227.5, $p = 0.89$), width 17.28 ± 8.74 mm and 17.58 ± 9.33 mm (U-test 229.5, $p = 0.92$), and height 21.67 ± 16.56 mm and 23 ± 15.64 mm, respectively (U-test 223.5, $p = 0.82$). **Conclusion:** The size of thyroid nodules is not a reliable factor indicating malignancy in follicular thyroid tumors. Further studies are needed to confirm these findings on a larger sample.

THYROID SURGERY

1113492 - REVOLUTIONIZING THYROID CANCER SURGERY: SUCCESSFUL TOETVA FOR PAPILLARY THYROID CARCINOMA – A CASE REPORT

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Case Presentation: Case 1: A 36-year-old female with a history of hypothyroidism presented with a one-year history of cervical discomfort and a palpable thyroid nodule. Ultrasound imaging revealed a 2x2 cm right-lobe solid-cystic nodule and a 1x0.5 cm left-lobe solid nodule, both hypoechoic with peripheral vascularity. Fine-needle aspiration biopsy (FNAB) classified the right nodule as Bethesda IV. A TOETVA total thyroidectomy was performed, and histopathology confirmed bilateral papillary thyroid carcinoma (pT1aN0M0) with clear surgical margins. Case 2: A 37-year-old asymptomatic female with a history of Graves' disease presented with a suspicious right-lobe thyroid nodule (TI-RADS 5). FNAB confirmed a diagnosis of papillary thyroid carcinoma (Bethesda VI). She underwent TOETVA total thyroidectomy, which revealed a 1.5 cm papillary carcinoma with positive margins (pT1a, pNx). Postoperatively, she received 100 mCi of radioactive iodine (I-131) and is currently undergoing levothyroxine therapy. **Discussion:** TOETVA offers a minimally invasive, cosmetically superior alternative to conventional thyroid surgery. Our cases demonstrate its feasibility in treating papillary thyroid carcinoma, showing that it can achieve favorable oncologic outcomes. However, one patient experienced positive surgical margins, emphasizing the importance of surgical technique and careful patient selection. While TOETVA is oncologically safe for small, well-differentiated tumors, its application in cases with high-risk features remains a topic for further discussion. Notably, common complications, such as transient mental nerve injury and subcutaneous emphysema, were absent in our patients. **Final Comments:** TOETVA is a promising and effective approach for managing papillary thyroid carcinoma, delivering excellent cosmetic outcomes without compromising oncologic safety. With proper patient selection and surgical expertise, TOETVA may become a viable option for selected papillary thyroid carcinoma patients. Further studies are necessary to evaluate its long-term oncologic efficacy and its role in high-risk cases.

THYROID SURGERY

1112528 - RISK PREDICTORS FOR TRANSIENT AND PERMANENT HYPOPARATHYROIDISM AFTER THYROIDECTOMY AT A UNIVERSITY HOSPITAL: A RETROSPECTIVE COHORT STUDY

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Introduction: Hypocalcemia (hypoCa), commonly related to Hypoparathyroidism (HypoPT), arises 30%-50% of thyroidectomies, being in its majority transient. **Objective:** To describe the frequency and predictors of transient and permanent HypoPT following thyroidectomy at a university hospital. **Methods:** A retrospective cohort, where data were collected from medical records of 462 patients since surgery up to 12 months after. Comparisons were done between groups, based on surgical indication: malignancy, benign nodular disease (BND), and Graves disease (GD). Postoperative HypoCa (<8.5 mg/dL) and/or hyperphosphatemia (>4.5 mg/dL) was defining criterion for postsurgical HypoPT. Permanent HypoPT was defined by the ongoing need for calcitriol or cholecalciferol (>10,000 IU/day), hyperphosphatemia, or persistently low serum PTH after 12 months. **Results:** Of the entire cohort, 141 underwent surgery for BND, 60 for GD, and 261 for cancer. Postsurgical HypoPT was common (34.5%), being more frequent in cancer surgery (39.3%) and GD (35.6%) compared to BND (18%). The frequency of postoperative hypoCa reached up to 63.2% ($p<0.01$) when combining total thyroidectomy with cervical dissection (CD). Other risk factors were the use of cervical drains (63.6%) and procedures performed during the first six months of medical residency (50 vs 18%; $p=0.05$ for GD and 29.2 vs 13.3%; $p=0.04$ for BND). Permanent HypoPT represented 6% of HypoPT cases and was less common in GD (6.3%) compared to malignancy surgery combined with CD (9.3%; $p<0.03$). No permanent cases occurred in BND group. Postoperative serum phosphate was associated with permanent HypoPT (6.5 ± 1.0 vs. 4.5 ± 0.9 ; $p<0.01$). **Conclusion:** Frequency of postsurgical HypoPT was consistent with the literature, predominantly transient. The main risk factors included cancer surgery with CD, the use of cervical drains, and less surgical experience of the residents. Higher serum Phosphate were related to permanent HypoPT development.

THYROID SURGERY

1114208 - RURAL INDIA EMBRACING ADVANCED TECHNIQUES IN SURGERY OF THYROID: - A SERIES OF 87 CASES OF TRANSORAL ENDOSCOPIC THYROIDECTOMY - VESTIBULAR APPROACH (TOETVA) TECHNIQUE WITH RESPECT TO SAFETY & FEASIBILITY IN SMALL SETUP HOSPITAL IN RURAL INDIA

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Introduction: TransOral Endoscopic Thyroidectomy - Vestibular Approach (TOETVA), an alternative surgical technique for thyroid surgery is gaining widespread popularity. Amongst all endoscopic approaches for thyroid, TOETVA leaves no cutaneous scar. **Objective:** Majority of TOETVA surgeries are performed in the Tertiary Care institutes. It's safety & Feasibility in small setup hospitals has not been reported until now. This series makes an attempt to study the Safety & Feasibility in smaller operative setups in rural India. **Methods:** Total of 87 TOETVA procedures were performed. Patient selection was done with predefined inclusion criteria: Medically fit (ASA I & 2), Lobe size less than 6 cm, No previous neck surgery, No mediastinal extension & FNAC negative for malignancy (Bethesda I, II & III). Each one of the patients were monitored for: 1. Occurrence of complications, 2. Postoperative recovery, 3. Intraoperative blood loss, 4. Ease of surgical dissection, 5. Surgical time, 6. Postoperative pain. **Results:** Total 87 patients were operated TOETVA Technique from May 2018 till February 2025. In all 59 Total Thyroidectomies & 28 Hemithyroidectomies were performed. After analysis of the patient's data, significant advantages were observed with respect to safety and feasibility. All the procedures could be performed with same safety as in tertiary care institute. Essential parameters considered as proper training in TOETVA technique and proper patient selection. **Conclusion:** TOETVA can be considered safe and feasible with several benefits such as less trauma, faster wound healing in the oral cavity, and earlier recovery with a superior cosmetic outcome. This study wants to emphasize that TOETVA can be performed with safety & feasibility in small setup hospitals if proper selection of patients is done along with necessary training and essential instrumentation.

THYROID SURGERY

1113795 - SINGLE-INCISION ROBOTIC AREOLAR APPROACH THYROIDECTOMY (SIRA): AN INITIAL EXPERIENCE

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Introduction: The anterior cervical approach has been the standard procedure for thyroid surgery for over a century. However, in the past two decades, minimally invasive surgery techniques have advanced using endoscopes and robots, allowing precise surgery to be performed through small incisions. To further improve these techniques, we have performed the world's first single-incision robotic thyroidectomy using the areola approach (SIRA). This revolutionary procedure suggests that single-incision robotic thyroid surgery may be the future of minimally invasive and precise thyroid surgery. **Objective:** There are various methods used in endoscopic and robotic thyroid surgery, including the transaxillary approach (TA), bilateral axillary breast approach (BABA), retroauricular approach (RA), and transoral vestibular approach. **Methods:** BABA is considered advantageous as it provides optimal visibility of important structures, allowing for complete thyroidectomy similar to open surgery. However, it has a drawback in that it is more invasive, requiring four skin incisions on the axilla and breast instead of just one on the neck. In 2023, Yi et al. presented a new approach called single-port robotic areola-access thyroidectomy (SPRA) to overcome these drawbacks of BABA. Additionally, we developed the first single-incision robotic areola approach thyroidectomy (SIRA). **Results:** In March 2024, a patient with suspected right thyroid cancer underwent a Single Incision Robotic Areolar Approach Thyroidectomy (SIRA) on the both thyroid lobe. Following the surgery, the patient experienced no complications and was discharged. The pathologic report showed that the thyroid cancer was 1.7 cm in size, and had clear margins. Additionally, 10 out of 10 lymph nodes were found to have cancer. **Conclusion:** Robotic thyroid surgery using a single port is expected to play a crucial role in the future of endocrine surgery.

THYROID SURGERY

1113796 - STUDY DESIGN AND RISK OF BIAS MODIFY THE ASSOCIATION BETWEEN VITAMIN D DEFICIENCY AND POSTOPERATIVE HYPOCALCEMIA: A SECONDARY ANALYSIS OF A SYSTEMATIC REVIEW

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Introduction: Post-thyroidectomy hypocalcemia is the most frequent complication after total thyroidectomy. Preoperative vitamin D deficiency has been suggested as a potential risk factor, but inconsistencies exist in the literature, possibly related to methodological differences. **Objectives:** to evaluate whether study design and risk of bias influence the association between preoperative vitamin D deficiency and postoperative hypocalcemia in patients undergoing total thyroidectomy. **Methods:** This is a secondary analysis of a previously conducted systematic review. We included observational studies evaluating the association between preoperative vitamin D levels and postoperative hypocalcemia. Methodological quality was assessed using the QUIPS tool. Subgroup analyses were performed based on study design (prospective vs. retrospective) and overall risk of bias (high vs. low/moderate). Meta-regression adjusted for the threshold effect of vitamin D deficiency was also conducted. **Results:** Twenty-eight studies comprising 4,994 patients were included. Nineteen studies had a prospective design. Both prospective and retrospective studies showed an association between vitamin D deficiency and hypocalcemia; however, the effect size was lower in prospective studies (OR 1.95; 95% CI 1.28-2.97) compared to retrospective ones (OR 2.18; 95% CI 1.02-4.7). Studies with high risk of bias showed a significant association (OR 2.55; 95% CI 1.4-3.6), while those with low/moderate risk did not (OR 1.71; 95% CI 0.96-3.06). Meta-regression showed no significant modification after adjusting for threshold definitions. **Conclusion:** Study design and methodological quality influence the reported association between vitamin D deficiency and postoperative hypocalcemia. These findings suggest caution when recommending preoperative vitamin D supplementation based solely on observational data.

THYROID SURGERY

1112620 - SUBSEQUENT THYROID HORMONE TREATMENT IN PATIENTS WITH SMALL, LOW RISK PAPILLARY THYROID CANCER WHO CHOSE ACTIVE SURVEILLANCE OR SURGERY: A PROSPECTIVE COHORT STUDY

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Introduction: Patients with small, low risk papillary thyroid cancer (PTC) may choose active surveillance (AS) over surgery to avoid future thyroid hormone (TH) treatment. **Objective:** We ascertained subsequent rates of TH treatment in patients with small, low risk PTC who chose AS or surgery and were not taking TH at the time of enrollment. **Methods:** We conducted a prospective cohort study, offering 200 adult patients with low-risk PTC measuring < 2 cm in maximal diameter the choice of AS or immediate surgery. TH treatment for strict TSH suppression was not mandated in the AS group. Descriptive data are presented on TH utilization at last follow-up. **Results:** We included 172 patients who were not taking TH treatment at enrollment, including 136 who chose AS and 36 who chose surgery. At baseline, the mean baseline TSH was 1.70 mIU/L, standard deviation [SD] 0.99 (N = 172) and the prevalence rate of positive thyroglobulin antibodies was 25% (42/165). Patients were followed for a mean of 67 months (SD 17). In the AS group, 22% (30/136) of patients crossed over to active treatment or met disease progression criteria for surgery. The rate of suspected disease progression under AS was 13% (17/136). The rates of TH treatment at last follow-up according to initial choice were: AS - 13% (18/136, 95% CI - 9%, 20%), initial surgery - 75% (27/36, 95% CI - 58%, 88%). Of the 18 patients in the AS group who were treated with TH at last follow-up, 83% (15/18) had crossed over from AS to surgery or met cross-over criteria. **Conclusions:** We observed that not mandating TH treatment for TSH suppression in patients with small, low risk PTC under AS enables most patients to avoid subsequent TH treatment. More research is needed examining the utility of TH treatment in AS.

THYROID SURGERY

1112475 - THE IMPACT OF LEARNING CURVE ON THE OUTCOMES OF RADIOFREQUENCY ABLATION FOR BENIGN THYROID NODULES: A SINGLE-CENTER EXPERIENCE

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Introduction: Radiofrequency ablation (RFA) is an emerging minimally invasive technique for the treatment of benign thyroid nodules (BTNs). Although RFA has shown promising results in terms of nodule volume reduction and preservation of thyroid function, its effectiveness can be influenced by the experience of the operator. **Objective:** Describe the learning curve on the reduction of nodule volume in patients treated with RFA, comparing outcomes from the first year of experience with those from the second, third and fourth years. **Methods:** This prospective cohort study includes 119 RFA procedures performed between 2021-2024. All patients had benign thyroid nodules with Bethesda II cytology and were treated with RFA as an alternative to surgery. Data collected included: - Volume reduction at 6 post-treatment. - Complications and adverse events - Correlation between the operators experience and procedural efficiency. **Results:** The cohort consisted of 119 patients, with a mean age of 55 years (22-80), and 80,6% were female. Of the 119 patients, 104 were evaluated at 6 months post-ablation. 2021 - n 2 58%. Vol 16.14 2022 - n 17 67.2%. 18.18 2023 - n 45 71.7%. 22.8 2024 - n 40 73.7% We presented 3 cases (2.5%) of temporary dysphonia (with complete resolution before the third month), 1 case of Claude Bernard-Horner syndrome (0,84%), and 1 case of ecchymosis (0.84%). **Conclusion:** The learning curve plays a significant role in improving the outcomes of radiofrequency ablation for benign thyroid nodules. As the operator gains experience, there is a clear improvement in nodule volume reduction, procedural time, and complication rates. Our results highlight the importance of continued practice and technique refinement, as well as the use of intra-procedural ultrasound, to achieve optimal treatment results. This study underscores the value of long-term experience in minimizing complications and improving the success rate of RFA for BTNs.

THYROID SURGERY

1112380 - THE TRANSORAL VESTIBULAR APPROACH IN THYROID CANCER: WHY NOT?

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Introduction: Although cervicotomy remains the most common procedure, the transoral endoscopic vestibular approach (TOETVA) offers superior cosmetics, though concerns remain about its safety and oncological outcomes. **Objective:** The aim was to assess the viability of TOETVA as a minimally invasive surgical option for DTC, comparing it to traditional approaches in terms of safety, complication rates, recurrence, and overall patient outcomes. **Methods:** A total of 143 patients (p) who underwent thyroid lobectomy (TL) for differentiated thyroid cancer (DTC) from 2015 to 2024 were retrospectively analyzed. Patients aged ≥ 18 years with fine needle aspiration biopsy (FNAB) categories V, VI, I, II, or indeterminate nodules (2017 Bethesda System) were included. Surgery, consisting lobectomy with isthmectomy, was performed via either conventional or transoral approaches. The risk of recurrence was classified as low or intermediate based on 2015 American Thyroid Association (ATA) guidelines. Follow-up included thyroid tests, clinical exams, and neck ultrasounds every six months. **Results:** A total of 143 patients (p) were included at a single institution, a median age was 44 years (18-69), and 81% of them were women (117). Of these, 114 p underwent TL for DTC via conventional cervicotomy, while the remaining 29 through an endoscopic approach, in one of them completion thyroidectomy was successfully performed with the same procedure. All patients were classified as stage I according to the 8th edition of the AJCC/TNM staging system. Based on the ATA risk of recurrence classification, 95% were categorized as low-risk, and only 10 patients were intermediate-risk. Transient recurrent nerve paresis occurred in 5.4% (2 p) of TOETVA procedures compared to 5.7% (6 p) in those with conventional approach. **Conclusions:** TOETVA achieves comparable disease control outcomes to the conventional approach in patients with low and intermediate-risk DTC, offering optimal cosmetic results and no significant postoperative complications.

THYROID SURGERY

1113707 - THYROID SURGERY WITHOUT USE OF DRAIN OUR EXPERIENCE AND COMPARISON

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Introduction: Thyroidectomy is an operation that involves the surgical removal of all or a part of thyroid gland. General endocrine or ENT surgeon often perform thyroidectomy when patient has thyroid cancer, colloid goitre and adenoma. Routine use of drain after thyroidectomy arises from the past in order to decrease the risk of acute airway obstruction caused by haemorrhage or post operative hematoma. However, many problems have been reported by the use of drainage. **Objective:** To compare the feasibility of patients undergoing thyroid surgery with and without placement of drain in term of hospital stay, post operative pain, fluid collection in the neck and other post operative complications. **Methods:** This study was conducted at Dr. Jaulkar Ent Hospital and Research Centre, Raipur (C.G.) India (Urban Centre of Raipur Institute of Medical Sciences) from 2007-2025. Important variables of the study were duration of hospital stay, post operative pain score, amount of fluid collection in the wound as detected on ultrasound and post operative complications. Visual analog scale was used to assess post operative pain on completion of 24 hours. **Results:** This study included 860 patients. The duration of hospital stay was found less in patients without drain. The average length of hospital stay was between 12-13 hours for patient without drain and about 48-72 hours with patients with drain. Comparatively, the post operative complication was found to be very less in group without drain. Suture reaction, transient recurrent nerve palsy and wound infection was observed as most prevalent post operative complications in patients with drain. **Conclusion:** The current practice of post surgical drain in thyroidectomy does not offer any significant advantage. On the contrary, post surgery complications and duration of stay was higher in patients with drain.

THYROID SURGERY

1114323 - THYROIDECTOMY TRAINING BOX (TTB): CERVICAL SIMULATOR FOR TRAINING IN ENDOSCOPIC AND ROBOTIC TRANSORAL THYROIDECTOMY

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Introduction: Trans Oral Endoscopic Thyroidectomy Vestibular Approach (TOETVA) and Transoral Robotic Thyroidectomy (TORT) have been increasingly gaining ground, with the great benefit of leaving the scar hidden. Despite this advantage, the spread of the technique has been limited by the difficulty of training. Realistic simulation plays a major role in learning surgical techniques and reducing costs and time. **Objective:** to develop and validate a TOETVA/TORT simulator. **Methods:** the first phase of the project consisted of designing and developing a Transoral Thyroid Surgery simulator based on real surgeries. The product has the oral cavity for attaching the three trocars and the cervical part containing the thyroid and adjacent structures. In the second phase, the simulator was validated by specialists who performed an endoscopic thyroidectomy procedure. They all filled a questionnaire about the simulator and the simulation based on the LIKERT scale. **Results:** The simulator had excellent results in the visual evaluation (face validity), with 100% of responses between good and excellent for the following characteristics: synthetic structures, design, visibility of the surgery field, resistance, resilience, fulcrum effect, ergonomics, surgical material, and practicality. The last three were rated higher, with more votes for excellent. For content validity, the items that received the best ratings were, precisely, the steps relating to the surgical procedure: opening the intermuscular midline, isthmotomy, and thyroidectomy. **Conclusion:** the TTB showed great ability to simulate a TOETVA and a TORT, with satisfactory evaluations concerning its visual and content validation.

THYROID SURGERY

1114272 - THYROWELL FEDERAL CENTERS FOR SAFE THYROID SURGERY

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Introduction: The development of diagnostic tools and screening methods for thyroid diseases is accompanied by an increase in the frequency of detected pathologies, which in turn requires the development of a surgical treatment system at the federal level. **Objective:** The study was conducted between May 2024 and February 2025. **Methods:** During this period, the total number of hospitals participating in the study increased to 8 centers. The total number of patients who underwent surgical treatment during the operation of the centers is 170 people. **Results:** The concept of patient care in the Thyrowell Safe Surgery Centers includes pre-, intra- and postoperative monitoring and treatment of patients. At the preoperative stage, all patients underwent the procedure of fine needle aspiration puncture biopsy of formations, the selected material was sent to a single central high-quality diagnostic laboratory. At this stage of preparation, all patients undergo a standardized set of tests, including a study of the general condition of the body and a study of hormone levels. An examination by highly specialized specialists is mandatory. If necessary, teleconference with an oncological psychologist. At the stage of surgical intervention, standardized stowage and equipment of the operating team has been prepared in each center for safe surgery. Routine use of an intraoperative neuromonitor during surgery. Each patient underwent a histological examination of the surgical material. All patients are referred to endocrinologists for monitoring and correction of hormonal status. **Conclusion:** The described system helps to reduce the frequency of postoperative complications in patients

THYROID SURGERY

1114104 - TRACHEAL FISTULA AFTER THYROIDECTOMY FOR THYROID CANCER MANIFESTED AS CERVICAL BULGING AFTER THE THIRD WEEK OF SURGERY

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Case Presentation: A 32-year-old patient with a 0.6 mm unilateral thyroid carcinoma and no suspicious lymph nodes on preoperative ultrasound underwent partial thyroidectomy that resulted in cervical hematoma eight hours after surgery due to the cricothyroid artery entering high behind the laryngeal nerve, which lost its ligature, and was controlled during the surgical review. The patient was discharged on the 4th postoperative day in good condition, but on the 22nd postoperative day she developed a new cervical bulge that, when treated in the emergency room, turned out to be emphysema bulging the entire anterior region of the neck. The patient was hemodynamically stable and eupneic. Hospitalization and bronchoscopy were indicated and proceeded the following day in the surgical center when a tiny punctual lesion orifice in the laryngotracheal junction, almost in the subglottic region, was identified in the trachea, which explained the tracheal fistula to the skin and the emphysema bulging the neck. decided to adopt a clinical approach only, avoiding an open surgical approach. Continuous cervical bandaging was implemented for ten days, with the bulging completely resolved with three-month follow-up after resolution. **Discussion:** Tracheal fistula or thyroidectomy can occur due to inadvertent trauma to the trachea, either by sharp instruments or by heat, especially vessel-sealing scissors. In this case, the initial procedure already presented difficulty in ligating the cricothyroid artery because it passes high behind the nerve, almost at the nerve's entrance into the larynx. When the hematoma occurred and surgical re-approach occurred, we decided to apply suture with needle thread with an X stitch in the described region and the needle pierced part of the trachea, causing ischemia and punctiform fistula 3 weeks later. **Final Comments:** Post-thyroidectomy tracheal fistula is a rare occurrence and should be remembered especially in late emphysematous bulges from 3 weeks after the procedure.

THYROID SURGERY

1112464 - TREATMENT OF LYMPH NODE METASTASIS OF PAPILLARY THYROID CANCER WITH MICROWAVE ABLATION

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Case Presentation: A 76-year-old patient with a history of stroke, healing with facial paralysis, without other sequelae. He underwent total thyroidectomy for papillary thyroid carcinoma by a general surgeon about 30 years ago, with postoperative dose of radioiodine treatment. The patient evolved with definitive paralysis of the left vocal fold in the median position. One month ago, he presented a lump at right level IV. He underwent ultrasound imaging that showed two suspicious lymph nodes, the largest being laterally the internal jugular vein measuring 1.42 x 1.30 x 1.20 cm, at right level IV. Another smaller lymph node, medially the internal jugular vein, measuring 0.99 x 0.56 x 0.56 cm, in the transition between levels IV and VI on the right. Fine needle aspiration cytology showed papillary carcinoma metastases with high thyroglobulin (into the lymph node aspiration fluid). The patient opted for microwave thermoablation because he did not want to undergo another surgical procedure since the first one ended up being traumatizing. The ablation was performed with local anesthesia and mild sedation with a total ablation time less than two minutes for each lymph node. **Discussion:** Surgical removal of lymph node metastases from papillary thyroid cancer is the best treatment for disease eradication. In selected cases with few lymph nodes involved thermal ablation can achieve Propper disease control with less morbidities and complications. **Final Comments:** Thermal ablation of metastatic lymph nodes from papillary thyroid cancer can be a safe alternative to surgery in selected cases.

THYROID SURGERY

1113722 - UNVEILING THE UNCOMMON: A RARE SKULL METASTASIS AS THE INITIAL MANIFESTATION OF A WELL-DIFFERENTIATED THYROID CARCINOMA

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Case Presentation: Papillary thyroid carcinoma is the most common histological type of differentiated thyroid carcinoma. Rarely, metastasis to the skull occur in 2.5% with only 14 reported cases, commonly in parietal area with 5 cases in frontal region. The present case is rare and unique due to the shape and size of the skull base metastatic tumor. This case presents a 49-year-old female with anterior neck and enlarging cranial mass. In the interim, she was asymptomatic. Cranial MRI revealed meningeal hemangiopericytoma on left frontal region. Neck ultrasound showed thyroid nodules suggesting FNAB, which unveiled malignant thyroid neoplasm. She was admitted for craniotomy but proceeded first with excision of thyroid mass with histopathological findings of follicular thyroid carcinoma. No postoperative complications were noted. Excision of the tumor was done with perioperative diagnosis of Follicular Thyroid Carcinoma, Stage I with Meningeal Hemangiopericytoma. Biopsy of brain mass confirmed papillary thyroid carcinoma. Biopsy of thyroid was re-evaluated thereafter which confirmed to be papillary in origin. **Discussion:** The largest recorded cranial metastasis measured 10.5 x 10.2 x 7.5 centimeters. The present case is rare due to location and size measuring 13 x 10.5 x 7 centimeters found in frontal region claiming the largest skull metastasis. No complications post-operatively, she recovered well and discharged after a week. She was prescribed medications and advised to undergo RAI therapy as an outpatient. **Final Comments:** Accurate diagnosis has major implications for tumor management as different tumor types respond differently. This case highlights the importance of having high index of suspicion when approaching patients who present with skull mass. Not all skull mass originates primarily in the skull but can also be a metastasis from a distant primary.

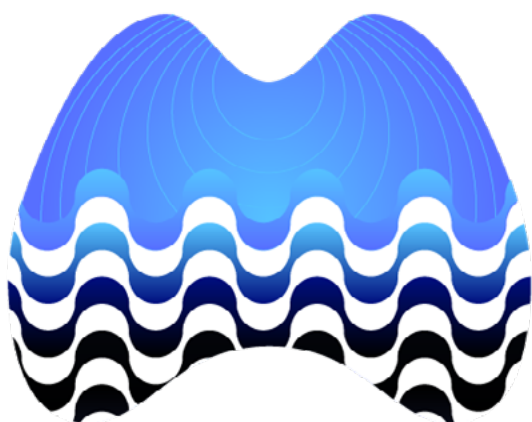
THYROID SURGERY

1114113 - UTILITY OF A NEAR-INFRARED IMAGING CAMERA SYSTEM IN SURGERY FOR PRIMARY HYPERPARATHYROIDISM

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Introduction: Primary hyperparathyroidism (PHPT) often necessitates precise preoperative localization of the responsible parathyroid lesion, commonly facilitated by MIBI scintigraphy, computed tomography, and ultrasound imaging. During surgery, confirmation relies on intraoperative PTH measurements and frozen-section analysis. However, these procedures can be time-consuming or unavailable in certain clinical contexts. Notably, parathyroid glands exhibit intrinsic autofluorescence in the near-infrared spectrum (approximately 780 nm), offering a unique marker for rapid identification. This study evaluates the utility of the PDE-neo[®] near-infrared imaging system in pinpointing parathyroid tissue during PHPT operations. **Objective:** Our main goal was to determine whether the PDE-neo[®] device could enhance intraoperative detection of parathyroid glands by visualizing their autofluorescence in real time. Additionally, we aimed to explore its capability as a supplementary or alternative modality to conventional intraoperative frozen-section pathology and intact PTH assays. **Methods:** Between January 2014 and December 2023, 37 patients underwent surgical treatment for PHPT at our institution. Standard imaging (MIBI, CT, and ultrasound) guided preoperative planning. For 19 of these patients, the PDE-neo[®] camera was used to identify parathyroid autofluorescence. After resection, all specimens were examined histologically to confirm the presence of parathyroid adenoma or other pathology. Postoperative serum PTH levels were measured to validate surgical success. **Results:** Among the 19 cases utilizing PDE-neo[®], 18 exhibited clear autofluorescence, and all fluorescent lesions were confirmed pathologically as adenomas. Each patient, including the one without detectable fluorescence, demonstrated significant postoperative PTH reduction, indicating successful surgical intervention. **Conclusion:** Near-infrared imaging using the PDE-neo[®] system provides a rapid, precise adjunct for locating hyperfunctioning parathyroid glands in PHPT. By exploiting tissue-specific autofluorescence, this method can streamline intraoperative decision-making and enhance outcomes when used alongside – or potentially in place of – conventional PTH assays and frozen-section pathology.

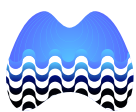


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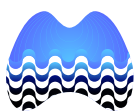


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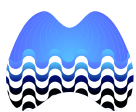
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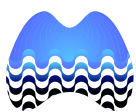
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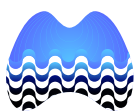
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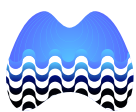


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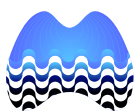
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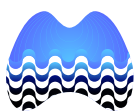


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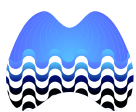


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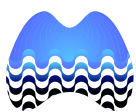


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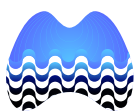
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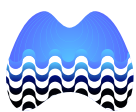
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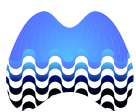
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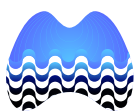
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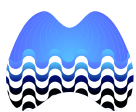
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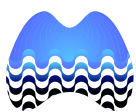
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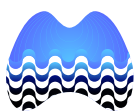
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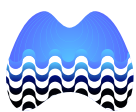
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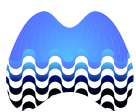
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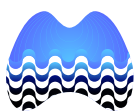


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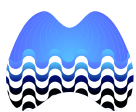
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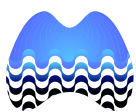
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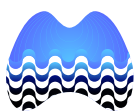
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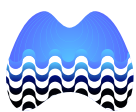
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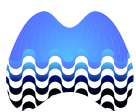
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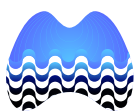


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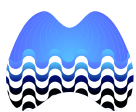
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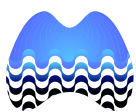


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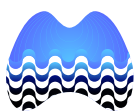
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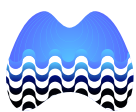
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