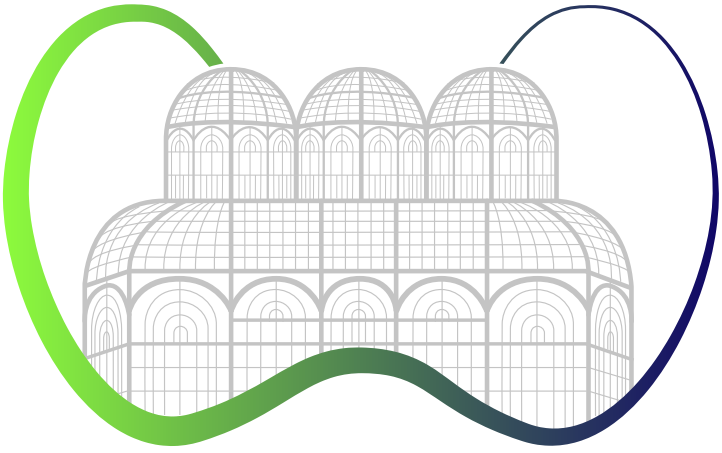
ISSN 2446-5321

Archives of Endocrinology and Metabolism

OFFICIAL JOURNAL OF THE BRAZILIAN SOCIETY OF ENDOCRINOLOGY AND METABOLISM

Vol. 67 – Supplement 01 – April – 2023



XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

SBEM
Sociedade Brasileira de Endocrinologia e Metabologia

Archives of Endocrinology and Metabolism

OFFICIAL JOURNAL OF THE BRAZILIAN SOCIETY OF ENDOCRINOLOGY AND METABOLISM

Editorial assistant: Roselaine Monteiro
roselaine@endocrino.org.br

Rua Botucatu, 572 – conjunto 83 – 04023-062 – São Paulo, SP
Telefax: (11) 5575-0311 / 5082-4788

Online submission / Electronic publishing
www.aem-sbem.com • www.scielo.br/abem

Segmento Farma editores

Rua Anseriz, 27, Campo Belo
04618-050 – São Paulo, SP. Fone: 11 3093-3300
www.segmentofarma.com.br • segmentofarma@segmentofarma.com.br

Publication code: 30316.4.23

Indexed in Biological Abstracts, Index Medicus, Latindex, Lilacs, MedLine, PubMed, SciELO, Scopus, ISI-Web of Science

BRAZILIAN ARCHIVES OF ENDOCRINOLOGY AND METABOLISM
Brazilian Society of Endocrinology and Metabolism – São Paulo, SP:
Brazilian Society of Endocrinology and Metabolism, volume 5, 1955-
Six issues/year
Continued from: Brazilian Archives of Endocrinology (v. 1-4), 1951-1955
ISSN 2359-4292 (online issues)

1. Endocrinology – journals 2. Metabolism – journals
I. Brazilian Society of Endocrinology and Metabolism II. Brazilian Medical Association

CDU 612.43 Endocrinology
CDU 612.015.3 Metabolism

Archives of Endocrinology and Metabolism

OFFICIAL JOURNAL OF THE BRAZILIAN SOCIETY OF ENDOCRINOLOGY AND METABOLISM

Archives of endocrinology and metabolism
Official journal of **SBEM** – Brazilian Society of Endocrinology and Metabolism (Department of the Brazilian Medical Association), **SBD** – Brazilian Diabetes Society, **ABESO** – Brazilian Association for the Study of Obesity and Metabolic Syndrome

SBEM – Brazilian Society of Endocrinology and Metabolism

SBEM BRAZILIAN BOARD OF DIRECTORS 2023-2024

President	Paulo Augusto Carvalho Miranda (MG)
Vice-President	Neuton Dornelas Gomes (DF)
Executive Secretary	Karen Faggioni de Marca Seidel (RJ)
Adjunct Executive Secretary	Fábio Ferreira de Moura (PE)
Treasurer-General	Carolina Ferraz da Silva (SP)
Adjunct Treasurer	Ana Luiza Silva Maia (RS)

Rua Humaitá, 85, cj. 501
22261-000 – Rio de Janeiro, RJ
Fone/Fax: (21) 2579-0312/2266-0170
www.endocrino.org.br
sbem@endocrino.org.br

Scientific Departments - 2023/2024

ADRENAL AND HYPERTENSION

President	Madson Queiroz de Almeida (SP) madson.a@hc.fm.usp.br
Vice-President	Leonardo Vieira Neto (RJ)
Directors	Flávia Amanda Costa Barbosa (SP) Guilherme Asmar Alencar (SC) Adriane Maria Rodrigues (PR) Claudio Elias Kater (SP) Milena Coelho Fernandes Caldato (PA)

DIABETES MELLITUS

President	Levimar Rocha Araújo (MG) levimar@diabetes.med.br
Vice-President	Melanie Rodacki (RJ)
Directors	Cristiane Bauermann Leitão (RS) João Eduardo Nunes Salles (SP) Rodrigo de Oliveira Moreira (RJ) Rodrigo Nunes Lamounier (MG) Wellington Santana da Silva Junior (MA)

DYSLIPIDEMIA AND ATHEROSCLEROSIS

President	Joaquim Custódio da Silva Junior (BA)i jocsjunior@uol.com.br
Vice-President	Márcio Weissheimer Lauria (MG)
Directors	Joana Rodrigues Dantas Vezzani (RJ) Cynthia Melissa Valério (RJ) Marcello Casaccia Bertoluci (RS) Renan Magalhães Montenegro Junior (CE) Maria Helane Costa Gurgel Castelo (CE)

BASIC ENDOCRINOLOGY

President	Maria Tereza Nunes (SP) mtnunes@icb.usp.br
Vice-President	Luciani Renata Silveira de Carvalho (SP)
Directors	Beatriz D´Agord Schaan Denise Pires de Carvalho (RJ) Luciana Mattos Barros Oliveira (BA) Caroline Serrano do Nascimento (SP) Célia Regina Nogueira (SP) Rafael Loch Batista (SP)

Scientific Departments - 2023/2024

Women Endocrinology, Andrology and Transgenerity

President	Marcelo Fernando Ronsoni (SC) ronsoni.marcelo@gmail.com
Vice-President	Alexandre Hohl (SC)
Directors	Poli Mara Spritzer (RS) Dolores Perovano Pardini (SP) Ricardo Martins da Rocha Meirelles (RJ) Mônica de Oliveira (PE) Tayane Muniz Fighera (RS)

Pediatric Endocrinology

President	Sonir Roberto Rauber Antonini (SP) antonini@fmrp.usp.br
Vice-President	Margaret Cristina da Silva Boguszewski (PR)
Directors	Fabiano Sandrini (PR) Eveline Gadelha Pereira Fontenele (CE) Alexander Augusto de Lima Jorge (SP) Nathália Lisboa Rosa Almeida Gomes (MG) Everlayny Fiorot Costalonga (ES)

Bone and Mineral Metabolism

President	Bárbara Campolina Carvalho Silva (MG) barbaracampolina@mac.com
Vice-President	Catarina Brasil D´Alva (CE)
Directors	Narriane Chaves Pereira de Holanda (PB) Francisco José Albuquerque de Paula (SP) Monique Nakayama Ohe (SP) Leonardo Costa Bandeira e Farias (PE) Miguel Madeira (RJ)

Neuroendocrinology

President	Leandro Kasuki Jomori de Pinho (RJ) kasuki.leandro@gmail.com
Vice-President	Andrea Glezer (SP)
Directors	Manoel Ricardo Alves Martins (CE) Heraldo Mendes Garmes (SP) Vania dos Santos Nunes Nogueira (SP) Paula Condé Lamparelli Elias (SP) Guilherme Alcides Flôres Soares Rollin (RS)

Obesity

President	Bruno Halpern (SP) brunohalpern@hotmail.com
Vice-President	Márcio Corrêa Mancini (SP)
Directors	Fábio Rogério Trujilho (BA) Maria Edna de Melo (SP) Fernando Gerchman (RS) Simone Van de Sande Lee (SC) Lívia Lugarinho Corrêa de Mello (RJ)

Thyroid

President	Danilo Glauco Pereira Villagelin Neto (SP) dvillagelin@gmail.com
Vice-President	Rafael Selbach Scheffel (RS)
Directors	Fernanda Vaisman (RJ) Gláucia Maria Ferreira da Silva Mazeto (SP) Cléo Otaviano Mesa Júnior (PR) Susan Chow Lindsey (SP) Raquel Andrade Siqueira (GO)

Permanent Commissions - 2023/2024
Brazilian Society of Endocrinology and Metabolism

SCIENTIFIC COMISSION

President	Neuton Dornelas Gomes (DF) neuton@endocrino.org.br
Indicated by the directories	Cristiane Bauermann Leitão (RS) Cristiane Jeyce Gomes Lima (DF) Fernanda Vaisman (RJ) Juliana Beaudette Drummond (MG) Larissa Garcia Gomes (SP) Luciana Ansaneli Naves (DF) Marise Lazaretti de Castro (SP) Milena Coelho Fernandes Caldato (PA) Milena Gurgel Teles Bezerra (CE) Thaísa Dourado Guedes Trujilho (BA)

PROFESSIONAL ETHICS AND DEFENCE – CDEP

President	Diana Viegas Martins (BA) diana.viegas@terra.com.br
Vice-Inspector	Luciana Antunes de Almeida Secchi (MS)
1st member	Itairan da Silva Terres (SC)
2nd member	Angela Maria Spinola e Castro (SP)

SOCIAL COMMUNICATION – CCS

President	Fábio Ferreira de Moura (PE) fmoura@endocrino.org.br
AE&M Editor	Beatriz D'Agord Schaan (RS)
Members	Mateus Dornelles Severo (RS) Ximene Antunes (RJ) Lúcia Helena Oliveira Cordeiro (PE) Márcio Krakauer (SP)

HISTORY OF ENDOCRINOLOGY – CHE

President	Henrique de Lacerda Suplicy (PR) hsuplicy@gmail.com
Members	Adriana Costa e Forti (CE) Cláudio Elias Kater (SP) Mauro Antônio Czepielewski (RS)

TITLE OF SPECIALIST IN ENDOCRINOLOGY AND METABOLISM – CTEEM

President:	Rodrigo de Oliveira Moreira (RJ) rodrigo.moreira@endocrino.org.br
Vice-President:	Maria Edna de Melo (SP)
Members:	Margaret de Castro (SP) Miguel Madeira (RJ) Monike Lourenço Dias Rodrigues (GO) Cléo Otaviano Mesa Júnior (PR) Marcelo Fernando Ronsoni (SC)i

STATUTES, RULES AND REGULATIONS – CERN

President	Rui Monteiro de Barros Maciel (SP) rui.maciel@unifesp.br
Members	César Luiz Boguszewski (PR) Fernanda Vaisman (RJ) Rafael Selbach Scheffel (RS) João Roberto Maciel Martins (SP) Wellington Santana da Silva Junior (MA)

MEDICAL TRAINING IN ENDOCRINOLOGY AND METABOLOGY – CFMEM

President	Milena Coelho Fernandes Caldato (PA) milenacaldato@hotmail.com
Members	Marcia Helena Soares Costa (RJ) Alexis Dourado Guedes (BA) Cristiane Bauermann Leitão (RS) Michelle Patrocínio Rocha (SP)

INTERNATIONAL – CI

President	César Luiz Boguszewski (PR) clbogus@uol.com.br
Members	Ruy Lyra da Silva Filho (PE) Ana Luiza Silva Maia (RS)

VALORIZATION OF NEW LEADERSHIPS CVNL

President	Tayane Muniz Fighera (RS) tayane.fighera@ufrgs.br
Members	Isabella Santiago de Melo Miranda (DF) Nathália Lisboa Rosa Almeida Gomes (MG) Victoria Rodrigues Granja Alencar (PE) Flora Ladeiro Craveiro (SP)

ENDOCRINOLOGY CAMPAIGNS – CCE

President	Mariana Guerra Paulino Guerra (ES) marianaguerr@yahoo.com.br
Members	Ana Augusta Motta Oliveira Valente (PA) Émerson Cestari Marino (PR) Rosalia do Prado Padovani (SP) Erika Bezerra Parente (SP) Priscilla Gil (RJ)

ENDOCRINOLOGY OF SPORT AND EXERCISE – CEEE

President	Clayton Luiz Dornelles Macedo (RS) clayton.macedo@uol.com.br
Vice-President:	Andréa Messias Britto Fioretti (SP)
Members	Cristiano Roberto Grimaldi Barcellos (SP) Rogério Friedman (RS) Cristina da Silva Schreiber de Oliveira (SC) Ricardo de Andrade Oliveira (RJ) Fulvio Clemo Santos Thomazelli (SC)

CONTINUOUS MEDICAL EDUCATION – CEMC

President	Rafael Selbach Scheffel (RS) rscheffe@gmail.com
Members	Sergio Setsuo Maeda (SP) Wellington Santana da Silva Junior (MA) Ciciliana Maila Zilio Rech (RS) Vania dos Santos Nunes Nogueira (SP) Mateus Dornelles Severo (RS)

TEMPORARY COMMISSION ON DIVERSITY, EQUITY AND INCLUSION - CDEI

President	Fernanda de Azevedo Corrêa (SP) fernandacorrea@alumni.usp.br
Members	Amanda de Araújo Laudier (RJ) Ana Pinheiro Machado Canton (SP) Jorge Eduardo da Silva Soares (RJ) Karen Faggioni de Marca Seidel (RJ) Luciana Mattos Barros Oliveira (BA) Tayane Muniz Fighera (RS)

TEMPORARY COMMISSION ON ENVIRONMENTAL ENDOCRINOLOGY – CEA

President	Elaine Maria Frade Costa (SP) elainefradecosta@gmail.com
Members	Maria Izabel Chiamolera (SP) Vivian Carole Moema Ellinger (RJ) Eveline Gadelha Pereira Fontenele (CE)

TEMPORARY COMMISSION ON DEFENSE OF PROFESSIONAL AFFAIRS – CDAP

President	Ana Karina de Melo Bezerra Sodré (CE) karenegreg@uol.com.br
Members	Lino Sieiro Netto (RJ) Adriano Namo Cury (SP) Adauto Versiani Ramos (MG)

Committees

XIX LATIN AMERICAN THYROID CONGRESS
20TH | 23RD APRIL 2023
CURITIBA | PR | BRAZIL

Congress President

Fabian Pitoia
XIX Latin American Thyroid Congress President

Local Organizing Committee

Cleo Otaviano Mesa Junior
Local Organizing Committee President

Fabiola Yukiko Miasaki

Gisah Amaral de Carvalho

Evandro Vasconcelos

Scientific Committee

Janete Maria Cerutti
Scientific Committee President

Alvaro Sanabria

Juan Pablo Nicola

Lorena Mosso

Laura Sterian Ward

Ana Amelia Hoff

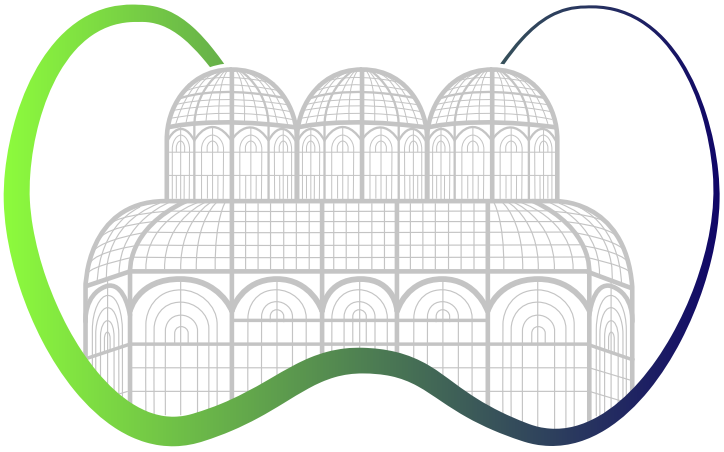
Gabriela Brenta

Fernando Jerkovich

Simone Wajner

Caroline Serrano Do Nascimento

Patricia de Fatima Teixeira



XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Scientific Program

• Thursday, April 20, 2023

Time	Activity	Room
• KOCHER CONFERENCE		
08:30 - 09:10	Kocher Conference **WELCOME AND OPENING** Chair: ERIVELTO MARTINHO VOLPI (Brazil) Chair: EVANDRO VASCONCELOS (Brazil) **LECTURE: THE QUALITY OF LIFE CHALLENGE IN THYROID SURGERY - WHAT TO EXPECT?** - Time: 30 min. Speaker: VICTORIA BANUCHI (United States)	Room 3
• THYROID IN THE ERA OF PRECISION MEDICINE		
08:50 - 09:00	THYROID IN THE ERA OF PRECISION MEDICINE **NEW CONCEPTS AND TECHNOLOGIES** **WELCOME AND OPENING** Chair: JANETE MARIA CERUTTI (Brazil) Chair: CAROLINE SERRANO DO NASCIMENTO (Brazil) Chair: JUAN PABLO NICOLA (Argentina)	Room 4
• COURSE THYROID ULTRASOUND MASTERCLASS		
09:00 - 12:00	COURSE **THYROID ULTRASOUND MASTERCLASS** **OPENING** - Time: 10 min. Chair: ROSALINDA YOSSIE ASATO DE CAMARGO (Brazil) Chair: EDUARDO KIYOSHI TOMIMORI (Brazil) **NODULE OR PSEUDONODULE IN THE THYROID GLAND** - Time: 20 min. Speaker: PABLO MORIKAWA (Paraguay) **CLINICALLY RELEVANT NODULES AND PARENCHYMAL CHANGES NOT CHARACTERIZED BY ULTRASONOGRAPHIC CLASSIFICATIONS** - Time: 20 min. Speaker: MARCO ANTONIO ALVAREZ ARRAZOLA (México) **SONOGRAPHIC-PATHOLOGIC CORRELATION FOR PUNCTATE ECHOGENIC FOCI IN PAPILLARY THYROID CARCINOMA** - Time: 20 min. Speaker: VICTOR HUGO NORIEGA RUIZ (Peru) **CLINICAL CASES** - Time: 110 min. Coordinator: ROSALINDA YOSSIE ASATO DE CAMARGO (Brazil) Speaker: FERNANDA NASCIMENTO FARO (Brazil) Speaker: NATÁLIA AMARAL CANÇADO (Brazil) Speaker: VANESSA CHERNIAUSKAS DE SOUZA MORIKAWA (Brazil) Panelist: JUAN PABLO DUEÑAS (Colombia) Panelist: GABRIELA BRENTA (Argentina) Panelist: PABLO MORIKAWA (Paraguay) Panelist: LUIS FELIPE SANCHEZ ARRIAGA (Mexico)	Room 2
• THYROID IN THE ERA OF PRECISION MEDICINE		
09:00 - 10:40	THYROID IN THE ERA OF PRECISION MEDICINE **SESSION: NEXT GENERATION SEQUENCING-BASED DIAGNOSIS OF THYROID DISEASES** Chair: JUAN PABLO NICOLA (Argentina) **WHAT ARE THE DIFFERENT NGS STRATEGIES TO IDENTIFY DISEASE-ASSOCIATED GENETIC VARIANTS?** - Time: 20 min. Speaker: GABRIEL COLOZZA GAMA (Brazil) **NGS AND COPY-NUMBER IN SCREENING OF HYPOTHYROIDISM AND RESISTANCE TO THYROID-HORMONE** - Time: 20 min. Speaker: JUAN PABLO NICOLA (Argentina) **WHEN TO USE NGS STRATEGY ON DIAGNOSIS AND PROGNOSIS OF A THYROID NODULE AND THERAPEUTIC DECISIONS?** - Time: 40 min. Speaker: YURI NIKIFOROV (United States) **Discussion** - Time: 20 min.	Room 4
• KOCHER CONFERENCE		
09:10 - 10:30	Kocher Conference **ROUND TABLE 1 – INITIAL APPROACH TO THYROID NODULES – NEW TRENDS** Chair: ALESSANDRO CURY OGATA (Brazil) Moderator: PRISCILA COSTA TINCANI (Brazil) Moderator: IDALIA MEDINA ARAUJO (Paraguay) **UPDATING THE USG RISK STRATIFICATION – ATA X TI-RADS X EU-TIRADS** - Time: 10 min. Speaker: ARTURO MADRID (Chile) **NEW USG TOOLS (MICROBUBBLES AND ELASTOGRAPHY) – ARE THEY USEFUL?** - Time: 10 min. Speaker: MARCO ANTONIO ALVAREZ ARRAZOLA (Mexico) **THE CENTIMETER CUT-OFF – STILL ON?** - Time: 10 min. Speaker: JOSEPH SCHARP (United States) **THE FNAB – MULTIPLE SHADES OF GRAY** - Time: 10 min. Speaker: FABIANO CALLEGARI (Brazil) **MOLECULAR MARKERS - HOW WORTHY?** - Time: 10 min. Speaker: HERNAN GONZALEZ (Chile) **Q&A** - Time: 10 min.	Room 3

10:50 - 12:00	Kocher Conference **ROUND TABLE 2 – ARE THE SURGEONS ASTRONAUTS?** Chair: LUIZ PAULO KOWALSKI (Brazil) Moderator: IVAN MARCELO AGRA (Brazil) Moderator: LUIZ ROBERTO MEDINA DOS SANTOS (Brazil) **REMOTE ACCESS TO THE NECK – A NEW TOOL OR A NEW PHILOSOPHY** - Time: 10 min. Speaker: VICTORIA BANUCHI (United States) **ENDOSCOPIC THYROIDECTOMY – ALWAYS OR NEVER?** **ALWAYS** - Time: 10 min. Speaker: ANTONIO AUGUSTO BERTELLI (Brazil) **NEVER** - Time: 10 min. Speaker: CARLOS SIMÓN DUQUE (Colombia) **CURRENT IONM STANDARDS** - Time: 10 min. Speaker: JOSEPH SCHARP (United States) **PARATHYROID PRESERVATION – WHEN FLUORESCENCE HELPS** - Time: 10 min. Speaker: ANA INES VOOGD (Argentina) **Q&A**	Room 3
• THYROID IN THE ERA OF PRECISION MEDICINE		
11:00 - 12:30	THYROID IN THE ERA OF PRECISION MEDICINE **SESSION: DECIPHERING HUMAN GENETIC VARIANTS AND APLICATIONS OF GENOME EDITING THECNOLOGY** Chair: CAROLINE SERRANO DO NASCIMENTO (Brazil) **HOW TO REPORT A GENETIC VARIANT? DATABASES THAT PROVIDE VARIANT-LEVEL INFORMATION AND PHENOTYPIC FEATURES** - Time: 30 min. Speaker: NARA LYGIA DE MACENA SOBREIRA (United States) **CRISPR GENOME EDITING: OVERVIEW OF METHODOLOGIES AND PERSPECTIVES IN THYROID CARCINOMAS** - Time: 30 min. Speaker: CESAR SEIGI FUZIWARA (Brazil) **Q&A** - Time: 30 min.	Room 4
• COURSE THYROID ULTRASOUND MASTERCLASS		
13:00 - 16:00	COURSE **THYROID ULTRASOUND MASTERCLASS** **VARIATION IN ULTRASONOGRAPHY ASSESSMENT OF THYROID NODULES** - Time: 20 min. Speaker: ANA IRIS RAMÍREZ BENÍTEZ (Paraguay) **ULTRASONOGRAPHIC APPEARANCE OF AGRESSIVE VARIANTS OF PAPILLARY THYROID CARCINOMA** - Time: 20 min. Speaker: FERNANDO MUNIZAGA (Chile) **SONOGRAPHIC CRITERIA FOR ACTIVE SURVEILLANCE OF PAPILLARY THYROID MICROCARCINOMA** - Time: 20 min. Speaker: DEBORA LUCIA SEGURO DANILOVIC (Brazil) **CLINICAL CASES** - Time: 120 min. Coordinator: EDUARDO KIYOSHI TOMIMORI (Brazil) Speaker: FERNANDA NASCIMENTO FARO (Brazil) Speaker: NATÁLIA AMARAL CANÇADO (Brazil) Speaker: VANESSA CHERNIAUSKAS DE SOUZA MORIKAWA (Brazil) Panelist: MARCOS ABALOVICH (Argentina) Panelist: ROSA NOEMI VEGA MEDINA (Paraguay) Panelist: CELSO FRIGUGLIETTI (Brazil) Panelist: BERNARDO LOPES CANÇADO FONSECA (Brazil) **CLOSURE**	Room 2
• KOCHER CONFERENCE		
13:15 - 14:15	Kocher Conference **ROUND TABLE 3 - MINIMALLY INVASIVE TREATMENTS - A NEW ERA OR JUST TRENDING** Chair: GABRIEL DAMIANO (Argentina) Moderator: CRISTHIAN RAMIRO GARCIA CEVALHOS (Ecuador) Moderator: LEONARDO RANGEL (Brazil) **THERMAL ABLATION FOR BENIGN NODULES – IS THE SKY THE LIMIT?** **PROBABLY** - Time: 10 min. Speaker: JOSE HIGINO STECK (Brazil) **I PREFER SUGERY** - Time: 10 min. Speaker: CELSO FRIGUGLIETTI (Brazil) **THERMAL ABLATION IN MALIGNANCIES – SIN OR VIRTUE?** **FIRST TREATMENT** - Time: 10 min. Speaker: JUAN PABLO DUEÑAS (Colombia) **RECURRENCES** - Time: 10 min. Speaker: ERIVELTO MARTINHO VOLPI (Brazil) **Q&A** - Time: 10 min.	Room 3

• THYROID IN THE ERA OF PRECISION MEDICINE		
13:30 - 15:30	THYROID IN THE ERA OF PRECISION MEDICINE **SESSION: THE ARENA OF LIQUID BIOPSY AND SINGLE CELL: CONCEPTS AND APPLICATIONS** Chair: JANETE MARIA CERUTTI (Brazil) **MULTI-ANALYTE ANALYSES FOR LIQUID BIOPSY: OVERVIEW OF CONCEPTS, AND TECHNIQUES TO DETECT AND ANALYZE CIRCULATING TUMOUR CELLS (CTCS), CELL FREE TUMOR DNA (cfDNA), CELL FREE TUMOUR RNA (cfRNA) AND PROTEINS:** **ORIGIN AND METHODS FOR ANALYSIS** - Time: 30 min. Speaker: LUDMILLA T.D. CHINEN (Brazil) **IS LIQUID BIOPSY APPLICABLE TO THYROID?** - Time: 30 min. Speaker: CAROLINA FERRAZ (Brazil) **ADVANCING PRECISION MEDICINE THROUGHT SINGLE-CELL PROFILING: APPROACHES AND APLICATIONS** - Time: 30 min. Speaker: ROBSON FRANCISCO CARVALHO (Brazil) **Q&A** - Time: 30 min. **CLOSING REMARKS**	Room 4
• KOCHER CONFERENCE		
14:40 - 15:10	Kocher Conference **LECTURE GRAVES DISEASE – FROM THE SURGEONS STANDPOINT** - Time: 30 min. Speaker: MICHAEL SINGER (United States)	Room 3
15:10 - 15:50	Kocher Conference **ROUND TABLE 4 – CONSERVATIVE SURGERY FOR WDTC – WHAT'S GOING ON** Chair: GUSTAVO PHILIPPI DE LOS SANTOS (Brazil) Moderator: FELIPE CAPDEVILLE (Chile) Moderator: EMERSON FAVERO (Brazil) **GOODBYE** - Time: 10 min. Speaker: SANTIAGO ALBERTO ZUND (Argentina) **SEE YOU SOON** - Time: 10 min. Speaker: DANIEL ANDRES RAPPOPORT WURGAFT (Chile) **FOLLOW-UP ISSUES** - Time: 10 min. Speaker: MICHAEL SINGER (United States) **Q&A** - Time: 10 min.	Room 3
15:50 - 16:55	Kocher Conference **ROUND TABLE 5 - DTC – A NEW SURGICAL PERSPECTIVE** Chair: FERNANDO WALDER (Brazil) Moderator: GENIVAL BARBOSA DE CARVALHO (Brazil) **ACTIVE SURVEILLANCE AS A FIRST STEP** - Time: 10 min. Speaker: ALVARO SANABRIA (Colombia) **RESCUE SURGERY FOR ACTIVE SURVEILLANCE** - Time: 10 min. Speaker: EVANDRO VASCONCELOS (Brazil) **HOW MUCH SURGERY IS NEEDED TO THE LYMPH NODES?** - Time: 10 min. Speaker: ANDRE IWATA DE CARVALHO (Brazil) **BALANCING MORBIDITY AND RISK OF RECURRENCE** - Time: 10 min. Speaker: SIMONE DUTENHEFNER (Brazil) **Q&A** - Time: 10 min. **CLOSING REMARKS**	Room 3
• KOCHER CONFERENCE		
17:00 - 18:00	**YEAR IN THYROIDOLOGY** **CLINICAL YEAR - HIGHLIGHTS** - Time: 20 min. Speaker: VERONICA ILERA (Argentina) **BASIC YEAR - HIGHLIGHTS** - Time: 20 min. Speaker: CLAUDIA GABRIELA PELLIZAS (Argentina) **SURGICAL YEAR - HIGHLIGHTS** - Time: 20 min. Speaker: LUIZ PAULO KOWALSKI (Brazil)	Room 1
18:00 - 19:00	**LATS SENIOR PRIZE 2023** **INTRODUCTION** ANA MARIA MASINI-REPISO (Argentina) **RECIPIENT** CLAUDIA GABRIELA PELLIZAS (Argentina) **CONFERENCE:** **MY JOURNEY ACROSS THYROID HORMONE ACTION: FOCUS ON IMMUNITY**	Room 1
19:00 - 19:30	Opening Ceremony **OPENING CEREMONY** **LATS PRESIDENT** FABIAN PITOIA (Argentina) **SCIENTIFIC COMMITTEE PRESIDENT** JANETE MARIA CERUTTI (Brazil) **LOCAL ORGANIZING COMMITTEE PRESIDENT** CLEO OTAVIANO MESA JUNIOR (Brazil) **LATS SECRETARY** CLAUDIA GABRIELA PELLIZAS (Argentina)	Room 1
19:30 - 20:30	**Opening Cocktail**	Exhibition area

• Friday, April 21, 2023

Time	Activity	Room
08:30 - 09:30	Conference **ACTIVE SURVEILLANCE OF SMALL LOW RISK PAPILLARY THYROID CARCINOMA** Chair: FABIAN PITOIA (Argentina) Chair: LAURA STERIAN WARD (Brazil) Time: 45 min. Speaker: ANNA M. SAWKA (Canada) **Q&A** - Time: 15 min.	Room 1
09:30 - 10:30	**YOUNG INVESTIGATOR AWARDS - CLINICAL** **ID 117030 - CARDIOMETABOLIC RISK AND INSULIN RESISTANCE IN PATIENTS WITH RESISTANCE TO THYROID HORMONE B** - Time: 10 min. ***Presenter: Pryscilla Moreira de Souza Domingues Hajj*** **Discussion** - Time: 5 min. **ID 117082 - CHARACTERIZATION OF MIR-146B AS PROGNOSTIC BIOMARKER TO PREDICT CLINICAL-PATHOLOGICAL PHENOTYPES ASSOCIATED WITH AGGRESSIVE BEHAVIORS IN THYROID DIFFERENTIATED CARCINOMAS FROM PREOPERATIVE FNA CYTOLOGY** - Time: 10 min. ***Presenter: Marcos Tadeu dos Santos*** **Discussion** - Time: 5 min. **ID 117065 - HIGH ACCURACY OBSERVED IN PRELIMINARY PERFORMANCE RESULTS OF THE VALIDATION OF A MICRORNA AND DNA-BASED THYROID MOLECULAR CLASSIFIER IN A PEDIATRIC COHORT** - Time: 10 min. ***Presenter: Marcos Tadeu dos Santos*** **Discussion** - Time: 5 min. **ID 117027 - IDENTIFICATION OF CIRCULATING MICRORNAS OF POTENTIAL USE IN THE DIAGNOSIS OF THYROID CANCER** - Time: 10 min. ***Presenter: Karina Colombera Peres*** **Discussion** - Time: 5 min.	Room 1
09:30 - 10:30	**YOUNG INVESTIGATOR AWARDS - BASIC** **ID 117164 - POLYCHLORINATED BIPHENYLS STIMULATE THYROID GENE TRANSCRIPTION THROUGH EPIGENETIC MECHANISMS AND ACTIVATION OF THE CREB SIGNALING PATHWAY** - Time: 10 min. ***Presenter: Vinicius Gonçalves Rodrigues*** **Discussion** - Time: 5 min. **ID 117151 - BISPHENOL A EXPOSURE DURING THE INTRAUTERINE PERIOD DISRUPTS THE PITUITARY-THYROID AXIS OF THE OFFSPRING RATS DURING ADULTHOOD** - Time: 10 min. ***Presenter: Guilherme Henrique*** **Discussion** - Time: 5 min. **ID 117066 - INHIBITION OF EZH2 METHYLTRANSFERASE ACTIVITY INDUCES AN ANTITUMORAL EFFECT AND IMPROVES CELL DIFFERENTIATION IN ANAPLASTIC THYROID CANCER** - Time: 10 min. ***Presenter: Diego Claro de Mello*** **Discussion** - Time: 5 min. **ID 117157 - POLYCHLORINATED BIPHENYLS EXPOSURE DISRUPTS THE PITUITARY-THYROID AXIS OF F1 OFFSPRING ANIMALS DURING ADULTHOOD** - Time: 10 min. ***Presenter: Evelyn Franciny Cardoso Tavares*** **Discussion** - Time: 5 min	Room 2
10:30 - 11:00	Scientific Arena **Eli Lilly - RESTRITO PARA PRESCRITOR E DISPENSADOR DE MEDICAMENTO***	Scientific Arena
11:00 - 12:30	Hot Topics **WHAT ARE THE CONCERNS ABOUT ADVERSE EFFECTS OF ENDOCRINE DISRUPTORS IN THE THYROID?** Chair: HELTON ESTRELA RAMOS (Brazil) **20 YEARS AFTER THE 9/11: IT MAY NOT ALL BE OVERDIAGNOSIS IN DETECTION OF CANCER INCREASE INCIDENCE** - Time: 20 min. Speaker: MAAIKE VAN GERWEN (United States) **COULD PESTICIDES BE ASSOCIATED WITH INCREASE INCIDENCE OF THYROID DISEASE WORLDWIDE?** - Time: 20 min. Speaker: RENATA MARINO ROMANO (Brazil) **ENDOCRINE DISRUPTORS EXPOSURE DURING PREGNANCY: WHAT IS THE DEAL WITH THE THYROID AXIS?** - Time: 20 min. Speaker: MARIA IZABEL CHIAMOLERA (Brazil) **Q&A**	Room 1

Time	Activity	Room
11:00 - 12:30	Symposium **IN THE ERA OF MINIMALLY INVASIVE APPROACH, WHO WILL BENEFIT?** Chair: CLAUDIO R. CERNEA (Brazil) Chair: ALVARO SANABRIA (Colombia) **RADIOFREQUENCY ABLATION IN THE MANAGEMENT OF THYROID BENING NODULE, WHEN?** - Time: 15 min. Speaker: ERIVELTO MARTINHO VOLPI (Brazil) **RADIOFREQUENCY IN MALIGNANT NODULE AND RECURRENCES: IS THERE AN OPTIMAL AGE AND TUMOR SIZE?** - Time: 15 min. Speaker: LEONARDO RANGEL (Brazil) **ROBOTIC SURGERY: IS PATIENT SELECTION A PARAMOUNT IN THIS PROCEDURE?** - Time: 15 min. Speaker: VICTORIA BANUCHI (United States) **FLUORESCENCE HELPS TO DETECT PARATHYROIDS DURING THYROIDECTOMY?** - Time: 15 min. Speaker: MARCO AURÉLIO VAMONDES KULCSAR (Brazil) **Q&A** - Time: 30 min.	Room 2
11:00 - 12:30	Symposium **WHAT ARE THE LATEST ADVANCES IN THE DIAGNOSIS AND TREATMENT OF MEDULLARY THYROID CARCINOMA?** Chair: NELSON WOHLLK (Chile) Chair: RUI MONTEIRO DE BARROS MACIEL (Brazil) **UPDATE ON CMT PROGNOSTIC FACTORS: HOW TO IDENTIFY AN AGGRESSIVE TUMOR WHICH WILL EVENTUALLY REQUIRE SYSTEMIC TREATMENT?** - Time: 20 min. Speaker: ANA AMELIA HOFF (Brazil) **SYSTEMIC THERAPIES FOR METASTATIC MTC: SEVERAL GOOD OPTIONS, WHICH ONE TO CHOOSE?** - Time: 20 min. Speaker: ANA LUIZA MAIA (Brazil) **AN UPDATE ON SURGICAL TREATMENT OF CMT: DO PREOPERATIVE CALCITONIN LEVELS MATTER?** - Time: 20 min. Speaker: FELIPE A. BRASILEIRO VANDERLEI (Brazil) **ORAL COMUNICATION: ID 117061 - ROLE OF RET POLYMORPHISMS IN MEN2A-ASSOCIATED HYPERPARATHYROIDISM** - Time: 10 min. ***Presenter: Nathalie Lobo de Figueiredo Feitosa*** **Q&A** - Time: 20 min.	Room 3
11:00 - 12:30	Symposium **THYROID HORMONE ACTION IN A TISSUE-DEPENDENT MANNER** Chair: CLAUDIA GABRIELA PELLIZAS (Argentina) Chair: CARMEN CABANELAS PAZOS DE MOURA (Brazil) **THYROID HORMONE SIGNALING IN TUMOR INFILTRATING MACROHAGES** - Time: 20 min. Speaker: LAURA FOZZATTI (Argentina) **THYROID HORMONE ACTION IN IMMUNE CELLS** - Time: 20 min. Speaker: MARIA DEL MAR MONTESINOS (Argentina) **THYROID HORMONE ACTION ON METABOLISM - POTENTIAL THERAPEUTIC APPLICATIONS** - Time: 20 min. Speaker: MARIA TEREZA NUNES (Brazil) **Q&A** - Time: 30 min.	Room 4
12:30 - 13:30	**Satellite Symposium - Merck**	Room 1
12:30 - 13:30	**Satellite Symposium - Horizon Therapeutics - RESTRICTED FOR PRESCRIBERS**	Room 3
13:30 - 15:00	Panel Discussion **THE 5th WHO NOMENCLATURE OF THYROID NEOPLASM** Chair: GISAH AMARAL DE CARVALHO (Brazil) Chair: ANA CAROLINA PANIZA (Brazil) **A SUMMARY OF THE 2022 WHO CLASSIFICATION OF THYROID NEOPLASM. NEW CATEGORIES? WHY?** - Time: 20 min. Speaker: FABIANO CALLEGARI (Brazil) **HOW TO INCORPORATE THE WHO CHANGES IN THE CLINICAL PRACTICE?** - Time: 20 min. Speaker: ROSA PAULA MELLO BISCOLLA (Brazil) **THE MOLECULAR SIGNATURE OF FOLLICULAR-DERIVED TUMORS. DOES IT CORRELATE WITH HISTOLOGICAL SUBTYPES?** - Time: 20 min. Speaker: MATTHEW D. RINGEL (United States) **Q&A** - Time: 30 min.	Room 1
13:30 - 15:00	Symposium **THYROID HORMONE SIGNALING** Chair: CLAUDIA RIEDEL (Chile) Chair: MIRIAM OLIVEIRA RIBEIRO (Brazil) **WHAT IS NEW IN THYROID HORMONE SIGNALING?** - Time: 20 min. Speaker: ANTONIO C. BIANCO (United States) **THYROID HORMONE ACTION IN PERIPHERAL TISSUES** - Time: 20 min. Speaker: MARINA MALTA LETRO KIZYS (Brazil) **SPECTRUM OF DISEASES AFFECTED BY THYROID HORMONE RESISTANCE** - Time: 20 min. Speaker: CÉLIA REGINA NOGUEIRA (Brazil) **Q&A** - Time: 30 min.	Room 2

Time	Activity	Room
13:30 - 15:00	Symposium **IMPACT OF COVID-19 ON THE THYROID** Chair: ALICIA TERESA GAUNA (Argentina) Chair: DANILO GLAUCO PEREIRA VILLAGELIN NETO (Brazil) **EFFECT OF COVID-19 PANDEMIC ON THE DIAGNOSIS AND TREATMENT OF THYROID CANCER** - Time: 20 min. Speaker: JOSE MIGUEL DORA (Brazil) **THYROID DYSFUNCION AND COVID-19: WHAT DO WE KNOW SO FAR?** - Time: 20 min. Speaker: HELTON ESTRELA RAMOS (Brazil) **ARE THYROID DISORDERS ASSOCIATED WITH SARS-COV-2 VACCINATION?** - Time: 20 min. Speaker: LAURA CAROLINA DELFINO (Argentina) **Q&A** - Time: 30 min.	Room 3
15:00 - 16:00	**YOUNG INVESTIGATOR AWARDS - CLINICAL AND BASIC** **ID 117142 - IDENTIFICATION OF NOVEL PREDISPOSITION GENES TO THE DEVELOPMENT OF NON-SYNDROMIC FAMILIAL NON-MEDULLARY THYROID CANCER BY EXOME DATA ANALYSIS** - Time: 10 min. ***Presenter: Isabela Nogueira Nunes*** **Discussion** - Time: 5 min. **ID 117063 - THE TRANSCRIPTIONAL CONTROL OF EZH2 HISTONE METHYLTRANSFERASE IN AGGRESSIVE THYROID CANCER** - Time: 10 min. ***Presenter: Marcella Maringolo Cristovão*** **Discussion** - Time: 5 min. **ID 117090 - THE IMPACT OF AGE ON THE MALIGNANCY RATE OF THYROID NODULES CLASSIFIED ACCORDING TO THE ACR-TIRADS** - Time: 10 min. ***Presenter: Leonardo Barbi Walter*** **Discussion** - Time: 5 min. **ID 117145 - AGK-BRAF ACTIVATES THE MAPK AND PI3K/AKT SIGNALING PATHWAYS, DISRUPTS NIS ACTIVITY AND INDUCES GENOMIC INSTABILITY IN NORMAL THYROID CELLS** - Time: 10 min. ***Presenter: Luiza de Mello Oliveira Sisdelli*** **Discussion** - Time: 5 min.	Room 1
16:30 - 18:00	Symposium **HIGH-RISK ADVANCED THYROID CARCINOMA: IS IODINE REDIFFERENTIATION A REALITY?** Chair: ANA LUIZA MAIA (Brazil) Chair: FABIAN PITOIA (Argentina) **THE RATIONALE FOR THYROID REDIFFERENTIATION THERAPY** - Time: 20 min. Speaker: NANCY CARRASCO (United States) **A SUMMARY OF THE AMERICAN AND EUROPEAN EXPERIENCE OF REDIFFERENTIATION THERAPY FOR RADIOIODINE-REFRACTORY CANCER** - Time: 20 min. Speaker: INÉS CALIFANO (Argentina) **WHAT IS THE BEST TIME TO TREAT, THE BEST PROTOCOL TO USE AND THE BEST CANDIDATE FOR RE-DIFFERENTIATION THERAPY?** - Time: 20 min. Speaker: FERNANDA VAISMAN (Brazil) **Q&A** - Time: 30 min	Room 1
16:30 - 18:00	Symposium **ARE THYROID AUTOANTIBODIES THE CAUSE OF THYROIDAL AND NON-THYROIDAL DISEASES?** Chair: SUEMI MARUI (Brazil) Chair: MONICA SUSANA SALA (Argentina) **IS GENDER A RISK FACTOR FOR THYROID AUTOIMMUNE DISEASES?** - Time: 20 min Speaker: NATASSIA ELENA BUFALO (Brazil) **WHAT ARE THE OTHER RISK FACTORS FOR THYROID AUTOIMMUNE DISEASES?** - Time: 20 min Speaker: ALEJANDRA LANAS (Chile) **ARE THYROID AUTOANTIBODIES A RISK FACTOR TO MORTALITY?** - Time: 20 min Speaker: ISABELA J BENSEÑOR (Brazil) **Q&A** - Time: 30 min	Room 2
16:30 - 18:00	Symposium **REDOX STATUS AND THYROID FUNCTION** Chair: CAROLINE SERRANO DO NASCIMENTO (Brazil) Chair: LAURA FOZZATTI (Argentina) **NOX4 IN THYROID PHYSIOLOGY AND PATHOLOGY** - Time: 20 min. Speaker: DENISE PIRES DE CARVALHO (Brazil) **IODOLIPIDS, ROS GENERATION AND THYROID FUNCTION** - Time: 20 min. Speaker: LISA THOMASZ (Argentina) **ENDOCRINE -DISRUPTING CHEMICAL AND THYROID REDOX STATUS** - Time: 20 min. Speaker: LEANDRO MIRANDA-ALVES (Brazil) **Q&A** - Time: 30 min.	Room 3

Time	Activity	Room
16:30 - 18:00	Symposium **THYROID DYSFUNCTION** Chair: ILEANA G. S RUBIO (Brazil) Chair: NICOLE LUSTIG FRANCO (Chile) **THYROID DYSFUNCTION AND METABOLIC SYNDROME** - Time: 20 min. Speaker: CARMEN CABANELAS PAZOS DE MOURA (Brazil) **FETAL AND CHILDREN NEURODEVELOPMENT: TO WHICH EXTENT IS THYROID RELEVANT?** - Time: 20 min. Speaker: MIRIAM OLIVEIRA RIBEIRO (Brazil) **THYROID DYSFUNCTION AS A RISK FOR RECURRENT MISCARRIAGE** - Time: 20 min. Speaker: GRACIELA ALCARAZ (Argentina) **Q&A** - Time: 30 min	Room 4
18:00 - 19:00	Conference **AMERICAN THYROID ASSOCIATION CENTENNIAL CELEBRATION: FEATURE PAPERS FROM THE EDITOR'S CHOICE** Chair: MARIO VAISMAN (Brazil) Chair: JOSÉ AUGUSTO SGARBI (Brazil) **THYROID** Speaker: ANNA M. SAWKA (Canada) **CLINICAL THYROIDOLOGY** Speaker: ANGELA M. LEUNG (United States) **MEET THE EDITORS OF THE AMERICAN THYROID ASSOCIATION-MAL-JOURNAULS** Speaker: CATHERINE SINCLAIR (Australia) **Q&A** - Time: 15 min.	Room 1

• Saturday, April 22, 2023

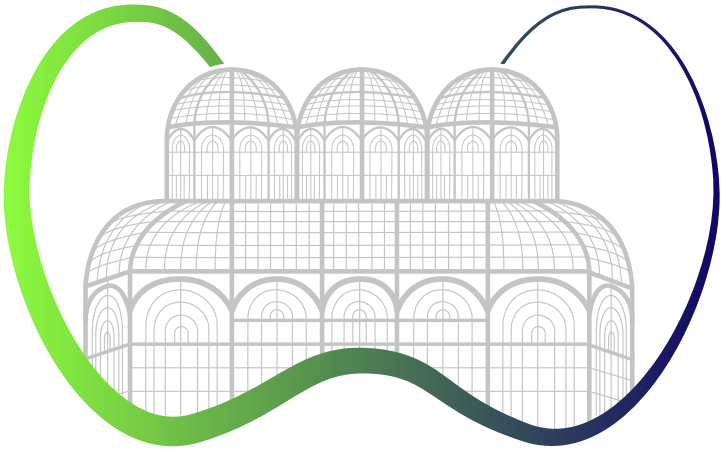
Time	Activity	Room
08:30 - 09:30	Conference **PROGRESSION OF METASTATIC THYROID CARCINOMA: NEW CONCEPTS AND CLINICAL IMPLICATIONS** Chair: ANA AMELIA HOFF (Brazil) Chair: GABRIELA BRENTA (Argentina) Time: 45 min. Speaker: MATTHEW D. RINGEL (United States) **Q&A** - Time: 15 min.	Room 1
09:30 - 11:00	Hot Topics **LOW RISK THYROID CARCINOMA** Chair: CAROLINA FERRAZ (Brazil) Chair: FERNANDO JERKOVICH (Argentina) **IS LOBECTOMY ENOUGH FOR BETHESDA V THYROID NODULE?** - Time: 20 min. Speaker: JORGELINA GUERRA (Argentina) **MANAGEMENT OF THYROID CANCER AFTER LOBECTOMY** - Time: 20 min. Speaker: DENISE P MOMESSO (Brazil) **QUALITY OF LIFE IN LOW RISK DIFFERENTIATED THYROID CANCER: CONSIDERATIONS ON THE EXTENT OF SURGERY** - Time: 20 min. Speaker: ANNA M. SAWKA (Canada) **ORAL COMUNICATION: ID 117047 - ACTIVE SURVEILLANCE IS A FEASIBLE AND SAFE STRATEGY IN SELECTED PATIENTS WITH PAPILLARY THYROID CANCER AND LOCOREGIONAL STRUCTURAL DISEASE** - Time: 10 min. ***Presenter: Jose Miguel Dominguez*** **Q&A** - Time: 20 min.	Room 1
09:30 - 11:00	Symposium **HYPERTHYROIDISM IS STILL AND UNSETTLED MATTER** Chair: CLEO OTAVIANO MESA JUNIOR (Brazil) Chair: GLÁUCIA MARIA FERREIRA DA SILVA MAZETO (Brazil) **SUBCLINICAL HYPERTHYROIDISM: WHO, WHY AND HOW TO TREAT** - Time: 20 min. Speaker: JOSÉ AUGUSTO SGARBI (Brazil) **HYPERTHYROIDISM - THE SURGEONS VIEW** - Time: 20 min. Speaker: MICHAEL SINGER (United States) **OVERT HYPERTHYROIDSM TREATMENT OPTIONS: IS THERE ANY ADVANTAGE OF LONG TERM ANTITHYROID DRUGS COMPARED TO DEFINITE THERAPY?** - Time: 20 min. Speaker: DANILO GLAUCO PEREIRA VILLAGELIN NETO (Brazil) **Q&A** - Time: 30 min.	Room 2

Time	Activity	Room
09:30 - 11:00	Symposium **WHY IS DEIODINATION IMPORTANT?** Chair: SIMONE WAJNER (Brazil) Chair: FABIOLA YUKIKO MIASAKI (Brazil) **DEIODINATION AND DISEASES - WHERE ARE WE AND WHY DOES IT MATTER** - Time: 20 min. Speaker: JOSI VIDART (Brazil) **THE ROLE OF IODOTHYRONINE DEIODINASES IN HUMAN NEOPLASIAS** - Time: 20 min. Speaker: IURI GOEMANN (Brazil) **DEREGULATION OF THE EXPRESSION AND ACTIVITY OF DEIODINASES DURING GESTACIONAL DIABETES** - Time: 20 min. Speaker: ENRIQUE GUZMAN (Chile) **Q&A –** Time: 30 min.	Room 3
09:30 - 11:00	**YOUNG INVESTIGATOR AWARDS - CLINICAL AND BASIC** **POSTER PRESENTATION Highlighted Posters from Basic (5) and Clinical (5) areas** - Time: 5 min. ***Presenter: Luciana Audi de Castro Neves*** **QUESTION** - Time: 3 min. **117133 - CLINICAL AND MOLECULAR ANALYSIS OF A MEN2A KINDRED HABORING THE RARE RET VARIANT P. SER904PHE** - Time: 5 min. ***Presenter: Jessica Oliboni Scapineli*** **QUESTION** - Time: 3 min. **ID 117128 - FUNCTIONAL ANALYSIS OF CONGENITAL HYPOTHYROIDISM-ASSOCIATED SLC5A5 GENE VARIANTS** - Time: 5 min. ***Presenter: Juan Pablo Nicola*** **QUESTION** - Time: 3 min. **ID 117122 - ASSOCIATION BETWEEN PROTEINURIA AND THYROID FUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGES 3 AND 4** - Time: 5 min. ***Presenter: Karina Schiavoni Scandelai Cardoso dos Reis*** **QUESTION** - Time: 3 min. **ID 117102 - ECTOPIC EXPRESSION OF MIR-200C CONTROLS ANAPLASTIC THYROID CANCER (ATC) DIFFERENTIATION AND AGGRESSIVENESS** - Time: 5 min. ***Presenter: Edna T. Kimura*** **QUESTION** - Time: 3 min. **ID 117092 - WHOLE-BODY SCAN (WBS) EVALUATION BEFORE 131 IODINE TREATMENT MIGHT HAVE LIMITED USE FOR DETECTION OF DISTANT METASTASIS IN PEDIATRIC DIFFERENTIATED THYROID CARCINOMA** - Time: 5 min. ***Presenter: Paulo Alonso G Alves Junior*** **QUESTION** - Time: 3 min. **ID 117087 - SPHINGOSINE KINASE 1 IS INVOLVED IN TRIIODOTHYRONINE EFFECTS IN MURINE DENDRITIC CELLS AND THE DRIVEN ADAPTIVE IMMUNITY** - Time: 5 min. ***Presenter: Claudia Gabriela Pellizas*** **QUESTION** - Time: 3 min. **ID 117080 - THE ROLE OF MICRORNAS IN THE REGULATION OF TERT EXPRESSION IN THYROID CANCER** - Time: 5 min. ***Presenter: Cesar Seigi Fuziwara*** **QUESTION** - Time: 3 min. **ID 117055 - IDENTIFYING NUCLEAR GROOVES IN WHOLE-SLIDE IMAGES OF PAPILLARY THYROID CARCINOMA CYTOLOGY IN DIFF-QUIK STAINING USING ARTIFICIAL INTELLIGENCE** - Time: 5 min. ***Presenter: Pedro Resende Ferreira Rende*** **QUESTION** - Time: 3 min. **ID 117069 - MOLECULAR ANALYSIS OF MIR146B PROMOTER ACTIVATION IN THYROID CANCER** - Time: 5 min. ***Presenter: Cesar Seigi Fuziwara*** **QUESTION** - Time: 3 min.	Room 4
11:00 - 11:30	Scientific Arena **Abbott**	Scientific Arena
11:30 - 12:20	Hot Topics **ENDOCRINE DISRUPTORS AND HEAVY METALS IN THYROID CANCER** Chair: DENISE PIRES DE CARVALHO (Brazil) Chair: MARIA TEREZA NUNES (Brazil) Time: 35 min. Speaker: MAAIKE VAN GERWEN (United States) **Q&A** - Time: 15 min.	Room 2
11:30 - 12:20	Hot Topics **SUBCLINICAL HYPOTHYROIDISM** Chair: JOSE MIGUEL DORA (Brazil) Chair: RUI MONTEIRO DE BARROS MACIEL (Brazil) Time: 35 min. Speaker: GABRIELA BRENTA (Argentina) **Q&A** - Time: 15 min.	Room 1

Time	Activity	Room
12:30 - 13:30	**Satellite Symposium - Eli Lily**	Room 1
12:30 - 13:30	**Satellite Symposium - Grupo Fleury**	Room 2
14:30 - 15:20	Meet the Professor **THYROID CANCER OF INTERMEDIATE RISK** **DEFINITION, GENETIC CHARACTERIZATION IN THE RISK STRATIFICATION AND UTILITY OF RAI TREATMENT** Speaker: CAMILA MOSCI (Brazil)	Room 1
14:30 - 15:20	Meet the Professor **PEDIATRIC THYROID CARCINOMA IN THE ERA OF PRECISION MEDICINE** Speaker: MARIA ISABEL CUNHA VIEIRA CORDIOLI (Brazil) Speaker: FERNANDA VAISMAN (Brazil)	Room 2
14:30 - 15:20	Meet the Professor **microRNA IN THYROID DEVELOPMENT AND CANCER** Speaker: EDNA T KIMURA (Brazil) Speaker: CESAR SEIGI FUZIWARA (Brazil)	Room 3
15:30 - 17:00	Hot Topics **ONCOCYTIC THYROID CARCINOMA** Chair: JANETE MARIA CERUTTI (Brazil) Chair: LAURA STERIAN WARD (Brazil) **WHAT IS NEW FROM PATHOLOGICAL PERSPECTIVES?** - Time: 20 min. Speaker: ICLEIA SIQUEIRA BARRETO (Brazil) **WHAT IS NEW FROM THE GENETIC PERSPECTIVES AND TREATMENT IN ONCOCYTIC THYROID CANCER?** - Time: 20 min. Speaker: DEBORA LUCIA SEGURO DANILOVIC (Brazil) **IMMUNILOGICAL BASIS FOR IMMUNOTHERAPY: DOES IT WORK IN THYROID CANCER?** - Time: 20 min. Speaker: LUCAS LEITE CUNHA (Brazil) **Q&A** - Time: 30 min.	Room 1
15:30 - 17:00	Symposium **WHAT IS THE RELASHIONSHIP BETWEEN MICRONUTRIENTS THAT ARE VITAL TO HEALTHY DEVELOPMENT AND THYROID DYSFUNCTION?** Chair: ADRIANA REYES (Argentina) Chair: ISABELA J BENSEÑOR (Brazil) **IODINE EXCESS OR DEFICIENCY ON THYROID FUNCTION DURING PREGNANCY AND BREASTFEEDING** - Time: 25 min. Speaker: CLAUDIA RIEDEL (Chile) **EPIGENETIC ASPECTS OF THYROID PROGRAMMING BY IODINE** - Time: 25 min. Speaker: CAROLINE SERRANO DO NASCIMENTO (Brazil) **SELENIUM AND GRAVES DISEASE** - Time: 10 min. Speaker: MARCOS ABALOVICH (Argentina) **Q&A** - Time: 30 min.	Room 2
15:30 - 17:00	Symposium **CONGENITAL HYPOTHYROIDISM, WHAT'S NEW IN GENETIC SCREENING, ASSOCIATION WITH HEARING DISEASES AND TREATMENT?** Chair: MARINA MALTA LETRO KIZYS (Brazil) Chair: ANA MARIA MASINI-REPISO (Argentina) **IS GENETIC SCREENING HELPING THE DIAGNOSIS OF CONGENITAL HYPOTHYROIDISM?** - Time: 20 min. Speaker: JUAN PABLO NICOLA (Argentina) **AN OVERVIEW OF THE TREATMENT OF CONGENITAL HYPOTHYROIDISM** - Time: 20 min. Speaker: LEA MARIA ZANINI MACIEL (SP) **IS CONGENITAL HYPOTHYROIDISM IS A RISK FACTOR FOR HEARING AND VOICE-SPEECH DISORDERS?** - Time: 20 min. Speaker: SUZANA NESI FRANCA (Brazil) **Q&A** - Time: 30 min.	Room 3
17:00 - 18:00	Conference **THE TALE OF THE SODIUM/IODIDE SYMPORTER(NIS): FROM CLONING TO STRUCTURE** Chair: ANA MARIA MASINI-REPISO (Argentina) Chair: DENISE PIRES DE CARVALHO (Brazil) Time: 45 min. Speaker: NANCY CARRASCO (United States) Time: 15 min.	Room 1
18:00 - 20:00	**LATS General Assembly**	Room 1

• Sunday, April 23, 2023

Time	Activity	Room
08:30 - 09:30	Conference **THYROID DISEASE AND PREGNANCY: A 2023 UPDATE** Chair: PATRICIA DE FATIMA TEIXEIRA (Brazil) Chair: GRACIELA ALCARAZ (Argentina) Time: 45 min. Speaker: ANGELA M. LEUNG (United States) **Q&A** - Time: 15 min.	Room 1
09:30 - 11:00	Panel Discussion **FROM A SUSPICIOUS NODULE TO SURGERY** Chair: HERNAN GONZALEZ (Chile) Chair: LENARA GOLBERT (Brazil) **ULTRASOUND RISK STRATIFICATIONS IS KEY TO NODULAR IDENTIFICATION AND FNA INDICATION?** - Time: 20 min. Speaker: RAFAEL SELBACH SCHEFFEL (RS) **HOW THE DIAGNOSIS OF NIFTP IMPACT THE PREOPERATIVE DIAGNOSIS AND THE PERFORMANCE OF MOLECULAR TESTS** - Time: 20 min. Speaker: ANA MARIA ORLANDI (Argentina) **PERSONALIZED SURGERY: EXTENT OF SURGERY BASED ON PROGNOSTICATION** - Time: 20 min. Speaker: JOSÉ GUILHERME VARTANIAN (Sao Paulo) **Q&A** - Time: 30 min.	Room 1
09:30 - 11:00	Panel Discussion **MANAGEMENT OF THYROID CANCER** Chair: ROSANA SKLATE (Argentina) Chair: ANA AMELIA HOFF (Brazil) **NEW THERAPIES FOR RECURRENT DIFFERENTIATED THYROID CARCINOMA** - Time: 20 min. Speaker: ERIKA ABELLEIRA (Argentina) **CURRENT STATUS OF SYSTEMIC TREATMENT OF ANAPLASTIC THYROID CARCINOMA** - Time: 20 min. Speaker: RAMONA DADU (United States) **THE ROLE OF SURGERY AFTER NEOADJUVANT THERAPY** - Time: 20 min. Speaker: SANTIAGO ALBERTO ZUND (Argentina) **ORAL COMUNICATION: ID 117049 - USE OF TYROSINE KINASE INHIBITORS AND PROGRESSIVE IMPLEMENTATION OF GENOMIC INTERROGATION FOR PATIENTS WITH ADVANCED THYROID TUMORS DERIVED FROM THE FOLLICULAR EPITHELIUM** - Time: 10 min. ***Presenter: Fernando Jerkovich*** **Q&A** - Time: 20 min.	Room 2
11:15 - 12:00	Session **CHALLENGES IN THYROID CARE: CLINICAL CASES** Chair: FERNANDA VAISMAN (Brazil) Chair: MARIO VAISMAN (Brazil) **CURRENT CONTROVERSIES IN THE DIAGNOSIS AND MANAGEMENT OF DIFFERENTIATED THYROID CANCER: CASES FROM THE CLINIC** Speaker: ANGELA M. LEUNG (United States)	Room 1
11:15 - 12:00	**THYROID SURGERY IN A CLINICAL CASE CONTEXT** Moderator: ALVARO SANABRIA (Colombia) Moderator: LUIS EDUARDO BARBALHO DE MELLO (Brazil) Moderator: FLÁVIO CARNEIRO HOJAIJ (Brazil)	Room 2
12:00 - 12:30	Closing Ceremony **YOUNG INVESTIGATOR AWARD AND CLOSING CEREMONY** FABIAN PITOIA (Argentina) JANETE MARIA CERUTTI (Brazil)	Room 1



XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Content

ORAL COMMUNICATION

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

ORAL PRESENTATION – LATS YOUNG INVESTIGATOR AWARD 2023 – BASIC

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

ORAL PRESENTATION – LATS YOUNG INVESTIGATOR AWARD 2023 – CLINICAL

CLINICAL/THYROID AND METABOLISM

CLINICAL/THYROID AND PEDIATRIC DISEASE

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID NODULE

CLINICAL/THYROID NODULE

CLINICAL/THYROID NODULE

POSTER EXHIBITION

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

BASIC/HYPERTHYROIDISM

BASIC/HYPERTHYROIDISM

BASIC/THYROID AND PREGNANCY

BASIC/THYROID AND REPRODUCTION

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID EPIDEMIOLOGY

BASIC/THYROID EPIDEMIOLOGY

BASIC/THYROID GENETICS

BASIC/THYROID GENETICS

BASIC/THYROID GENETICS

BASIC/THYROID GENETICS

BASIC/THYROID HORMONE ACTION

BASIC/THYROID HORMONE ACTION

BASIC/THYROID NODULE

BASIC/THYROID PHYSIOLOGY

BASIC/THYROID SURGERY

BASIC/THYROID SURGERY

BASIC/THYROID SURGERY

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPERTHYROIDISM

CLINICAL/HYPOTHYROIDISM

CLINICAL/HYPOTHYROIDISM

CLINICAL/HYPOTHYROIDISM

CLINICAL/HYPOTHYROIDISM

CLINICAL/HYPOTHYROIDISM

CLINICAL/IODINE DEFICIENCY

CLINICAL/THYROID AND COVID-19

CLINICAL/THYROID AND COVID-19

CLINICAL/THYROID AND COVID-19

CLINICAL/THYROID AND COVID-19

CLINICAL/THYROID AND METABOLISM

CLINICAL/THYROID AND METABOLISM

CLINICAL/THYROID AND PEDIATRIC DISEASE

CLINICAL/THYROID AND PEDIATRIC DISEASE

CLINICAL/THYROID AND PEDIATRIC DISEASE

CLINICAL/THYROID AND PEDIATRIC DISEASE

CLINICAL/THYROID AND PEDIATRIC DISEASE

CLINICAL/THYROID AND PREGNANCY

CLINICAL/THYROID AND PREGNANCY

CLINICAL/THYROID AND PREGNANCY

CLINICAL/THYROID AND REPRODUCTION

CLINICAL/THYROID AUTOIMMUNITY

CLINICAL/THYROID AUTOIMMUNITY

CLINICAL/THYROID AUTOIMMUNITY

CLINICAL/THYROID AUTOIMMUNITY

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID GENETICS

CLINICAL/THYROID GENETICS

CLINICAL/THYROID GENETICS

CLINICAL/THYROID GENETICS

CLINICAL/THYROID NODULE

CLINICAL/THYROID NODULE

CLINICAL/THYROID NODULE

CLINICAL/THYROID NODULE

CLINICAL/THYROID NODULE

CLINICAL/THYROID NODULE

CLINICAL/THYROID NODULE

CLINICAL/THYROID REGULATION

CLINICAL/THYROID SURGERY

CLINICAL/THYROID SURGERY

CLINICAL/THYROID SURGERY

POSTER PRESENTATION – BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID CANCER BASIC

BASIC/THYROID GENETICS

BASIC/THYROID HORMONE ACTION

POSTER PRESENTATION – CLINICAL

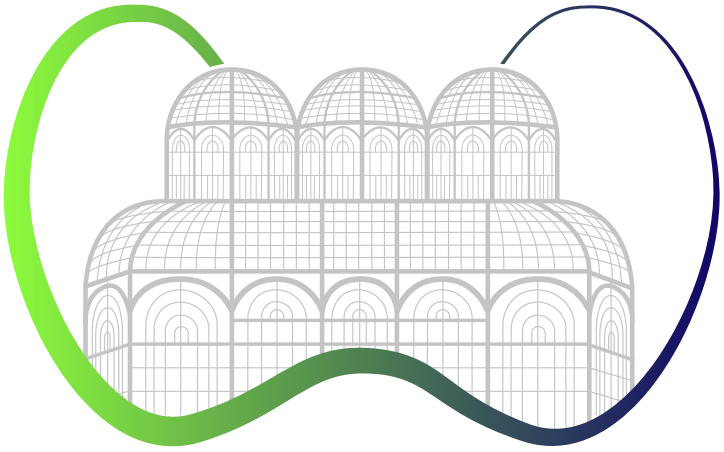
CLINICAL/THYROID AND METABOLISM

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL

CLINICAL/THYROID CANCER CLINICAL



XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Oral Communication

CLINICAL/THYROID CANCER CLINICAL

117047 ACTIVE SURVEILLANCE IS A FEASIBLE AND SAFE STRATEGY IN SELECTED PATIENTS WITH PAPILLARY THYROID CANCER AND LOCOREGIONAL STRUCTURAL DISEASE

Jose Miguel Dominguez[1], Marlín Solórzano[1], Nicole Lustig[1], Lorena Mosso[1], Hernan Gonzalez[2], Pablo H. Montero[2], Francisco Cruz[3], Antonieta Solar[4], Martín Espinoza[5], Roberto Santana[5]

[1] Department of Endocrinology, CETREN, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile.[2] Department of Surgical Oncology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile.[3] Department of Radiology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile.[4] Department de Pathology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile.[5] Department of Endocrinology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile

Introduction: After initial treatment, up to 30% of patients with papillary thyroid cancer (PTC) have incomplete response, mainly cervical lymph node (LN) disease. It has been suggested that, in selected patients, active surveillance (AS) is a safe alternative for these patients, with a frequency of structural progression between 10% and 25%. **Objective:** To report the results of AS in patients with PTC and cervical LN disease. **Design:** Retrospective observational study. **Methods:** Adult patients consecutively treated and followed prospectively for PTC, who presented with cervical LN disease (≥5 mm in the smallest diameter) with suspicious ultrasound or positive fine needle aspiration biopsy (FNA), and were managed with AS. We excluded patients with LN ≥20 mm in the largest diameter, 18F FDG PET(+) disease or unsolved distant metastases. Patients were followed every 6-12 months with neck ultrasound, Tg and TgAb. Additional imaging was performed at the discretion of the treating physician. TSH was maintained <0.1 or 0.1-0.5 uUI/mL depending on the presence of individual comorbidities. Growth was defined as an increase ≥3 mm in either diameter. **Results:** We included 32 patients, 27 (84.4%) women, aged 39 ± 14 years, all initially treated with total thyroidectomy and 22 (69%) with therapeutic neck dissection. Cervical LN disease was diagnosed 1 year (0.3-12.6) after initial management; diameter 9.0 mm (6.0-19.0); FNA was performed in 18 (56%) patients. After a median AS of 4.3 years (0.6-14.1), 4 (12.5%) patients had LN growth, 2 (50%) of whom were surgically removed, 1 (25%) was effectively treated with radiotherapy, and 1 (25%) has a scheduled surgery. Additionally, 6 (19.0%) patients received some treatment by their own preference. Tg increase was the only predictive factor of LN growth, evaluated as both the delta Tg ($p < 0.0366$) and percentage of Tg change ($p < 0.0140$). None of the included patients died, had local complications due to LN growth or salvage therapy, nor developed distant metastases during follow-up. **Conclusions:** In selected patients with PTC and locoregional structural disease, AS is a feasible and safe strategy as it allows to identify and effectively treat the minority of patients who progress.

CLINICAL/THYROID CANCER CLINICAL

117061 ROLE OF RET POLYMORPHISMS IN MEN2A-ASSOCIATED HYPERPARATHYROIDISM

Nathalie Lobo de Figueiredo-Feitosa[1], Patrícia Künzle Ribeiro Magalhães[1], Lucieli Ceolin[2], Ana Luiza Maia[2], Léa Maria Zanini Maciel[1]

[1] Department of Internal Medicine, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, SP, Brazil.[2] Endocrine Division, Thyroid Section, Porto Alegre Clinical Hospital, Rio Grande do Sul Federal University, Porto Alegre, RS, Brazil

Introduction: Multiple endocrine neoplasia type 2A (MEN2A) is an autosomal dominant inherited disease characterized by medullary thyroid carcinoma (MTC), pheochromocytoma and hyperparathyroidism (HPT), with high penetrance and variability of expression. HPT is the less common component of the syndrome (10% to 30% of patients). Several authors have suggested that RET polymorphisms could be associated with susceptibility and prognosis of MTC. **Objectives:** To evaluate the frequencies of RET polymorphisms (G691S, L769L, S836S e S904S) in MEN2A-patients and verify the association of RET variants with susceptibility and age-dependent penetrance of HPT. **Methods:** The RET variants G691S, L769L, S836S, and S904S were evaluated in a cohort of 157 MEN2A patients (M = 70, F = 87) attending tertiary teaching hospital. A comparison of RET variants frequencies between patients with and without HPT was performed. Kaplan-Meier curves and Cox regression analysis were used to estimate the effect of RET polymorphisms on the age-dependent penetrance. **Results:** A total of 28 (16.6%) patients presented MEN2A-associated hyperparathyroidism. The mean age at diagnosis was 35.27 ± 12.72 years, 55.4% of patients were women. Female subjects had higher risk of HPT development (OR = 2.61; 95%CI = 1.04-6.55). Ninety percent of the patients had RET mutation at codon 634 and 60% had some RET polymorphisms. RET mutations frequencies were similar between patients with or without HPT (P = 0.632). The frequencies of RET variants were as follows: 33.7% G691S, 33.1% L769L, 12.7% S836S and 33.7% S904S and no association was found between the frequencies of these RET polymorphisms and HPT development. However, Kaplan-Meier estimates of cumulative HPT diagnosis yielded distinct curves for patients harboring no or one polymorphism and two or more polymorphisms (P = 0.017). Patients harbored two RET variants exhibited an increase risk for earlier HPT development regardless gender (P = 0.015; OR 3.03; 95%CI 1.24-7.39). **Conclusion:** RET polymorphism alleles have an additive effect on the estimated risk of age-related HPT development in MEN2A patients.

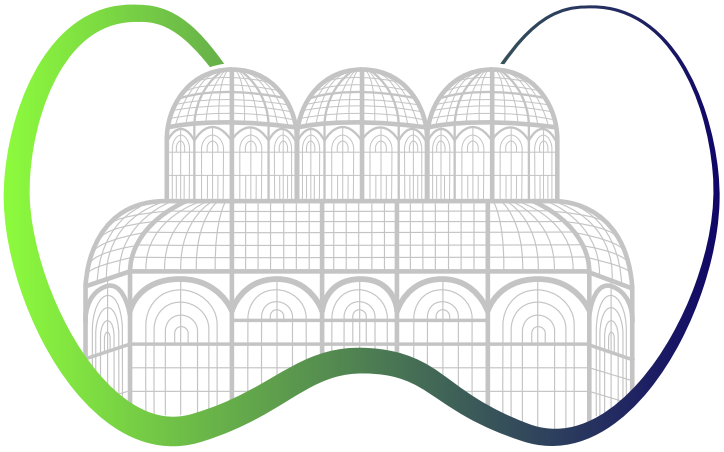
CLINICAL/THYROID CANCER CLINICAL

117049 USE OF TYROSINE KINASE INHIBITORS AND PROGRESSIVE IMPLEMENTATION OF GENOMIC INTERROGATION FOR PATIENTS WITH ADVANCED THYROID TUMORS DERIVED FROM THE FOLLICULAR EPITHELIUM

Fernando Jerkovich[1], María Soledad Capalbo[1], Erika Abelleira[1], María del Cisne Ochoa[1], Fernanda Bueno[1], Fabián Pitoia[1]

[1] División Endocrinología, Hospital de Clínicas, Universidad de Buenos Aires, Buenos Aires, Argentina

Introduction: The advent of tyrosine kinase inhibitors (TKIs) and genomic interrogation revolutionized the management of patients with advanced thyroid cancer (TC). **Objective:** To report our experience with the use of TKIs in patients with radioiodine-refractory differentiated thyroid carcinoma (RR-DTC) and anaplastic thyroid cancer (ATC). Secondly, to describe the implementation of genomic interrogation in this cohort of patients. **Methods:** Retrospective study of patients who received TKIs (March 2011 to December 2022). Tumor responses were evaluated according to RECIST v1.1. We estimated the median progression-free survival (PFS) and the overall survival (OS). Adverse effects (AEs) were recorded according to the CTCAE v5.0. We assessed the frequency of access to genomic interrogation and the results obtained with Oncomine FocusTM® or Foundation One®CDx platforms for RR-DTC patients and RT-PCR for BRAF mutations in ATC patients. **Results:** We included 36 patients with RR-DTC: 22 with papillary carcinoma, 9 with follicular carcinoma, and 5 with oncocytic carcinoma. Four additional patients had an ATC. RR-DTC: Sorafenib was prescribed to 32 patients (30 as first-line and 2 as second-line treatment). The best responses under sorafenib were: partial response (PR) in 10% and stable disease (SD) in 66%. Lenvatinib was prescribed in 23 patients (1° line in 5, 2° line in 17, and 3° line in 1). Tumor responses with lenvatinib were: i) complete response (CR): 12%, PR: 24%, and SD: 35%. A patient with an NTRK fusion (ETV6-NTRK3) received 3° line larotrectinib with an initial CR and then presented progressive disease (PD) at 12 months. Selitrectinib (4° line) was indicated after finding an on-target mutation in the TRK kinase domain. This patient died of pulmonary PD after 11 months of TKI initiation. Additionally, a patient who had PD under sorafenib and then lenvatinib received cabozantinib and currently has 28 months of treatment with SD. Median PFS with sorafenib was 16.5 months (95% CI 12.3-20.6), and 14 months (95% CI 0.3-27.7) with lenvatinib. The median PFS for the total cohort was 32 months (95% CI 29.5-34.5), with a median OS of 39 months (95% CI 31.8-46.2). ATC: Three out of 4 patients with ATC received the combination dabrafenib and trametinib (D-T) with an OS of 8 months. The remaining patient with ATC died due to PD before the authorization of D-T by his health insurance. Genomic interrogation was offered to 28/36 (78%) patients with RR-DTC and 4/4 (100%) unresectable ATC. Sixteen patients (12 with CDT-RR and all 4 with CAT, 40%) were able to access these studies. Actionable mutations were detected in 8/16 (50%) patients. **Conclusions:** Objective response and PFS progression rates were similar to those observed in other real-life studies. Detection of actionable mutations in patients with advanced TC is a promising scenario that will undoubtedly improve OS with a lower incidence of AEs.



XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Oral Presentation – LATS Young Investigator Award 2023 – Basic

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

117151 BISPHENOL A EXPOSURE DURING THE INTRAUTERINE PERIOD DISRUPTS THE PITUITARY-THYROID AXIS OF THE OFFSPRING RATS DURING ADULTHOOD

Guilherme Henrique[1], Érica Kássia Sousa-Vidal[2], Renata Elen Costa da Silva[1], Bruno Fiorelini Pereira[1], Gisele Giannocco[1], Caroline Serrano-Nascimento[1]

[1] Universidade Federal de São Paulo, São Paulo, SP, Brasil.[2] Instituto Israelita de Ensino e Pesquisa Albert Einstein, Hospital Israelita Albert Einstein, São Paulo, SP, Brasil

Introduction: Bisphenol A (BPA) is used in the production of polycarbonate plastics, and it is a known endocrine disruptor that interferes with thyroid hormone (TH) synthesis and action. However, the impact of intrauterine exposure to BPA in the programming of thyroid function of the offspring has never been reported. **Objective:** To investigate the effects of maternal exposure to BPA during gestation on the pituitary-thyroid axis gene expression and function of the adult F1 offspring rats. **Methods:** Pregnant Wistar rats were exposed or not to water supplemented with 0.1 or 1 ppm BPA throughout the gestation. The treatment was interrupted after the birth of the offspring animals. The female and male offspring rats were euthanized at the postnatal day 90 (PND90). Pituitary, thyroid, and serum were collected. Gene and protein expression was evaluated by RT-qPCR and Western Blotting, respectively. Thyroid histological analysis was also performed. Global DNA methylation was assessed by ELISA. Fluorometric or chemiluminescence immunoassays were performed to measure TH and TSH serum levels. **Results:** Intrauterine exposure to both doses of BPA significantly increased the gene and protein expression of the TSH beta subunit in the pituitary of the adult F1 female rats. However, in the male rats, this effect was observed only in animals exposed to the lowest treatment dose. Interestingly, the TSH serum levels were reduced in the female rats but were increased in the BPA-exposed male rats. Moreover, the intrauterine exposure to BPA increased the expression of several genes/proteins involved in the synthesis and secretion of TH as NIS, TPO, TSHR, TG, MCT8, PAX8, NKX2.1, and FOXE1 in both genders. In agreement, BPA-exposed animals presented increased T4 serum levels. Thyroid morphology was altered in the BPA-exposed offspring rats. Both concentrations of BPA exposure induced similar effects in both genders; the thyroid follicles showed hyperplasia and hypertrophy of epithelial cells, and some of the follicles degenerated. BPA-exposed animals also presented fibrosis in the thyroid gland. Finally, the BPA-exposed female and male rats presented decreased global methylation of DNA, increased expression of histone acetyltransferases (Hat1, Kat14) and demethylases (Kdm6a, Kdm1a), and decreased expression of histone methyltransferases (Ezh1, Ezh2). These data are coherent with the increased transcriptional activity that was observed. **Conclusion:** BPA exposure during a critical development period disrupted the function of the pituitary-thyroid axis and increased the susceptibility of the female and male offspring rats to develop hyperthyroidism during adult life.

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

117157 POLYCHLORINATED BIPHENYLS EXPOSURE DISRUPTS THE PITUITARY-THYROID AXIS OF F1 OFFSPRING ANIMALS DURING ADULTHOOD

Evelyn Franciny Cardoso Tavares[1], Guilherme Henrique[1], Vinicius Gonçalves Rodrigues[1], Nuha Ahmad Dsouki[1], Gisele Giannocco[1], Caroline Serrano-Nascimento[1]

[1] Universidade Federal de São Paulo (Unifesp), São Paulo, SP, Brasil

Introduction: Polychlorinated biphenyls (PCB) are flame-retardant compounds widely used as lubricants in the industry and electronic devices. Although PCBs were banned over 25 years ago, they are highly persistent in the environment and remain in the food chain until this day. PCBs are lipophilic and concentrate in the adipose tissue and serum. Exposure to PCBs has been previously associated with altered thyroid function. However, the impact of PCBs on the hypothalamic-pituitary-thyroid axis function programming has never been reported. **Objectives:** To investigate the consequences of maternal exposure to PCBs during pregnancy on the function of the pituitary-thyroid axis of the F1 offspring during adulthood. **Methods:** Pregnant Wistar rats were orally treated with corn oil (control) or corn oil supplemented 50 or 500 µg of Aroclor 1254/kg/day throughout the gestation period. Of note, Aroclor 1254 is a polychlorinated biphenyl mixture. After the birth of the offspring, the treatment was interrupted. The male and female offspring rats were euthanized at PND90. The pituitary, thyroid, and liver were collected. Gene and protein expression was evaluated by RT-qPCR and Western Blotting. Thyroid histological analysis was also performed. **Results:** PCBs exposure during the intrauterine period significantly reduced the mRNA expression of Tshb and Dio2 in the pituitary of male and female F1 offspring rats. In agreement, there was a significant reduction in the protein content of TSHB in the pituitary of these animals. Interestingly, the mRNA expression of Gh was increased in the pituitary, exclusively in female F1 rats. Intrauterine exposure to PCBs increased thyroid gene/protein expression of NIS and TG in the male rats and the gene/protein expression of NIS, TPO, TSHR, TG, and MCT8 in the female F1 adult rats. Thyroid morphology was also altered in the PCB-exposed animals in both doses and genders. In fact, the thyroid follicles of PCB-exposed animals were enlarged and filled with higher amounts of TG than the follicles of the control rats. Moreover, inflammatory infiltration in the follicles was observed, especially in the female rats' thyroid. Fibrosis signals were also observed. Finally, the expression of Sult1e1, an enzyme involved in the peripheral metabolism of thyroid hormones, was decreased in the PCB-exposed offspring rats, while the expression of transthyretin, the main rat protein involved in the plasma transport of thyroid hormones, was only reduced in the liver of PCB-exposed female F1 adult rats. **Conclusions:** Maternal exposure to PCBs disrupts the pituitary-thyroid axis of adult female and male offspring rats in a sexually dimorphic pattern. Indeed, our data suggest that the female offspring rats were more susceptible to the deleterious effects of PCBs on thyroid function. The results also suggest that intrauterine exposure to PCBs leads to a hyperactivation of thyroid function in the F1 rats during adulthood.

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

117164 POLYCHLORINATED BIPHENYLS STIMULATE THYROID GENE TRANSCRIPTION THROUGH EPIGENETIC MECHANISMS AND ACTIVATION OF THE CREB SIGNALING PATHWAY

Vinicius Gonçalves Rodrigues[1], Evelyn Franciny Cardoso Tavares[1], Guilherme Henrique[1], Mikaeli Vieira Ribeiro Oliveira[1], Caroline Serrano-Nascimento[1]

[1] Universidade Federal de São Paulo (Unifesp), São Paulo, SP, Brasil

Introduction: Polychlorinated biphenyls, also known as PCBs, are organochlorine compounds and flame retardants used as coolant fluids and lubricants for transformers, capacitors, and other industrial equipment that have been banned for over 25 years in many countries. Due to their persistence in the environment, humans were exposed to PCBs mainly through consuming contaminated food. Studies demonstrated alterations in T3, T4, and TSH serum concentrations in humans and rodents exposed to PCBs. However, the mechanisms involved in this dysregulation of the thyroid function induced by PCBs have never been reported. **Objectives:** To evaluate the molecular mechanisms triggered by PCBs exposure in the disruption of thyrocytes gene/protein expression and function. **Methods:** PCCl3 cells were treated or not (control) for 24 h with 10-7 M or 10-9 M Aroclor 1254, a polychlorinated biphenyls mixture. Gene and protein expression was evaluated by qPCR and Western Blotting, respectively. To assess the transcriptional regulation of thyroid genes by PCBs, PCCl3 cells were transiently transfected with plasmids containing NIS, TG, and TPO promoters' regions. Moreover, the activation of MAPK and CREB signaling pathways was evaluated by Western Blotting in the cells exposed or not to PCBs. **Results:** The exposure of thyrocytes to PCBs significantly increased the gene and protein expression of PAX8, FOXE1, TPO, NIS, TSHR, and MCT8, especially in the lowest dose of treatment. Interestingly, the expression of TG was reduced in PCB-exposed cells. In accordance, the exposure of thyrocytes to Aroclor 1254 increased the transcriptional activity of NIS and TPO promoters but reduced the activity of the TG promoter, especially in the 10-9 M dose. PCB treatment has also decreased the gene and protein expression of DNMT3a and DNMT3b but did not alter the expression of DNMT1. Moreover, PCB-exposed cells presented reduced mRNA expression of the histone deacetylase Hdac3 and increased mRNA expression of the histone demethylase Kdm6a. These results agree with increased acetylation of the histones H3 and H4 and decreased trimethylation of the lysines 9, and 27 of the histone H3 observed in PCB-exposed cells. Finally, PCB-exposed cells presented increased phosphorylation of CREB and reduced phosphorylation of ERK, which are coherent with the activation of the thyroid expression of differentiation markers. **Conclusions:** Taken together, our data suggest that PCBs stimulate the transcription of thyroid differentiation markers through the activation of the CREB signaling pathway, which is crucial in the regulation of thyroid function, and through epigenetic mechanisms commonly involved in transcriptional activation.

BASIC/THYROID CANCER BASIC

117145 AGK-BRAF ACTIVATES THE MAPK AND PI3K/AKT SIGNALING PATHWAYS, DISRUPTS NIS ACTIVITY AND INDUCES GENOMIC INSTABILITY IN NORMAL THYROID CELLS

Luiza de Mello Oliveira Sisdelli[1], Maria Isabel Vieira Cordioli[1], Welbert Rocha[1], Roxane Hatanaka[1], Guilherme Henrique[2], Renata Elen Costa da Silva[2], Caroline Serrano-Nascimento [2], Janete Maria Cerutti[1]

[1] The Genetic Bases of Thyroid Tumors Laboratory, Discipline of Genetics, Department of Morphology and Genetics, Universidade Federal de São Paulo (Unifesp), São Paulo, SP, Brazil. [2] Laboratório de Endocrinologia Molecular e Translacional, Escola Paulista de Medicina, Unifesp, São Paulo, SP, Brazil

Introduction: We recently uncovered that gene fusions are more common in pediatric papillary thyroid carcinoma (PTC), while in adults, point mutations are more prevalent. Among the fusions, AGK-BRAF is a recurrent event in sporadic pediatric PTC, and it is associated with distant metastasis and early manifestation of the disease (mean 10.67 y.o.). However, the mechanism responsible for driving tumor aggressiveness remains poorly understood. **Objective:** To explore the effects of ectopic expression of the five most prevalent genetic alterations found in pediatric PTC in thyroid PCCL3 cells. **Methods:** We used the differentiated rat thyroid epithelial cells that express TSHR and NIS mRNAs and can take up iodine. We independently and permanently transfected PCCL3 cells with plasmid containing cDNA from AGK-BRAF, RET/PTC1, RET/PTC3, ETV6-NTRK3 fusions, BRAF V600E and BRAF Wild type. Immunoblotting was used to examine the effect of the mutations in MAPK and PIK3/AKT signaling pathways and NIS expression. NIS activity was analyzed by a nonradioactive iodide uptake assay. Genomic instability, a hallmark of dedifferentiated cancer, was investigated by micronuclei assay using DAPI and fluorescent microscopy. **Results:** Cells expressing AGK-BRAF fusion significantly activated MAPK ($p < 0.001$) and PIK3/AKT ($p < 0.05$) signaling pathways, while reducing NIS expression ($p < 0.001$) and iodide uptake ($p < 0.001$), more than cells transfected with other oncoproteins and control. A higher number of micronuclei was found in cells expressing ETV6-NTRK3 (47%), AGK-BRAF (24%) than cells transfected with RET/PTC3 (18%), BRAF V600E (17%) and RET/PTC1 (14%). Anaphase bridges, which are associated with DNA double strand breaks, were predominantly observed in the AGK-BRAF (20%) and ETV6-NTRK (18%) transfected cells. **Conclusion:** We demonstrated that AGK-BRAF fusion leads to higher activation of the MAPK and PIK3/AKT pathways and lower NIS expression and activity in PCCL3 cells. These were accompanied by a higher number of micronuclei and higher anaphase bridge, which enable the acquisition of additional genetic alterations during tumor progression. These results helped to elucidate the mechanisms by which the AGK-BRAF fusion cause dedifferentiation of the thyroid cells and a more aggressive behavior of tumor cells in pediatric cases of PTC with distant metastasis.

BASIC/THYROID CANCER BASIC

117066 INHIBITION OF EZH2 METHYLTRANSFERASE ACTIVITY INDUCES AN ANTITUMORAL EFFECT AND IMPROVES CELL DIFFERENTIATION IN ANAPLASTIC THYROID CANCER

Diego Claro de Mello[1], Marcella Maringolo Cristóvão[1], Kelly Cristina Saito[1], Edna Teruko Kimura[1], Cesar Seigi Fuziwara[1]

[1] Department of Cell and Developmental Biology, Institute of Biomedical Sciences, University of São Paulo, São Paulo, SP, Brasil

Introduction: Anaplastic thyroid cancer (ATC) is an undifferentiated form of thyroid carcinoma that is lethal. Although ATC treatment has improved in the last years, the loss of differentiation and high rates of recurrence and metastasis remain as challenges to overcome. In the last decade epigenetic reprogramming has emerged as a new cancer hallmark and epigenetic alterations caused by upregulation of Polycomb Repressive Complex 2 (PRC2) may contribute to cancer aggressiveness by acting in gene silencing through histone modifications. EZH2 is the core catalytic component of PRC2 as its methyltransferase causes the trimethylation of H3 histone on lysine 27 (H3K27me3), a transcription repression mark. Thus, strategies to inhibit PRC2/EZH2 function by blocking EZH2 methyltransferase activity pharmacologically or permanently using CRISPR/Cas9-mediated gene editing may contribute to ATC's treatment. **Objectives:** Investigate the role of PRC2/EZH2 in ATC's biology and dedifferentiation. **Methods:** To permanently inhibit EZH2, we targeted the EZH2 gene with CRISPR/Cas9-mediated gene editing in ATC cell SW1736 and assessed cell function by *in vitro* and *in vivo* assays such as cell counting, migration, invasion, clonogenic assay and xenotransplant in nude mice (CEUA protocol 2023150720). Additionally, we treated ATC cells KTC2 and SW1736 with the EZH2 methyltransferase inhibitor EPZ6438 alone or in combination with the MAPK inhibitor U0126. Then, thyroid differentiation and EMT (epithelial-mesenchymal transition) genes expression were analyzed by qPCR and western blot and tumor features by immunohistochemistry. **Results:** CRISPR/Cas9-induced EZH2 gene editing in SW1736 cells reduced cell migration and invasion and reduced cell growth *in vitro*. Moreover, we observed upregulation of thyroid differentiation genes NIS, TG, TSHR and GLIS3 and induction of a mesenchymal-epithelial transition (MET), by increasing E-cadherin and miR-200a/c expression and reducing ZEB1/2 and N-cadherin levels, which contributed for transition to an epithelial-like cell morphology. In addition, EZH2-mediated gene editing also repressed Wnt/β-catenin signaling activation. In the xenograft study, SW1736 EZH2-edited cells formed tumors with reduced volume (~10% of control tumor volume) that showed less proliferation in the anti-Ki67 immunostaining and impairment of recruitment of cancer associated fibroblasts stained with anti-alpha-SMA antibody. Furthermore, pharmacological inhibition of EZH2 with EPZ6438 decreased colony formation and improved thyroid differentiation-genes expression in KTC2 and SW1736 cells, but the treatment with MAPK inhibitor U0126 did not enhance these effects. **Conclusion:** In this work, we show that EZH2 inhibition induces a strong antitumoral effect *in vitro* and *in vivo* by inducing MET and improving differentiation of thyroid follicular cells.

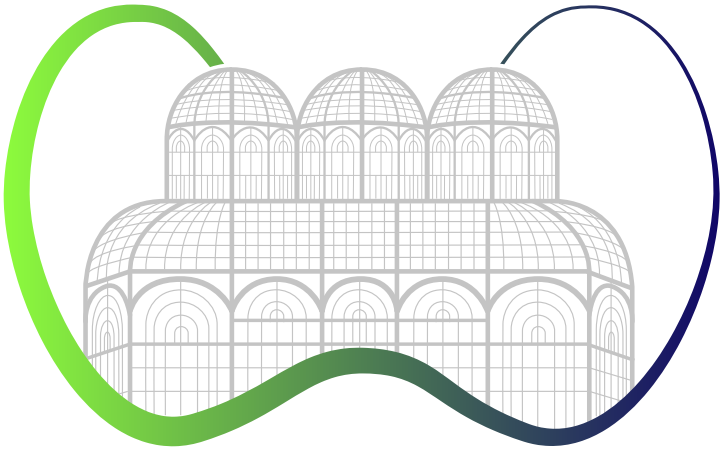
BASIC/THYROID CANCER BASIC

117063 THE TRANSCRIPTIONAL CONTROL OF EZH2 HISTONE METHYLTRANSFERASE IN AGGRESSIVE THYROID CANCER

Marcella Maringolo Cristóvão[1], Diego Claro de Mello[1], Edna Teruko Kimura[1], Cesar Seigi Fuziwara[1]

[1] Institute of Biomedical Sciences, University of São Paulo, São Paulo, SP, Brasil

Introduction: Anaplastic thyroid carcinoma (ATC) is the most aggressive type of endocrine cancer, presenting undifferentiated cells that are resistant to radioiodine therapy. Among the genetic alterations underlying ATC oncogenesis are mutations in the MAPK pathway, in the TP53 tumor suppressor gene and in the TERT promoter. Furthermore, ATC overexpresses EZH2, the catalytic subunit of the Polycomb 2 complex, responsible for promoting trimethylation of histone H3 at the lysine 27 (H3K27Me3) that leads to the formation of heterochromatin. Thus, EZH2 overexpression can lead to gene silencing, which can result in cell dedifferentiation and tumor progression. **Objective:** Investigate the mechanism underlying the transcriptional activation of the EZH2 gene in ATC. **Methods:** We chose the region around EZH2 exon 1 that shows high H3K27ac levels indicating an active promoter region (data from Genome Browser). We divided this region into fragments: E1, E2, E3, E4 and E5. The fragments E3 and E4 were divided into smaller pieces: E3A, E3B and E3/4 (intersection of E3 and E4). These fragments were PCR amplified and cloned upstream of the firefly luciferase gene in pGL4-20 minP plasmid. ATC cell lines – KTC2, SW1736, 8305C – and papillary thyroid carcinoma cell lines – TPC-1 and BCPAP were transfected and 24 hours later cells were lysed for luciferase reporter assays. Transcription factor (TF) prediction was performed on LASAGNA software and TFs with higher scores were chosen for gene expression analysis by qPCR. Moreover, site directed mutagenesis and deletion of TFs binding sites was performed in the E3/4 plasmid. We also treated ATC cells with a MAPK inhibitor (U0126) to assess the impact of this pathway on EZH2 expression and activation. **Results:** The E3 and E4 regions present the highest luminescence values, while for the small fragments, the E3/4 region showed the highest value. Based on TF prediction analysis for the E3/4 fragment, we selected YY1, E2F1, NKX2.5, NFYA, FOXM1 and KLF4 for gene expression analysis and found that most of TFs were upregulated in ATC, while only KLF4 was down-regulated. We observed a decrease in EZH2 promoter activation after deletion of NFYA and YY1 binding sites within E3/4 region, and when both of these sites were deleted the effect observed was additive. Deletion of SP1 binding site reduced E3/4 activation indicating a role for MAPK signaling in EZH2 control. Indeed, after MAPK inhibition with U0126, the EZH2 expression and promoter activation decreased significantly in ATC cells. **Conclusions:** The E3/4 fragment is the minimum promoter of EZH2 and presents binding sites for several TFs that are overexpressed in ATC. Deletions in NFYA, YY1 and SP1 binding sites in E3/4 reduced promoter activation levels, indicating that these TFs may play a role in EZH2 transcriptional activation. Moreover, MAPK blockage reduces promoter activation and EZH2 gene expression, indicating that the MAPK pathway can induce EZH2 transcription in ATC.



XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Oral Presentation – LATS Young Investigator Award 2023 – Clinical

CLINICAL/THYROID AND METABOLISM

117030 CARDIOMETABOLIC RISK AND INSULIN RESISTANCE IN PATIENTS WITH RESISTANCE TO THYROID HORMONE B

Pryscilla Moreira de Souza Domingues Hajj[1], Patrícia Moreira Gomes[1], Patrícia Künzle Ribeiro Magalhães[1], Léa Maria Zanini Maciel[1]

[1] Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, SP, Brazil

Introduction: In resistance to thyroid hormone due mutations in thyroid hormone receptor β (RTHβ), the peripheral tissues show variable refractoriness to the action of thyroid hormones (TH). The effect of TH on insulin sensitivity differs by tissue – it enhances glucose uptake in the muscle but reduces it in the liver. The overall net effect in hypothyroidism favors insulin resistance **Objectives:** To assess cardiometabolic risks and insulin sensitivity in RTHβ patients. **Methods:** 16 patients (8 adults and 8 children/teenagers) with RTHβ 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 with dosages of glycemia, lipids, insulin, interleukin-6 (IL-6), TNF-alpha, leptin and adiponectin, ultrasensitive c-reactive protein. Fat percentiles and lean mass were also evaluated using the Bioimpedance technique (BIA) and the trunk and peripheral fat percentiles using the dual emission X-ray absorptiometry technique (DXA). Insulin sensitivity was performed in adult patients and controls with the hyperinsulinemic euglycemic clamp (CEH); HOMA-IR was calculated in all individuals studied. **Results:** the mean ages (in years) of adult patients and controls and affected children/teenagers and controls were, respectively, 52.3 ± 16.3 *vs.* 48.5 ± 16.6 (P=0.5), and 10.88 ± 3.94 *vs.* 10.00 ± 3.08 (P = 0.4). By univariate analysis, there was no difference between waist-hip and waist-height ratio in both adult and children/teenagers groups. RTHβ patients exhibited higher cholesterol (P = 0,04) and LDL than controls (P = 0.03) but no difference in triglycerides levels. A significant difference was observed in IL-6 levels between RTHβ patients and controls (P < 0.01). There was no evidence of insulin resistance evaluated by CEH and HOMA-IR. **Conclusion:** We did not demonstrate insulin resistance in patients with RTHβ studied, using the gold standard method, the hyperinsulinemic-euglycemic clamp. However, higher levels of total cholesterol and LDL-cholesterol were found in adults patients, which implies the need for controlled and continuous patient monitoring to prevent increased cardiometabolic risks in this disease. We demonstrated for the first time the increase in IL-6 levels in patients with RTHβ, as occurs in autoimmune thyroid diseases and goiter. A larger number of patients should be studied to confirm these results.

CLINICAL/THYROID AND PEDIATRIC DISEASE

117065 HIGH ACCURACY OBSERVED IN PRELIMINARY PERFORMANCE RESULTS OF THE VALIDATION OF A MICRORNA AND DNA-BASED THYROID MOLECULAR CLASSIFIER IN A PEDIATRIC COHORT

Marcos Tadeu dos Santos[1], Bruno Mari Fredi[1], Andrei Félix de Oliveira[1], Isabela Fernanda Morales Martins[1], Miriane de Oliveira[1], Bruna Frizzo Rabelo[1], Nathalia de Campos Rodrigues[1], Diego Nogueira Vilela[1], Bruna Moretto Rodrigues[1], Yasmin de Macedo Mallon Couto[2], Paulo Alonso Garcia Alves Junior[2], Mario Lucio Cordeiro Araujo Junior[2], Fernanda Vaisman Balieiro[2]

[1] Onkos Molecular Diagnostics, Ribeirão Preto, SP, Brazil. [2] Brazilian National Cancer Institute (Inca), Rio de Janeiro, RJ, Brazil

Introduction: Thyroid nodules are very common in adults (20%-76%) but uncommon (~1.5%) in the pediatric population (children and adolescents under 18 years old). In addition, the risk of malignancy (RoM) in this population is higher when compared to adults, including in the indeterminate cytology categories: Bethesda III, 10%-30% *vs.* 50%-75% and Bethesda IV, 25%-40% *vs.* 75%-93%. Despite this, molecular testing is still recommended and useful in this population. However, the available molecular tests in Latin America are not yet validated in the pediatric population. **Objective:** To evaluate the diagnostic performance of a microRNA and DNA-based thyroid molecular classifier (mir-THYpe full) in the pediatric population. **Methods:** The initial cohort of this validation study was composed of FNA slides from 15 patients: seven from the National Cancer Institute (INCA) and eight from Onkos biorepository. Samples were subjected to the mir-THYpe full molecular test, which includes microRNA expression profiling and DNA analysis (BRAF V600E and pTERT C228/250T) by qPCR. Samples in which we were able to obtain enough RNA were also analyzed for the presence of PAX8/PPRAg, RET/PTC1 and RET/PTC3 fusions. The anatomopathological reports (AP data) were used as the gold standard to assess the test's performance. **Results:** Of the 15 samples (six Bethesda III, five Bethesda IV and four Bethesda VI) analyzed, one sample was classified as inconclusive, due to low material available in FNA and failing in quality control parameters of the test. From the remaining 14 samples, 12 were classified as positive for malignancy in the molecular classifier, of which 11 were in fact malignant nodules (91.6%) - papillary thyroid carcinomas and microcarcinomas, including two BRAF positive samples. The only false positive sample was a colloid goiter. Of the remaining two samples, both were classified as negative for malignancy in the molecular test and both were confirmed as truly benign nodules (100%) – follicular adenomas. In general, from the 14 valid pediatric samples included in this preliminary study, 13 were correctly classified by the molecular classifier, showing 92.8% of accuracy. None of the translocations analyzed were detected in this cohort. **Conclusion:** Although preliminary, the results suggest the technical applicability of the mir-THYpe full molecular classifier in pediatric thyroid nodules. A robust validation is still ongoing, including more samples and aiming to increase benign samples, to better assess the predictive values of this molecular test in the pediatric population.

CLINICAL/THYROID CANCER CLINICAL

117142 IDENTIFICATION OF NOVEL PREDISPOSITION GENES TO THE DEVELOPMENT OF NON-SYNDROMIC FAMILIAL NON-MEDULLARY THYROID CANCER BY EXOME DATA ANALYSIS

Isabela Nogueira Nunes[1], Thaise Nayane Ribeiro Carneiro[1,2], Luis Eduardo Barbalho de Mello[3], José Brandão Neto[3], Camila Xavier Alves[3], Janete Maria Cerutti[1]

[1] Genetic Bases of Thyroid Tumors Laboratory, Division of Genetics, Department of Morphology and Genetics, Federal University of São Paulo (Unifesp), São Paulo, SP, Brazil. [2] The Children's Hospital of Philadelphia, Philadelphia. [3] Liga Norte Riograndense Contra o Câncer, Natal, RN, Brasil

Introduction: According to the 2022 WHO classification, familial non-medullary thyroid carcinoma (FNMTC) represents 3 to 9% of all follicular cell-derived thyroid carcinoma and were classified as syndromic or non-syndromic FNMTC. The non-syndromic FNMTC is clinically characterized by the presence of at least 3 first-degree relatives affected by follicular cell-derived thyroid carcinoma, or 2 or more first-degree relatives affected by papillary thyroid carcinoma (PTC); both in the absence of environmental predisposing factors and inherited cancer syndromes. Although predisposing genes to syndromic FNMTC have been identified and genetic test is offered, genetic alterations in over 150 genes and several chromosomal loci have been associated with non-syndromic FNMTC, but most variants confer small increments in risk and explain just a small fraction of the family cluster. No genetic test is available to assess at-risk family members, continuous monitoring is needed. **Objective:** To identify genetic variants that are associated with non-syndromic FNMTC by whole exome sequencing (WES) analysis. **Methods:** WES was performed in affected (n = 27) and non-affected (n = 10) family members of 7 families with clinical diagnosis of non-syndromic FNMTC from Rio Grande do Norte state, Brazil. The exoma analysis was performed using Illumina NextSeq 550 platform. As a first step, visual inspection of variants in 157 genes previously related to non-syndromic FNMTC was conducted. Next, novel predisposing genes were investigated using PhenoDB and filtered using Genome Aggregation (gnomAD) and Online Archive of Brazilian Mutations (ABraOM) population databases. Functional prediction was performed using VEP interface. The identified variants were validated in affected and non-affected family members by Sanger sequencing. To better understand the role of the variants identified, their prevalence was assessed in over 1,500,00 sporadic cancer data available at COSMIC and IntOGen. **Results:** The visual inspection of variants identified in the 157 previously described genes disclosed missense variants in POLD1, KMT2C and SOX7 genes. However, the validation analysis showed that the variants in SOX7 and KMT2C did not segregate with the phenotype in these families. The WES analysis revealed variants in new candidate genes (MLH3, KMT2A, PRDM1, MUTYH) that segregate with the phenotype. The pedigrees of the 7 families showed a degree of clinical heterogeneity, reduced penetrance and distinct patterns of inheritance. Remarkably, the identified candidate genes encode protein associated with DNA repair (POLD1, MUTYH, MLH3) or histone modification (KMT2A, PRDM1). **Conclusion:** We identified variants in a gene previously associated with non-syndromic FNMTC and four novel candidate genes. These findings will certainly aid the development of a multigene panel test for genetic screening of non-syndromic FNMTC, which will better predict an individual's risk of cancer and guide therapy.

CLINICAL/THYROID NODULE

117082 CHARACTERIZATION OF MIR-146B AS PROGNOSTIC BIOMARKER TO PREDICT CLINICAL-PATHOLOGICAL PHENOTYPES ASSOCIATED WITH AGGRESSIVE BEHAVIORS IN THYROID DIFFERENTIATED CARCINOMAS FROM PREOPERATIVE FNA CYTOLOGY

Marcos Tadeu dos Santos[1], Isabela Fernanda Morales Martins[1], Andrei Félix de Oliveira[1], Bruno Mari Fredi[1], Miriane de Oliveira[1], Bruna Frizzo Rabelo[1], Nathalia de Campos Rodrigues[1], Diego Nogueira Vilela[1], Bruna Moretto Rodrigues[1], Gustavo Bittar Cunha[2], Rosália do Prado Padovani[2], Antonio Augusto Tupinambá Bertelli[2], Carolina Ferraz da Silva[2]

[1] Onkos Molecular Diagnostics, Ribeirão Preto, SP, Brazil. [2] Santa Casa de São Paulo School of Medical Sciences

Introduction: Thyroid cancer ranks as the ninth most-incident cancer worldwide, and although usually having a favorable outcome, some cases can progress to more aggressive behaviors. Recent studies have associated the high expression of microRNA-146b (miR-146b) in thyroid differentiated carcinomas with higher risk phenotypes, such as extrathyroidal invasion, lymph node metastasis and the presence of the BRAF V600E mutation, exhibiting its potential to predict the progression of the disease and a worse prognosis for patients. **Objective:** To characterize the miR-146b as a prognostic biomarker for clinical-pathological phenotypes in differentiated thyroid carcinoma from fine-needle aspiration (FNA) smear slides, for an early identification in the preoperative setting of potentially aggressive behavior thyroid carcinomas allowing a more accurate clinical management of patients. **Methods:** The cohort of this study consisted of 99 FNA samples of thyroid differentiated carcinomas obtained from Santa Casa de São Paulo School of Medical Sciences and Onkos biorepository. All samples were subjected to analysis of miR-146b normalized expression and the DNA for presence of BRAF V600E mutation by qPCR. The patients' anatomopathological reports (AP data) were examined and the clinical-pathological characteristics were identified at the time of surgery. The characteristics analyzed were: Extrathyroidal Invasion (EI), Vascular Invasion (VI), Lymph Node Metastasis (LNM) and ATA Recurrence Risk (RR). Using the Receiver Operator Characteristic (ROC) curve, two miR-146b expression cut-offs values for each characteristic were defined, generating three "miR-146b expression zones": low, moderate and high. **Results:** Based on the miR-146b expression, the risk of developing each characteristic in each respective "miR-146b expression zones" were: Presence of EI – 6.2% (low), 30.8% (moderate) and 40% (high); Presence of VI – 4.5% (low), 22.2% (moderate) and 40% (high); Presence of LNM – 12.8% (low), 27.3% (moderate) and 75% (high); Probability of being Intermediate/High risk at ATA RR – 13.6% (low), 48.6% (moderate) and 80% (high); Presence of BRAF V600E – 7.9% (low), 62.5% (moderate) and 91.7% (high). **Conclusion:** The results suggested that miR-146b normalized expression can be used as a prognostic biomarker to predict clinical-pathological phenotypes and potential aggressive behaviors of thyroid differentiated carcinomas, in order to support a more personalized patient management in the preoperative setting.

CLINICAL/THYROID NODULE

117027 IDENTIFICATION OF CIRCULATING MICRORNAS OF POTENTIAL USE IN THE DIAGNOSIS OF THYROID CANCER

Karina Colombera Peres[1], Alexandre Hilário Berenguer de Matos[1], Mateus Leandro Bezerra[1], Larissa Teodoro Rabi[1], Alfio José Tincani[1], Priscila Costa Tincani[1], Icléia Siqueira Barreto[1], Lucas Leite Cunha[2], Leonardo Augusto Marson[1], Natassia Elena Bufalo[1], Murilo Viera Geraldo[1], Laura Sterian Ward[1]

[1] Universidade Estadual de Campinas (Unicamp), Campinas, SP, Brasil. [2] Universidade Federal de São Paulo (Unifesp), São Paulo, SP, Brasil

There is an urgent need for biomarkers that can aid in the diagnosis of the growing population of patients with thyroid nodules, especially in patients classified as indeterminate by cytology. In addition, it is essential to distinguish patients that can be just monitored from those deserving more aggressive approaches. MicroRNAs (miRNA) are small non-coding RNAs that play a fundamental role in the regulation of gene expression and, therefore, in the pathogenesis and progression of different types of cancer. Due to their relatively easy manipulation, the detection of dysregulation of miRNA expression in liquid biopsies has proven useful in the management of various tumors. To search for potentially useful miRNAs in thyroid nodules patients' management, we submitted to Next Generation Sequencing (NGS), comprising the reading of the complete micro transcriptome, 18 serum samples obtained from peripheral blood collection. The experimental group included 14 patients with thyroid nodules measuring 0.4 to 6 cm in diameter (11 women, 3 men; mean age 46.4 ± 12.3 years) who underwent investigative surgery due to indeterminate cytology. Histology showed that there were 3 goiters, 3 follicular adenomas (FA), 4 papillary thyroid microcarcinomas (PTM), and 4 papillary thyroid carcinomas (PTC). NGS results were compared to a control group consisting of 4 individuals demonstrably without thyroid disease (4 females, mean age 38.9 ± 9.0 years old). Differential expression analyses between experimental and control groups were performed using the DEseq2 algorithm. miRNAs with p-value < 0.05 and that presented fold-regulation greater or less than 2 in the experimental group compared to the control group were considered significantly dysregulated. Fifty-nine dysregulated miRNAs were identified in the experimental group. Fourteen miRNAs were found dysregulated in goiter; 31 dysregulated miRNAs in FA; 35 miRNAs in PTM; and 20 in the PTC samples. To visualize clusters of significantly dysregulated miRNAs, unique to each analyzed experimental group, we performed the construction of a heat map: miR-224-5p and miR-486-5p were the most up and downregulated miRNAs in the goiter group with 2.8 UA and -3.2 AU, respectively; miR-197-3p (2.9 AU) was the most upregulated and miR-342-5p was -3.1 times downregulated in FA. Exclusively dysregulated miRs also distinguished PTM and PTC groups. The most up and downregulated miRs comparing PTM and controls were miR-215-5p (3.3 AU) and miR-1255-5p (-3.0 AU) respectively. In addition, miR-193b-5p was found 2.5 times upregulated in the PTC whereas miR-150-5p was 3.1 times downregulated in this same group. In conclusion, we demonstrated a miRNA profile that may characterize thyroid nodules and found novel miRNAs which can be used in liquid biopsies aiming at the diagnosis of malignancy upon a simple blood collection.

CLINICAL/THYROID NODULE

117090 THE IMPACT OF AGE ON THE MALIGNANCY RATE OF THYROID NODULES CLASSIFIED ACCORDING TO THE ACR-TIRADS

Leonardo Barbi Walter[1], Paula Martins Fernandes[1], Débora Lunkes Strieder[1], Anita Lavarda Scheinpflug[1], Andre Borsatto Zanella[1], Mauricio Farenzena[1], Carlo Sasso Faccin[1], Rafael Selbach Scheffel[1], José Miguel Dora[1], Iuri Martin Goemann[1], Ana Luiza Maia[1]

[1] Hospital de Clínicas de Porto Alegre, Porto Alegre, RS, Brasil

Introduction: The impact of age on malignancy prediction in thyroid nodules is not completely understood. The cornerstone of thyroid nodule evaluation is ultrasound-based risk stratification systems (RSSs), which dictate subsequent investigations regardless of clinical variables. **Objectives:** To evaluate the impact of age on malignancy risk in thyroid nodules and on the American College of Radiology – Thyroid Imaging Reporting and Data System (ACR-TIRADS) strategy. **Methods:** Retrospective cohort study of patients aged ≥ 20 years with thyroid nodules evaluated in a tertiary hospital from 2012 to 2019, submitted to fine-needle aspiration biopsy. The primary analysis consisted of stratification according to age to analyze the malignancy rate and the secondary analysis to evaluate the impact of age on the malignancy rate in thyroid nodules retrospectively classified according to the ACR-TIRADS. Cytology and cell block categories V and VI results were considered to define malignancy. **Results:** A total of 1,023 nodules from 921 patients were analyzed. Most patients were female (88.2%), and the median age was 58.5 (interquartile range [IQR], 41.1-66.6) years. The median nodules' size was 2.4 (IQR, 1.7-3.6) cm. The percentages of thyroid nodules classified as TR1, TR2, TR3, TR4, and TR5 were 1.4% (n = 14), 50.0% (n = 512), 25.9% (n = 265), 14.4% (n = 147), and 8.3% (n = 85) respectively, whose malignancy rates were, correspondingly, 0%, 0.8%, 3.4%, 13.6%, and 41.2%. The stratification by age strata revealed a significant difference in the prevalence of malignancy between the subgroups of 20-39, 40-59, and ≥60 years: 10.7%, 8.5%, and 3.7%, respectively (P < 0.002). For each year of life, there was a 2.8% reduction in the odds ratio for malignancy, adjusted for sex, multinodularity, and nodule size (confidence interval 95%: 1.1-4.8%; P = 0.003). Interestingly, the results were similar when we analyzed the different categories of ACR-TIRADS: in TR5, in the subgroups of 20-39 years (n = 17) and ≥60 years (n = 31), the malignancy rate decreased from 64.7% to 22.6%; and in TR4, from 21.4% (n = 14) to 10.4% (n = 77). In TR3, the malignancy rate was 1.7% (n = 118) in the subgroup of ≥60 years. In the multivariate analysis, adjusting for sex, multinodularity, and nodule size, malignancy was different among age strata (20-39, 40-59, and ≥60 years) in TR5 (P = 0.009) and TR3 (P < 0.001), but not in TR4 (P = 0.656). **Conclusion:** The "one-size fits all" approach for thyroid nodule management based on sonographic RSSs should be revisited. Patients older than 60 years have a substantial decrease in the malignancy rate, especially in TR3 nodules, whose malignancy rate is comparable to Bethesda II cytology.

XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Poster Exhibition

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

117129 COULD THE CYTOTOXIC EFFECT OF BISPHENOL A ON BCPAP THYROID CELLS BE DUE TO THE GENOTOXICITY OF THE PRODUCT?

Izabela Fernanda Dal'Bó[1], Elisangela de Souza Teixeira[1], Natassia Elena Bufalo[1], Laura Sterian Ward[1]

[1] Laboratory of Molecular Cancer Genetics, Faculty of Medical Sciences, State University of Campinas, Campinas, SP, Brazil

Introduction: We previously demonstrated that Bisphenol A (BPA) causes important but different cytotoxic effect on normal and papillary thyroid carcinoma (PTC) derived cells. Cell viability and cytotoxicity analysis were performed using the Trypan blue assay on three human cell lines: Nthy-ori 3-1 (normal thyroid follicular cells), TPC-1 (RET mutated cells from PTC) and BCPAP (BRAF mutated cells from PTC). We also measured the metabolic activity using Cell Counting Kit – 8 assay (CCK-8). Different concentrations of BPA, including the Specific Migration Limit (SML – considered the maximum permissible amount of a specific component transferred from the material to a food simulant, under assay conditions) = 1 µg/mL, according to our National Health Surveillance Agency (Anvisa), were tested in 24 and 48 hours. We observed that PTC cell lines were more resistant than the normal lineage to low concentrations of BPA, but this endocrine disruptor caused more than 90% of cell death of normal and both neoplastic thyroid lineages, reducing the metabolic activity and viability in all thyroid cells. However, BCPAP cells were resistant to BPA with less than 10% death rate at SML 1 µg/mL dose. Death rate augmented considerably with higher doses and almost all cells were killed with more than 100 µg/mL. **Objective:** To further investigate the causes of the observed cell death produced by BPA on BCPAP cells. **Methods:** We employed the DNA Comet assay to investigate the level of DNA fragmentation produced on BCPAP cells by BPA at different concentrations including 1 µg/mL; 4 µg/mL; 12.5 µg/mL; 40 µg/mL; and 100 µg/mL at 24 h and 48 h exposure. The percentage of DNA in the tail of exposed cells to different BPA concentrations were compared to a negative (non-BP) and a positive (H2O2) controls. **Results and discussion:** BPA caused very low DNA damage at 24 hours, with a fragmentation of DNA (5.56 + 4.54) similar to the negative control (4.91 + 1.13) when the cells were exposed to BPA at SML concentration. However, genotoxicity was reduced at 48h (17.46 + 3.33) compared to positive control (37.61 + 1.74), suggesting these BCPAP thyroid cells may recover from the chemical genotoxic damage. BPA doses above 4 µg/mL produced increasing DNA fragmentation in a dose-dependent manner at 24 h, but the percentage of DNA fragmentation tended to decrease after 48h in comparison to the positive control, suggesting again a reparatory and/or resistance mechanism. **Conclusion:** The cytotoxic effect of BPA at doses considered acceptable by Anvisa does not result from genotoxicity in BCPAP cells. Increasing concentrations of BPA have a genotoxic effect on BRAF mutated thyroid cells at 24 h of exposure, but these cells become resistant to this effect after 48 h.

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

117150 IDENTIFICATION OF PROTEIN CHANGES IN THE SERUM OF HYPOTHYROXINEMIC PREGNANT WOMEN

Jonathan Núñez[1], Enrique Guzmán Gutierrez[2], Felipe Aguilera[3], Jorge Fuentealba[4], Cecilia Opazo[5], Claudia Riedel[6], Evelyn Liliana Jara Fernández[7]

[1] Departamento de Farmacología, Facultad de Ciencias Biológicas, Universidad de Concepción, Concepción, Chile. [2] Facultad de Farmacia, Departamento de Bioquímica Clínica e Inmunología, Universidad de Concepción, Concepción, Chile. [3] Departamento de Bioquímica y Biología Molecular, Facultad de Ciencias Biológicas, Universidad de Concepción, Concepción, Chile. [4] Departamento de Fisiología, Facultad de Ciencias Biológicas, Universidad de Concepción, Concepción, Chile. [5] Instituto de Ciencias Naturales, Facultad de Medicina Veterinaria y Agronomía, Universidad de Las Américas, Chile. [6] Department of Biological Sciences, Faculty of Biological Sciences, Andres Bello National University, Santiago, Chile. [7] Laboratorio de Inmunofarmacología, Departamento de Farmacología, Facultad de Ciencias Biológicas, Universidad de Concepción, Concepción, Chile.

Introduction: Maternal thyroid hormones (THs) are essential for the appropriate development of the fetus and especially for the brain. The fetus thyroid gland during gestation will not properly function, the maternal thyroid gland will be responsible for adequately supply of THs to the fetus. In fact, the most important maternal TH for the fetus is T4, because T4 cross the placental barrier and achieve the fetus. Hypothyroxinemia is a lesser knowns thyroid hormone deficiency that hypothyroidism in clinical medicine. Maternal hypothyroxinemia is a TH deficiency characterized by low T4 and normal T3 and TSH levels. The hypothyroxinemic pregnant women will not have detectable symptoms given that levels of T3 are normal. However, the lack of T4 will impair irreversible the fetus development. In this study, we aimed to identify and characterize the serum proteome of the hypothyroxinemic women pregnant in comparison with euthyroid pregnant women. **Materials and methods:** We analyzed protein expression in sera from pregnant women diagnosed with hypothyroxinemia at week 12 of gestation compared to sera from euthyroid pregnant women. Written informed consent was obtained from all participants. Differences in the abundance of serum proteins between hypothyroxinemic women pregnant and euthyroid pregnant women were determined using mass spectrometer operated in data-dependent PASEF. Alterations in the abundance of serum proteins were analyzed by Progenesis software. **Results:** We found that sera from hypothyroxinemic pregnant women have a completely different protein expression pattern than sera in euthyroid women pregnant. The proteins identified in the study from hypothyroxinemic women pregnant are known to directly related to the activation of inflammatory pathways. **Conclusions:** The overexpressed proteins were directly related to the activation of inflammatory pathways suggesting that under hypothyroxinemia conditions an inflammatory environment predominates in the pregnant woman, and that could be responsible for the impact that this condition has on the development of the fetus.

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

117071 MOLECULAR CHARACTERIZATION OF DIFFERENTIATED THYROID CANCER IN CHILDREN AND YOUNG ADULTS: A MULTICENTER CROSS-SECTIONAL STUDY IN BRAZIL

Ana Clara Oliveira Tosta Telles[1,2], Juliana Lima Von Ammon[2], Rafael Reis Campos da Matta[2], Gabriel Jeferson Rodríguez Machado[2], Fabyan Esberard de Lima Beltrão[3], Alexandre Rolim da Paz[3], Fábio Hecht Castro Medeiros[4], Guilherme de Castro Lopes[5], Leonardo Freitas Boaventura Rios[6], Bruno da Silva Lisboa[6], Taíse Lima de Oliveira Cerqueira[7], Helton Estrela Ramos[7]

[1] Federal University of Bahia (UFBA), Salvador, BA, Brazil. [2] Postgraduate Program in Interactive Processes of Organs and Systems, Institute of Health Sciences, UFBA, Salvador, BA, Brazil. [3] Lauro Wanderley University Hospital, Federal University of Paraíba, João Pessoa, PB, Brazil. [4] The Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil. [5] Department of Molecular Genetics of Grupo Pardini, Vespasiano, MG, Brazil. [6] State University of Feira de Santana, Feira de Santana, BA, Brazil. [7] Department of Biorregulation, Health Sciences Institute, UFBA, Salvador, BA, Brazil

Introduction: The biological and molecular features underlying pediatric and adult differentiated thyroid cancer (DTC) pathogenesis could be responsible for differences in the clinical presentation and prognosis. Studies in Children and young adult (CAYA) population show that nearly 50% of tumors harbor some type of rearrangement. **Objective:** To determine the prevalence of molecular alterations in paraffin-embedded samples of DTC from children, adolescents and young adults treated at four cancer centers participating in the study. **Methods:** Tumor samples obtained from 79 CAYA patients (age < 21 years) with DTC were retrospectively recruited from four reference centers in the northeast region of Brazil: Hospital Aristides Maltez, IT – *Instituto Integrado Endocrinologia e Cirurgia*, *Hospital Dom Pedro de Alcântara* and *Hospital Universitário Lauro Wanderley*, between January 2010 and March 2021. Demographic information and anatomopathological data were reviewed by a pathologist. Paraffinized tumor DNA was extracted from paraffin-embedded samples and analysis through next-generation sequencing (NGS). In summary: HotSpot panel to determine five gene (KRAS, NRAS, BRAF, EGFR and PIK3CA) point mutations, and panel to identify gene fusions were performed. **Results:** The median age at diagnosis observed in the sample studied was 18 years, with patients ranging between 6 and 21 years. Thirty patients (37.9%) were under 18 years and forty-nine (62.1%) were aged between 18 and 21 years. The vast majority were female (61/79; 77.2%), with only 18 cases male (18/79; 22.8%). Initially, five samples positive for the BRAFV600E mutation and they were not submitted to the evaluation of gene fusions. NGS HotSpot: 21/79 (26.6%) had inconclusive results, 21/79 (26.6%) mutated and 37/79 (46.8%) were wild type for point mutations. Among the mutated, 10/21 (47.6%) cases were positive for BRAF mutation, 08/21 (38.1%) for EGFR, 04/21 (19%) for KRAS, 03/21 (14.3%) for NRAS and 01/21 (4.8%) for PIK3CA, with occurrence of simultaneous point mutations. Of the 10 mutations found in the BRAF gene, 60% of them were V600E. The remaining percentage was characterized by less common genetic alterations in this gene, the so-called BRAFnon-V600E, were identified: 01 BRAFG464R mutation, 01 BRAFG469E and 02 BRAFS467L. NGS gene fusions: 39/74 (52.7%) had inconclusive results, 10/74 (13.5%) were positive for a rearrangement and 25/74 (33.8%) were classified as wild type. Among the 10 positive cases for gene fusions: 03 were of the RET gene; 04 were of the NTRK gene; 02 were of PAX8:PPARG rearrangement; and 01 of the STRN:ALK gene fusion. **Conclusion:** In our CAYA patients: (i) BRAF gene mutations were the most prevalent, followed by EGFR, KRAS, NRAS and PIK3CA, (ii) novel BRAFnon-V600E were identified, (iii) 13,5% had gene rearrangements which were more frequent in subjects under 18 years old. *Supported by Bayer (21641).

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

117072 PAN-TRK IMMUNOHISTOCHEMISTRY FOR THE DETECTION OF NTRK FUSIONS IN CHILDREN AND YOUNG ADULTS DIFFERENTIATED THYROID CANCER PATIENTS

Ana Clara Oliveira Tosta Telles[1,2], Juliana Lima Von Ammon[2], Rafael Reis Campos da Matta[2], Gabriel Jeferson Rodríguez Machado[2], Fabyan Esberard de Lima Beltrão[3], Alexandre Rolim da Paz[3], Fábio Hecht Castro Medeiros[4], Guilherme de Castro Lopes[5], Leonardo Freitas Boaventura Rios[6], Bruno da Silva Lisboa[6], Taíse Lima de Oliveira Cerqueira[7], Helton Estrela Ramos[7]

[1] Federal University of Bahia (UFBA), Salvador, BA, Brazil. [2] Postgraduate Program in Interactive Processes of Organs and Systems, Institute of Health Sciences, UFBA, Salvador, BA, Brazil. [3] Lauro Wanderley University Hospital, Federal University of Paraíba, João Pessoa, PB, Brazil. [4] The Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil. [5] Department of Molecular Genetics of Grupo Pardini, Vespasiano, MG, Brazil. [6] State University of Feira de Santana, Feira de Santana, BA, Brazil. [7] Department of Biorregulation, Health Sciences Institute, UFBA, Salvador, BA, Brazil

Introduction: NTRK gene fusions have been implicated in oncogenic activity across several pediatric and adult cancers. Pan-Trk immunohistochemistry (IHC) staining using clone EPR17341 (Abcam, Cambridge, MA), a rabbit recombinant monoclonal antibody, can assess the protein expression and has been used in several recent studies. Little is known about its utility in differentiated thyroid cancer (DTC) samples from children and young adults (CAYA) patients. **Methods:** Tumor samples obtained from 79 CAYA patients (age < 21years) diagnosed with DTC between January 2010 and January 2021 were retrospectively recruited from four health centers from state of Bahia e Paraíba, Brazil. NTRK gene fusion testing of archival FFPE tumor samples: Pan-TRK IHC staining for TRKA, TRKB and TRKC protein expression were performed using antibody clone EPR17341 (Abcam, Cambridge, MA, USA) and OptiView DAB IHC detection kits on Dako Autostainer Link 48 (Agilent, Santa Clara, CA). NTRK fusion positive cases by NGS that were negative for pan-Trk IHC were re-stained with an increased concentration using a 1:25 antibody dilution. RNA-based NGS Sequencing: All 79 IHC pan-TRK tested samples were than analyzed with a RNA-based next-generation sequencing (NGS) assay in order to confirm IHC pan-TRK result and elucidate fusion partner. NGS was performed using the TST170 kit (Ilumina, San Diego, Ca, USA) and analyzed on a NextSeq 500. **Results:** 61% of the cases were female, the mean age at DTC diagnosis was 18 years. 7 of 79 patients had < 14 years old. Pan-Trk IHC with mAb EPR17341 was performed on 03 NGS positive cases for NTRK and on 64 negative control cases, including 21 cases with strong MAPK pathway (BRAF p.V600E, KRAS/NRAS hotspot) drivers. NGS sequencing: 04/35 valid tests (11,4%) were identified with NTRK gene fusion, (i) 03/35 (8,5%) ETV6-NTRK3 and 01/35 (2,8%) TPR-NTRK1. Pan-Trk IHC: overall, 12 of 79 (15%) cases had indeterminate staining and 3 of 79 (3,8%) cases had positive pan-Trk expression: less than 1% of cells (n = 1) and less than 10% (n = 2). While weak and focal, staining was always nuclear. Pan-Trk IHC was negative in all 4 NTRK NGS-positive cases. 25 of 74 (33,7%) NTRK NGS-negative control cases had concordant negative pan-TRK IHC results. Therefore, our rate of false positive pan-Trk IHC results was 3/25 (12%). The overall results for pan-Trk IHC in our cohort of NGS-negative cases was: (i) sensitivity (0%), (ii) specificity (96%), (iii) positive predictive value (94.7%), (iv) negative predictive value (91%). **Conclusions:** Pan-Trk IHC was not a tissue-efficient screen for NTRK fusions in DTC from CAYA patients. This is the largest cohort of CAYA DTC cases stained with pan-Trk IHC, and it is the first to detail the sensitivity and specificity of pan-Trk IHC regarding the data obtained by targeted RNA-based NGS panel in DTC.*Supported by Bayer (21641/IIR-BR-00018).

BASIC/ENDOCRINE DISRUPTORS AND THYROID FUNCTION

117158 TRICLOSAN EXPOSURE DURING THE INTRAUTERINE PERIOD DISRUPTS THE HYPOTHALAMUS-PITUITARY-THYROID AXIS OF THE OFFSPRING RATS DURING ADULT LIFE

Guilherme Henrique[1], Érica Kássia Sousa-Vidal[2], Evelyn Franciny Cardoso Tavares[1], Renata Elen Costa da Silva[1], Nuha Ahmad Dsouki[1], Gisele Giannocco[1], Caroline Serrano-Nascimento[1]

[1] Universidade Federal de São Paulo, São Paulo, SP, Brasil.[2] Instituto Israelita de Ensino e Pesquisa Albert Einstein, Hospital Israelita Albert Einstein, São Paulo, SP, Brasil

Introduction: Triclosan (TCS) is a bactericide widely used to produce personal care products. TCS exposure has been previously associated with thyroid disorders. Nevertheless, the effect of TCS exposure in the programming of thyroid dysfunctions has never been studied. **Objectives:** To investigate the impact of intrauterine exposure to TCS in the hypothalamus-pituitary-thyroid (HPT) axis of offspring rats during adult life. **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. Both TCS doses used in this study are considered safe by regulatory agencies in Europe and USA. The female and male offspring animals were euthanized at PND90. Hypothalamus, pituitary, thyroid, liver, and serum were collected. Gene and protein expression was evaluated by RT-qPCR and Western Blotting. Thyroid histological analysis was also performed. Global DNA methylation was assessed by ELISA. Chemiluminescence immunoassays were performed to measure TH and TSH serum levels. **Results:** Intrauterine exposure to TCS did not alter the protein content of TRH in the hypothalamus of the male offspring rats. However, TCS induced a significant reduction in the TRH protein content in the hypothalamus of female F1 animals. Interestingly, in both genders, TCS exposure decreased the pituitary expression of Gh, a gene positively controlled by TH. Moreover, there was a significant reduction in TSH serum levels in TCS-exposed male and female F1 rats. In addition, intrauterine exposure to TCS decreased the expression of Slc5a5, Tg, Tpo, Tshr, Foxe1, Pax8, and Nkx2.1 genes in the thyroid of male and female adult offspring rats. There was also a significant decrease in the NIS and TPO protein content in these animals‘ thyroids. Consistently, there was a reduction in the serum levels of T4 in males of the offspring at both doses and a tendency of decrease in the females exposed to the lowest TCS dose. Finally, the thyroid presented misshapen follicles, thyroid follicular cell destruction, and intense inflammatory infiltration in both studied doses. These thyroid morphology alterations were more prominent in male than female offspring rats. In both sexes, intrauterine exposure to TCS increased global DNA methylation and the protein content of methylated histone H3 at lysines 9 and 27 in the thyroid. Moreover, TCS exposure decreased the expression of transthyretin, Dio1, Ugt1a1, and Ugt1a6 in the liver of F1-exposed animals. **Conclusions:** Intrauterine exposure to TCS deregulates thyroid morphology and the synthesis, secretion, and peripheral metabolism of the TH in adult offspring. The data suggest that epigenetic mechanisms commonly involved in the repression of gene transcription are involved in the reduced gene expression of the thyroid gland of these animals. Exposure to TCS increased the susceptibility of males and females to developing thyroid hypofunction during adulthood.

BASIC/HYPERTHYROIDISM

117097 INFLUENCE OF NF-KB CARDIOMYOCYTE INACTIVATION IN THE ISCHEMIA-REPERFUSION MODEL IN HYPERTHYROIDISM

Denival Nascimento Vieira Júnior[1], Nathalia Senger[1], Aline Cristina Parletta[1], Sudhiranjan Gupta[2], Ivson Bezerra da Silva[3], Maria Luiza de Morais Barreto-Chaves[1]

[1] University of São Paulo, São Paulo, SP, Brasil.[2] Baylor University, Texas, USA.[3] Federal University of Paraíba, João Pessoa, PB, Brasil

Introduction: Thyroid diseases are closely related to changes in cardiac function and structure. Hyperthyroidism induces cardiac hypertrophy (CH) as a compensatory response, but it can evolve into a decompensated phenotype with relaxation impairment and arrhythmia. The myocardial ischemia-reperfusion (I-R) injury is associated with cardiomyocyte death and necrosis, which results in functional impairment. Some studies show that hyperthyroidism improves the contractile function of the heart after I-R in rats and mice. Previously, we demonstrated that activation of TLR4/MyD88/NF-kB pathway is crucial to cardiac hypertrophy observed in the hyperthyroidism, however the role of NF-kB in the cardiac function has not yet been elucidated. **Objectives:** To evaluate the role of NF-kB in the cardiac function of hyperthyroid mice after I-R injury. **Methods:** Experimental protocols were approved according to Animal Ethics Committee of the Institute of Biomedical Sciences – USP (nº 8434020221). Male mice (C57BL/6NTac strain or 3M strain containing NF-kB inactivation in the cardiomyocyte) were treated with T3 (7 ug/100 g) for 14 days (intraperitoneal, n = 5-8). The perfusion model of isolated heart was used to evaluate cardiac function. After treatment, the heart was removed and perfused in a Langendorff system and cardiac parameters (Left ventricular developed pressure (LVDP; dP/dt+, dP/dt-, heart rate (HR) and perfusion pressure) were continuously recorded following the protocol of 30 minutes of stabilization, 20 minutes of ischemia and 45 minutes of reperfusion. Data were analyzed by two-way ANOVA or Student’s t test and $p < 0.05$ was considered statistically significant. **Results:** Increased heart weight/body weight and heart weight/tibia length ratio in hyperthyroid groups indicated the CH phenotype (118% WT-T3 and 126% 3M-T3). There was no difference in the body weight between the groups. Preliminary data show increased HR in 3M hyperthyroid mice after I-R (WT control: 88%; WT T3: 89%; 3M control: 89%; 3M T3: 121%), while the LVDP (WT control: 77%; WT T3: 80%; 3M control: 87%; 3M T3: 83%), dP/dt+ (WT control: 84%; WT T3: 20%; 3M control: 89%; 3M T3: 90%), dP/dt- (WT control: 78%; WT T3: 77%; 3M control: 82%; 3M T3: 86%) and perfusion pressure (WT control: 91%; WT T3: 96%; 3M control: 101%; 3M T3: 103%) were not changed. **Conclusion:** Although preliminary, the data suggest a possible involvement of the NF-kB signaling in the cardiac function after I-R.

BASIC/HYPERTHYROIDISM

117017 TSH AT LOW NORMAL RANGE LEVELS ARE ASSOCIATED WITH INCREASE CARDIOVASCULAR DISEASE IN HYPERTENSIVE PATIENTS

Lia Lima de Araujo Cals[1], Simone Matsuda[1], Glaucia Carneiro[1], Maria Tereza Zanella[1], Marcelo Batista[1]

[1] Universidade Federal de São Paulo, São Paulo, SP, Brasil

Objective: To investigate the impact of serum TSH within normal reference range on vascular events in the population of hypertensive patients with higher body mass index (BMI) and dyslipidemia. **Methods:** A cross-sectional study of 463 middle-aged euthyroid hypertension patients (354 women and 109 men, mean age 56.2 ±11.4 years, and TSH between 0.5 and 5.2 mIU/L). The population was divided into tertiles of TSH and for analysis the subjects in the highest tertile [TSH upper normal range (N = 153) = 2.17-5.2 mIU/L] were compared to subjects in the other two tertiles [TSH low normal range (N = 310) = 0.5-2.16 mIU/L]. **Results:** Analyzing data from TSH at low normal range *versus* TSH at upper normal range, it was notice that the prevalence of cerebrovascular event (CVE) as well as cardiovascular disease (CVD) were higher in TSH low normal range group compared to the TSH upper normal range group, reaching statistically significant founds. CVE prevalence was (6.1% *versus* 2.0%, p = 0.034) and CVD prevalence was (12.9% *versus* 7.2%, p = 0.042). Analyzing the population by gender, in women the prevalence of CVD remained higher in the TSH low normal range group compared to TSH upper normal range group (10.8% *versus* 4.4%, p = 0.045), however this association was not demonstrated in men. A statistically significant difference was also found when compared the serum triglyceride levels (136.0 ± 72.7 in the TSH low normal range group *versus* 151.9 ± 74.9 mg/dL in the TSH upper normal range group, p = 0.030). **Conclusion:** The results suggest that low TSH levels within reference range may impact CVE and CVD, particularly in women. These results also reveals the importance of individualize TSH values according to the population under evaluation.

BASIC/THYROID AND PREGNANCY

117119 CHARACTERIZATION OF THYROID HORMONE TRANSPORT IN HTR8/SVNEO TROPHOBLAST CELLS UNDER HYPERINSULINEMIA CONDITIONS

Katherine Roble Riedemann[1], Enrique Guzmán Gutierrez[1]

[1] Universidad de Concepción, Concepción, Chile

Characterization of thyroid hormone transport in HTR8/SVneo trophoblast cells under hyperinsulinemia conditions. The transport of thyroid hormones (HT) guarantees normal fetal development, which includes its metabolism. Before 16 weeks of gestation, the fetus is exclusively dependent on maternal thyroxine (T4), and mild deficiency affects fetal neurological development. The placenta is responsible for regulating the passage of HT through membrane transporters in the trophoblast, and therefore any alteration in the activity and/or expression of thyroid hormone transporters (THT) could have repercussions in the newborn. Conditions prior to pregnancy, such as obesity and insulin resistance, generate a state of pathological hyperinsulinemia in the first trimester of pregnancy, which is related to an alteration in neonatal T4 concentration; however, the potential mechanism is still unknown. Therefore, the hypothesis is that pathological hyperinsulinemia, during the first trimester of pregnancy, modifies the transport of thyroid hormones in trophoblast cells. The main objective is to characterize the expression and activity of thyroid hormone transporters in trophoblast cells of the first trimester of pregnancy, HTR8/SVneo, under hyperinsulinemia conditions. For this, HTR8/SVneo cell cultures were used in the absence and presence of insulin (0-10 nM, 0-24 h), evaluating THT expression by immunocytochemistry. THT activity was assessed by T4 uptake (0-100 µM, 0-180 min) using the Sandell-Kolthoff technique. As results, the expression of THT from the Monocarboxylates 8 and 10 (MCT8-MCT10) family, organic anion transporter polypeptide 1A2 and 4A1 (OATP1A2-OATP4A1) and amino acid transporters LAT1-LAT2 was observed in HTR8/SVneo trophoblast cells. Regarding activity, a decrease in T4 uptake by THT was observed at a concentration of 0.1 nM insulin, while increasing the concentration to 1 nM and 10 nM insulin shows a significant increase in the activity of these transporters. These findings would reveal a regulation of THT by insulin, which could affect the correct development of the fetus during pregnancy.

BASIC/THYROID AND REPRODUCTION

117096 CONSEQUENCES OF HYPOTHYROIDISM AND HYPERTHYROIDISM ON TESTICULAR CIRCADIAN CLOCK EXPRESSION

Marianna Wirthmann Pompeo Flauzino[1], Jeane Maria de Oliveira[1], Ana Flavia de Melo Kaminski[1], Rafaela Paola Eleutério[1], Rodrigo A. Peliciari-Garcia[2], Renata Marino Romano[1], Paula Bargi-Souza[3]

[1] Department of Medicine, State University of Midwest (Unicentro), Guarapuava, PR, Brazil. [2] Department of Biological Sciences, Federal University of São Paulo (Unifesp), São Paulo, SP, Brazil. [3] Department of Physiology and Biophysics, Institute of Biological Sciences, Federal University of Minas Gerais (UFMG), Belo Horizonte, RJ, Brazil

Introduction: Rhythmic variations are present in several physiological processes, including daily oscillations in the pattern of gene expression and cellular function, metabolism and reproduction. The generation of circadian rhythms, either central or peripheral, relies on a set of genes called clock genes, which self-regulate through positive and negative transcriptional feedback loops over a 24-hour period. The circadian clock is directly associated with the functionality of the hypothalamic-pituitary-gonadal axis and disruption on daily pattern are associated to infertility, low gonadotropins and sexual hormones secretion and miscarriages. In parallel, disturbances in the hypothalamic-pituitary-thyroid axis alter the pituitary circadian clock expression, the daily pattern of gonadotropins synthesis and gonadal function in rats. **Objectives:** To characterize whether thyroid hormones modulate the rhythmicity of testis circadian clock and the consequences of hypothyroidism or hyperthyroidism in adulthood on daily expression pattern of testicular function markers. **Methods:** Male Wistar rats (45-50 days old, 180-200 g) were kept on a 12 h/12 h light/dark cycle (light phase: lights on at 06:00 am = Zeitgeber Time – ZT 0; dark phase: red filter Kodak 1A, 0.5 to 1 lux) in a temperature-controlled room (25 ± 2 °C) and had access to food and water ad libitum (CEUA ICB/USP 81, 21-03). The animals were divided into three experimental groups: Control (sham operated plus saline injection at ZTs 2 and 14), Hypothyroid [induced during puberty by surgical thyroidectomy plus 0.03% methylmercaptoimidazole (MMI) and 4.5 mM calcium chloride in the drinking water for 20 days] and Hyperthyroid by T3 intraperitoneal (i.p.) injections [0.75 µg/100 g], twice a day, at ZTs 2 and 14, for 5 consecutive days]. Euthanasia was performed under general anesthesia (60 mg/kg ketamine, 10 mg/kg xylazine and 3 mg/kg acepromazine, i.p.) and the testes were immediately collected, frozen in liquid nitrogen and stored at -80 °C. Transcript expression of the genes [Clock, Bmal1, Per2, Cry1, Nr1d1, Dbp and Star] was performed by reverse transcription followed by real-time PCR. Rpl19 was used as an internal control. One and Two-way ANOVA, and cosinor analysis were used to evaluate the time-of-day-dependent differential expression for each gene/group and their interactions. **Results:** The expression of core clock components exhibits a daily oscillation in testes, as evidenced by the temporal analysis of Bmal1, Per2 and Nr1d1 in euthyroid animals. In addition, the expression of gene that encodes Star enzyme also fluctuates over 24h. Both hypo- and hyperthyroidism impair the daily oscillatory pattern of core clock components and steroidogenesis markers in testes. **Conclusion:** Thyroid hormone disorders affect the rhythmicity of circadian clock in rat testes and markers of gonadal function, which might contribute for the reproduction impairments associated with thyroid dysfunction in male.

BASIC/THYROID CANCER BASIC

117098 A DNA METHYLATION-BASED CLASSIFICATION FOR THYROID NEOPLASMS USING AN UNSUPERVISED MACHINE LEARNING APPROACH

Vicente Rodrigues Marczyk[1], Mariana Recamonde-Mendoza[2], Ana Luiza Maia[1], Iuri Martin Goemann[1]

[1] Unidade de Tireoide, Hospital de Clínicas de Porto Alegre, Porto Alegre, RS, Brasil. [2] Instituto de Informática, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brasil

Introduction: Thyroid neoplasms are a heterogeneous group of tumors for which classification and diagnosis can be challenging. Alterations in DNA methylation are stable epigenetic events that can serve as clinical biomarkers. **Objectives:** We combined microarray DNA methylation data from previous studies to search for unique methylation patterns that could be used to classify thyroid tumors. **Methods:** We employed an unsupervised machine-learning strategy for class discovery to derive a classification based solely on methylation data without any clinical or histological information. We included a total of 810 thyroid samples (n = 256 for discovery and n = 554 for validation), encompassing benign and malignant follicular cell-derived thyroid neoplasms and normal thyroid tissue. **Results:** Our algorithm identified that samples could be separated into three distinct subtypes based on their methylation signature: (1) normal-like, (2) hypermethylated follicular-like, and (3) hypomethylated PTC-like. Follicular adenomas, follicular carcinomas, oncocytic adenomas, oncocytic carcinomas, and NIFTP samples were grouped within the follicular-like cluster, indicating that these pathologies shared numerous epigenetic alterations, with a predominance of hypermethylation events. Conversely, classic PTC and tall cell PTC formed a separate subtype characterized by the predominance of hypomethylated positions. Interestingly, follicular variant PTC (FVPTC) was as likely to be classified as follicular-like or PTC-like, suggesting that this histological subtype might be a heterogeneous group formed by more than one disease rather than a tumor subtype itself. FVPTC with follicular-like methylation patterns were enriched for RAS mutations, whereas FVPTC with PTC-like methylation patterns were enriched for BRAF and RET alterations. **Conclusion:** Our findings have broad implications for understanding thyroid tumor biology and classification. Since our algorithm does not employ any clinical or histological information, our results offer an unbiased classification based exclusively on epigenetic similarity.

BASIC/THYROID CANCER BASIC

117052 ANAPLASTIC THYROID CANCER CELL-SECRETED TGF-B1 INDUCES M2-LIKE MACROPHAGE POLARIZATION OF HUMAN MONOCYTES

Romina Celeste Geysels[1], Maria Victoria Braica[1], Maria Belén Brugo[1], Claudia Gabriela Pellizas[1], Juan Pablo Nicola[1], Sheue-Yann Cheng[2], Laura Fozzatti[1]

[1] Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas, Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.
[2] Laboratory of Molecular Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Rio de Janeiro, RJ, Brazil

Introduction: Anaplastic thyroid cancer (ATC) is a clinically aggressive form of undifferentiated thyroid cancer with limited treatment options. Tumor-associated macrophages (TAMs) constitute over 50% of ATC-infiltrating cells, and their presence is associated with a poor prognosis. The mechanisms of how TAMs promote ATC progression are not clear. We have previously shown that soluble factors secreted by ATC cells induced pro-tumor M2-like polarization of THP-1 cells (human monocytes). However, it remains to be identified which ATC cell-derived soluble factors drive macrophage activation. **Objective:** To investigate the effect of ATC cell-derived transforming growth factor β1 (TGF-β1) on macrophage phenotype. **Methods:** THP-1 cells (human monocytes) were treated with human ATC cell lines 8505C or C643-derived conditioned media (ATC-CM) or recombinant human TGF-β1 protein. THP-1 cell proliferation and polarization were assessed by flow cytometry, RT-qPCR and Western blot analysis. TGF-β1 levels in ATC-CM were quantified by ELISA. Gene expression profiles were obtained from the NCBI Gene Expression Omnibus database and analyzed using bioinformatics analysis. **Results:** Similar to our previous studies using ATC-CM, TGF-β1 treatment significantly influenced the phenotype of THP-1 cells. The changes involved increased expression of CD163 and CLEC7A, which are classic M2 phenotype markers of TAMs. In contrast, the levels of CCL13, another M2 marker, were decreased. TGF-β1 treatment decreased the proliferation of THP-1 cells and increased the mRNA expression of the pro-inflammatory cytokine IL-6. Moreover, we showed that TGF-β1 induced mRNA and protein levels of the transcription factors SNAIL and SLUG. Accordingly, TGF-β1 was detected in ATC-CM (DMEM, 10.42 ± 5.4 pg/mL; 8505C cell-derived CM, 3251 ± 162.5 pg/mL; C643 cell-derived CM, 2752 ± 213.1 pg/mL). We validated the clinical significance of the expression of TGF-β ligands and its receptors in human ATC by analyzing public microarray datasets, and found that the expression of TGF-β ligands as well as their receptors were significantly higher in human ATC tissue samples than in normal thyroid tissues. **Conclusions:** Our findings indicate that ATC cell-secreted TGF-β1 may play a key role in M2-like macrophage polarization of human monocytes possible involving the up-regulation of SNAIL and SLUG transcription factors. Thus, ours results uncovered a novel mechanism involved in the activation of TAMs by soluble factors released by ATC cells. Our findings have provided novel rationale basis for the development of original therapies for ATC.

BASIC/THYROID CANCER BASIC

117059 ANTI-TUMOR ACTIVITY OF SILVER BIONANOPARTICLES IN ANAPLASTIC THYROID CANCER CELLS

Agustina Jaroszewski[1], Maria Victoria Braica[1], Claudia Gabriela Pellizas[1], Paulina Laura Páez[2], Jack Zhu[3], Sheue-Yann Cheng[4], Laura Fozzatti[1]

[1] Centro de Investigaciones en Bioquímica Clínica e Inmunología, Consejo Nacional de Investigaciones Científicas y Técnicas, Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.
[2] Unidad de Tecnología Farmacéutica (Conicet), Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.[3] Cancer Genetic Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health.[4] Laboratory of Molecular Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Rio de Janeiro, RJ, Brazil

Introduction: Anaplastic thyroid cancer (ATC) is a highly aggressive type of thyroid cancer (TC). Currently, no effective target treatments are available that can improve overall survival, with ATC representing a major clinical challenge because of its remarkable lethality. A novel therapeutic modality for the treatment is therefore urgently needed. Recently, metal nanoparticles have been extensively explored in a variety of biological applications because of its versatile properties. Among them, silver bionanoparticles (AgNPs) have emerged as an useful agent for cancer treatment. AgNPs were previously biosynthesized by Pseudomonas aeruginosa culture supernatant with an important microbicide activity. However, their anti-tumor impact in ATC cells is not known. **Objective:** In this study we explored the anti-tumor effects of biogenic AgNPs on human ATC cells derived from patient tumors. **Methods:** ATC cells (8505C, C643, THJ-11T and THJ-16T cells) were treated with AgNPs (0.2–1.25 pM), for 24h. The anti-cancer potential of AgNPs was investigated by the MTT assay. Differentially expressed genes (DEGs) were detected by transcriptome sequencing (RNA-seq). The functional properties of DEGs were characterized by Reactome pathway analyses. Additionally, apoptosis in ATC cells was examined through the expression of cleaved caspase-3 and cleaved PARP by Western blot assay. **Results:** The exposure to AgNPs produced changes in ATC cell lines morphology and significantly decreased cell viability. DEG analysis between control and 0.75pM AgNPs-treated 8505c cells revealed 2242 DEGs, including 1501 upregulated genes and 741 downregulated genes. Among these DEGs, IL1A, MT2A, CTSL, MT1X, SBSN, SMAD7, MMP10, CRYAB, SERPINB2, SERPINE1, TPH2, RASD1, HSPA6, HSPA1A, ARC were identified as the top DEGs in AgNPs treated ATC cells. Reactome analysis revealed that “Attenuation phase”, “HSF1-dependent transactivation”, “NGF-stimulated transcription”, “HSF1 activation”, “Metallothioneins bind metals”, “Nuclear Events”, “Response to metal ions”, “Antagonism of Activing by Follistatin”, “Interleukin-33 signaling”, and “Activation of Matrix” were among the top enriched pathways in our AgNPs treatment comparisons. Additionally, AgNPs induced a significant increase in the expression levels of apoptotic markers cleaved caspase-3 and cleaved PARP in 8505c cells, as compared with untreated control cells. **Conclusions:** Our results indicate that the biogenic AgNPs have remarkable *in vitro* anti-tumor efficacy in ATC cells and provide an understanding of the potential genes and pathways involved in these effects. Therefore, AgNPs represent promising candidates as novel therapeutic agents for ATC. Validation of the gene expression profiles, and elucidation of their molecular mechanisms are being performed.

BASIC/THYROID CANCER BASIC

117134 ASSOCIATION OF CLDN1 OVEREXPRESSION WITH BRAF V600E MUTATION IN THYROID NODULES

Noemi Garcia Magallanes[1], Alejandra Paola Martínez Camberos[2], Marco Antonio Alvarez Arrazola[3], Anette Roxana Gastelum Quiroz[1], Andrea Ross Orozco[1], Fred Luque Ortega[4], Sigfrido Miracle Lopez[5], Eliakym Arámbula Meraz[4]

[1] Universidad Politécnica de Sinaloa, Sinaloa, México. [2] Universidad Autónoma de Occidente, Valle del Cauca, Colômbia. [3] Alvarez & Arrazola Radiólogos, Sinaloa, México. [4] Universidad Autónoma de Sinaloa, Sinaloa, México. [5] Universidad Anahuac México Norte, Ciudad de México, México

Introduction: Papillary thyroid cancer is the most frequent endocrine neoplasm. The V600E change in BRAF is the most common mutation in thyroid cancer (TC), which leads to the over-activation of the MAPK pathway. The interaction of this pathway with the deregulation of the expression of genes that facilitate tumorigenesis like CLDN1 could be useful for decision-making related to surgical removal and the degree of initial resection; however, there is poor information on the association of CLDN1 expression with BRAF V600E. **Objective:** Evaluate CLDN1 gene expression in BRAF mutated and BRAF unmutated thyroid nodules. **Methods:** BRAF genotyping (rs113488022) and CLDN1 expression were evaluated by RT-qPCR in 94 biopsies of thyroid nodules (TC = 48). Clinicopathological data were retrieved to further associations. **Results:** Mutated BRAF thyroid nodules were found to be 7.14 ± 0.293 times more expressed than those without the mutation ($p < 0.001$, N = 94). BRAF V600E mutation was identified exclusively in patients with TC. CLDN1 expression was 41.315 ± 0.554 times higher than those without TC ($p < 0.001$). Heterozygous patients had a change factor of 6.8, whereas mutated homozygotes had a change factor of 7.5 ($p < 0.001$, N = 94). The mean expression of CLDN1 in carriers of the A allele is much higher compared to normal homozygotes ($p < 0.001$). The behavior is maintained when analyzing only within the TC, which could suggest a possible relationship between the mutated allele and the expression of these genes. **Conclusion:** CLDN1 is significantly upregulated in TC patients carrying the BRAF V600E mutation. BRAF V600E is observed only in patients with TC, which could indicate a biological connection between them, which can be explained via MAPK; subsequent studies need to be realized to confirm the associations.

BASIC/THYROID CANCER BASIC

117016 BYSTANDER EFFECTS OF IONIZING RADIATION ON THYROID CANCER CELL

Carla Rodriguez[1], Marina Perona[1], Romina Oglio[1], Adriana Gambetta[1], Karen Nenna[1], Guillermo Juvenal[1], Alejandra Dagrosa[1], Lisa Thomasz[1]

[1] National Atomic Energy Commission, Buenos Aires, Argentina

Introduction: Thyroid cancer (TC) is the most prevalent malignant endocrine system disease. Patients with differentiated thyroid carcinomas have a good prognosis, while some may progress to more aggressive phenotypes such as undifferentiated or anaplastic thyroid carcinoma, which has a very poor prognosis. Ionizing radiation is frequently applied to tumors in patients suffering cancer, with curative or palliative purposes. Nevertheless, tumor resistance and metastasis remain as a clinical concern after radiotherapy. The tumor microenvironment plays a key role in cancer development and progression and ionizing radiation also affects non-tumoral cells in the surrounding tissue. The irradiated cells are believed to communicate signals by affecting the function of non-irradiated cells. We propose to study the expression of the H2O2 generating system, NADPH oxidases, in irradiated cells and the effect of soluble factors derived from irradiated thyroid cancer cells on cell proliferation and migration in non-irradiated thyroid cancer cells. **Methods:** The undifferentiated thyroid carcinoma cell line (8505c) was irradiated at 0, 2, 5, and 8 Gy. After 1, 24 and 72 h, RNA was extracted from the irradiated cells. On the other hand, the supernatants of the irradiated cells were collected after 24 and 72 h post-irradiation. The supernatants were used as conditioned media (CM) for cell proliferation assays (MTT), migration (wounding) and measurement of intracellular ROS levels. **Results:** When analyzing the H2O2 generating systems in the 8505c thyroid cancer line, we observed an increase in the expression of NOX-4 72 h post-irradiation and an increase in the expression of NOX-5 24 hours post-irradiation. We then analyzed the effect of conditioned media from irradiated cells on ROS levels, cell proliferation, and cell migration of non-irradiated cells. We observed that CM after 24 and 72 h post-irradiation produce an 20% and 32% increase of ROS levels ($p < 0.05$). Studies show that CM from irradiated cells after 1 and 24 h have no effect on cell proliferation and migration of non-irradiated cell. CM after 72 h significantly stimulated cell proliferation of non-irradiated cells (1.3-fold at 2 Gy, 1.4-fold at 5 Gy, and 1.4-fold at 8 Gy, $p < 0.01$). Migration studies show that conditioned medium from irradiated cells with 5 Gy and 8 Gy after 76 hours stimulated migration of non-irradiated cells by 1.8 and 2 fold ($p < 0.01$). **Conclusion:** Irradiated cells secreted factors to the medium with pro tumorigenic activity. In addition, irradiation induces the upregulation of NOX4 and NOX5 in the 8505c thyroid cancer cell line.

BASIC/THYROID CANCER BASIC

117033 MOLECULAR CHARACTERIZATION OF TT CELLS FROM MEDULLARY THYROID CARCINOMA: MICRORNAS AND THEIR CONNECTION WITH TUMOR SIGNALING PATHWAYS

Igor de Carvalho Deprá[1], Júlia Rezende Rolim e Silva[2], Célia Regina Nogueira[1], Gláucia Maria Ferreira da Silva Mazeto[1]

[1] Botucatu Medical School (Unesp), Botucatu, SP, Brazil. [2] Institute of Biosciences of Botucatu (Unesp), Botucatu, SP, Brazil

Introduction: Medullary thyroid carcinoma (MTC) is a relatively rare type of cancer, comprising about 5% of tumors affecting the gland. Although infrequent, it can present a very aggressive behavior, with high rates of persistence/recurrence and mortality. Deeper knowledge about the biology of these tumors may provide the establishment of targets for future therapeutic approaches. In this sense, the evaluation of the expression pattern of microRNAs (miRNAs) of tumor cells, as well as their target pathways, could provide greater knowledge about their role in the tumor microenvironment. **Objectives:** To investigate the expression of miRNAs in TT cells derived from CMT and to identify signaling pathways in which they could act. **Methods:** TT cells were initially authenticated and tested for Mycoplasma to confirm cell integrity. They were then cultured to 80% confluence and after being subjected to total RNA extraction, dividing the samples into six biological replicates. The concentration of RNA extracted from the cells was measured in a NanoDrop spectrophotometer. Cellular microRNA expression was determined using the nCounter instrument and the human miRNA panel (Nanostring). Prediction of the targets of the five most expressed miRNAs in cells was performed using TargetScan 8.0, and the enrichment analysis of KEGG pathways used RStudio, with the ClusterProfiler package. Pathways with $p < 0.05$ with Bonferroni correction were considered enriched. **Results:** The five most expressed miRNAs were: hsa-mir-125b-5p, hsa-mir-375, hsa-mir-16-5p, hsa-mir-4454, and hsa-mir-7975. These miRNAs enrich, in a statistically significant way ($p < 0.05$), the TGF-β, Hippo, Transcriptional Misregulation in Cancer, and mTOR pathways, respectively. Such pathways are related to angiogenesis, apoptosis, proliferation, and cell cycle. **Conclusion:** TT cells express microRNAs linked to molecular pathways relevant to CMT tumorigenesis/progression.

BASIC/THYROID CANCER BASIC

117135 SE-L-MET MODULATES MAPK AND PI3K/AKT PATHWAY AND INDUCES APOPTOSIS IN PAPILLARY AND ANAPLASTIC THYROID CANCER

Mariana Teixeira Rodrigues[1,2,3], Ana Paula Picaro Michelli[2], Gustavo Felisola Caso[2], Mirian Galliote Morale[2,4], Eric Chau[5], Biana V. Godin[5], Dorival Mendes Rodrigues-Junior[6], Joel Machado Júnior[7], Rodrigo E. Tamura[2,4], Jamile Calil-Silveira[2,8], Ileana Gabriela Sanchez de Rubio[2,3]

[1] Federal University of São Paulo (Unifesp), São Paulo, SP, Brazil. [2] Thyroid Molecular Sciences Lab, Biological Science Department, Unifesp, São Paulo, SP, Brazil. [3] Structural and Functional Biology Post-graduate Program, Genetic Department, Unifesp, São Paulo, SP, Brazil. [4] Biology-Chemistry Post-graduate Program, Institute of Environmental, Chemical and Pharmaceutical Science, Unifesp, São Paulo, SP, Brazil. [5] Godin's Lab, Department of Nanomedicine, Academic Institute Houston Methodist Research Institute, Houston, TX, USA. [6] Department of Medical Biochemistry and Microbiology, Science for Life Laboratory, Biomedical Center, Uppsala University, Uppsala, Sweden. [7] Biological Science Department, Unifesp, São Paulo, SP, Brazil. [8] Universidade Nove de Julho, São Paulo, SP, Brazil

Introduction: Most thyroid cancer cases are papillary thyroid carcinoma (PTC) and show a good prognosis, but around 10% progress aggressively. Along with anaplastic carcinomas (ATC), both correspond to more than 50% of TC deaths. For these cases, targeted therapies are the only therapeutic option. However, some patients do not respond or become resistant to these therapies or abandon it due to harsh side effects. In this scenario, the search for new treatment options is essential. Selenium, in adequate concentrations, is needed to maintain intracellular redox status and acts as an antioxidant. Nevertheless, higher concentrations of Se were related to cytotoxicity and increased ROS generation and may trigger antineoplastic responses. **Objective:** To evaluate the antineoplastic activity of Se-L-Methionine (Se-L-Met) in monolayer and spheroids cultures of PTC and ATC cell lines. **Methods:** This study used two ATC (KTC2 and HTH83) and two PTC (BCPAP and TPC1) cell lines. Cell viability was determined by PrestoBlue assay, followed by IC50 calculation. Cell migration was assayed by wound healing, cell death by annexin V-FITC, activation of caspase 3/7 by CellEvent assay, ROS generation with the DCF-DA reagent, and modulation of ERK/MAPK and PI3K/AKT pathways by Western Blot. Cell signaling pathways regulation was also analyzed by *in silico* tools PASS, SEA, and GO Biological Process. Spheroids were formed by the hanging drop technique, and viability was measured with PrestoBlue. **Results:** Se-L-Met reduced cell viability in all cell lines. KTC2 and TPC1 had lower IC50 values than HTH83 and BCPAP, which may depend on TP53 status. It also reduced colony formation and induced death by apoptosis, confirmed by the caspase 3/7 activation increasing. Se-L-Met did not increase ROS generation in KTC2 and BCPAP (BRAFV600E), whereas ROS was increased in HTH83 and TPC1 (BRAF wild type). ROS inhibition led to apoptosis reduction in HTH83. *In silico* analysis indicated that Se-L-Met may target MAPK3, linked to the MAPK pathway; MAPK6, involved in AKT phosphorylation; and NOS2, related to both PIK3-AKT and MAPK pathways. Indeed, we confirmed that Se-L-Met reduced pAKT and pERK expression in KTC2. Spheroids of all cell lines were more resistant to Se-L-Met treatment, requiring a chronic treatment of up to 14 days to reduce viability and, for KTC2, also a higher concentration. **Conclusions:** Our study showed that Se-L-Met could have potential antineoplastic activity in PTC and ATC through the induction of apoptosis in all four cell lines, despite the different sensitivities observed. ROS was an important mechanism to promote cell death in BRAF wild-type cells. *In vitro* and *in silico* analysis indicated that Se-L-Met modulates MAPK and PI3K/AKT pathways associated with oxidative stress. Our study also highlights the resistance of the spheroid model to Se-L-Met viability reduction and the importance of using other models in addition to the monolayer culture for drug testing.

BASIC/THYROID CANCER BASIC

117099 TERT PROMOTER MUTATION C228T IS ASSOCIATED WITH MAJOR TRANSCRIPTIONAL ALTERATIONS AND AGGRESSIVE CLINICAL COURSE IN PAPILLARY THYROID CARCINOMAS

Vicente Rodrigues Marczyk[1], Ana Luiza Maia[1], Iuri Martin Goemann[1]

[1] Unidade de Tireoide, Hospital de Clínicas de Porto Alegre, Porto Alegre, RS, Brasil

Introduction: Telomerase reverse transcriptase (TERT) promoter mutations C228T and C250T are found in approximately 12% of papillary thyroid carcinomas (PTC). Their presence has been consistently associated with disease aggressiveness and poor clinical outcomes. Very little is known, however, about the impact of TERT promoter mutations on the transcriptional activity of TERT in PTC and whether both C228T and C250T mutations carry the same oncogenic potential. **Objectives:** We employed data derived from The Cancer Genome Atlas to compare transcriptional alterations and clinical outcomes associated with each of these two mutations (C228T and C250T). **Methods:** Clinical and genomic data were retrieved from the GDC Data Portal. The following inclusion criteria were used: primary tumor sample; tested for TERT promoter mutations; and RNAseq data available. **Results:** A total of 380 PTC with known TERT promoter status were analyzed: 345 (91%) WT, 27 (7%) C228T, and 7 (2%) C250T. Both mutations were associated with increased TERT expression, but the magnitude of the effect was markedly different. C228T tumors showed a 15-fold increase in TERT mRNA levels compared to WT tumors (Fold-change = 15.4; P = 5.3 x 10-42), whereas C250T tumors showed only a 2-fold increase in expression (Fold-change = 15.4; P = 5.3 x 10-42). The C228T mutation was also associated with the activation of multiple signaling pathways controlling cell cycle, cellular division, and extracellular matrix degradation, supporting an important oncogenic role for this mutation. Clinical data demonstrated that the C228T mutation was associated with older age at diagnosis, larger tumor sizes, lymph node invasion, worse ATA risk, and distant metastasis at diagnosis compared to WT tumors. When we compared C228T against C250T tumors, we observed that C228T tumors were marginally associated with larger tumor sizes (P = 0.048), lymph node invasion (p = 0.050), and worse ATA risk (P = 0.034) in comparison to C250T tumors, although the small number of patients with the C250T mutation precludes more robust conclusions. During clinical follow-up, the C228T mutation was associated with metastatic recurrence (P = 0.009) but not with locoregional recurrence (P = 0.6). At 5 years, distant metastasis-free survival was 79.2% for C228T patients compared to 98.4% for those without it. **Conclusion:** Our findings indicate that the C228T mutation has a greater impact on TERT gene expression and is likely to confer greater oncogenic advantages for PTC. Patients with C228T tumors have more aggressive disease in comparison to WT tumors, including a strong association with distant metastasis at diagnosis and metastatic recurrence.

BASIC/THYROID CANCER BASIC

117088 THE POTENTIAL ANTITUMORAL ACTIVITY OF THE NATURAL COMPOUND LYSICAMINE THROUGH NECROSIS IN PAPILLARY AND ANAPLASTIC THYROID CANCER

Mariana Teixeira Rodrigues[1,2,3], Ana Paula Picaro Michelli[2], Gustavo Felisola Caso[2], Mirian Galliote Morale[2,4], Tamiris R. Cipriano Silva[5], Cristiano Raminelli[5], Eric Chau[6], Biana V. Godin[6], Dorival Mendes Rodrigues-Junior[7], Karina Ramalho Bortoluci[8], Rodrigo E. Tamura[2,4], Jamile Calil-Silveira[2,9], Ileana Gabriela Sanchez de Rubio[2,3]

[1] Federal University of São Paulo (Unifesp), São Paulo, SP, Brazil. [2] Thyroid Molecular Sciences Lab, Biological Science Department, Unifesp, São Paulo, SP, Brazil. [3] Structural and Functional Biology Post-graduate Program, Genetic Department, Unifesp, São Paulo, SP, Brazil. [4] Biology-Chemistry Post-graduate Program, Institute of Environmental, Chemical and Pharmaceutical Science, Unifesp, São Paulo, SP, Brazil. [5] Biology-Chemistry Post-graduate Program, Institute of Environmental, Chemical and Pharmaceutical Science, Unifesp, Diadema, SP, Brazil. [6] Godin's Lab, Department of Nanomedicine, Academic Institute Houston Methodist Research Institute, Houston, TX, USA. [7] Department of Medical Biochemistry and Microbiology, Science for Life Laboratory, Biomedical Center, Uppsala University, Uppsala, Sweden. [8] Department of Pharmacology, Unifesp, São Paulo, SP, Brazil. [9] Universidade Nove de Julho, São Paulo, SP, Brazil

Introduction: Although the good prognosis of differentiated thyroid cancer (DTC), about 10% evolve into more aggressive forms and, in conjunction with anaplastic thyroid cancer (ATC), both account for more than 50% of deaths. Despite the new targeted therapies being used, some patients do not respond or become resistant or abandon them due to the severe side effects. Hence the quest for novel therapeutical molecules is needed. Found in several plants, Lysicamine (Lys) is an alkaloid that is cytotoxic to breast and liver cancer cells but has never been tested before for TC models. **Objectives:** To evaluate the antineoplastic activity of Lys in monolayer and spheroids cultures of papillary TC (PTC) and ATC cell lines. **Methods:** Two ATC (KTC2 and HTH83) and two PTC (BCPAP and TPC1) cell lines were employed to evaluate the effect of Lys. After treatment, cell viability was determined by PrestoBlue™ assay, followed by IC50 calculation, cell migration by wound healing, cell death by annexin V-FITC in the presence of the inhibitor of RIPK-dependent necrosis NEC-1, activation of caspase 3/7 by the CellEvent assay, and generation of reactive oxygen species (ROS) with the DCF-DA reagent. Signaling pathways were analyzed by *in silico* tools, such as PASS, SEA, and GO Biological Process. The hanging drop technique was used to form spheroids, which were submitted to chronic treatment for cell viability evaluation with PrestoBlue™. **Results:** Lys reduced about 60% of cell viability after 72h of treatment and showed an anti-clonogenic effect in all cell lines, and reduced cell migration between 18 to 48 hours in TPC1. Moreover, Lys induced cell death by necrosis in all cell lines, while caspase activity was not detected. We observed an increased ROS generation in HTH83 and TPC1 after treatment, but ROS removal did not affect cell death. In KTC2, inhibition of RIPK1/RIPK3 decreased cell death, which could indicate necroptosis. Our in-silico analysis has predicted 82 proteins that Lys could modulate. Among them, Lys could target ERK1 and other MAPK family proteins; RIPK4, an NF-κβ activator and member of RIPK family; and GAPDH, which has an essential role in cell metabolism. Ultimately, spheroids of all cell lines were more resistant to treatment when compared to the monolayer culture. It required a chronic treatment of up to 14 days, and except for TPC1, spheroids were treated with twice the IC50 concentration to reduce viability. **Conclusion:** We report the antitumor potential of Lys for PTC and ATC modulating pathways associated with oxidative stress, cell metabolism, cycle, and death. Our results indicated that Lys leads to cell death due to necrosis, probably through necroptosis which has to be confirmed. Chronic treatment and higher doses were critical to decrease spheroid viability as in monolayer culture. Hence, our study also highlights the importance of using other models in addition to the monolayer culture for drug testing.

BASIC/THYROID CANCER BASIC

117136 THYROID WITH BONE METAPLASIA MIMICKING NEOPLASM: A CASE REPORT

Helvécio Neves Feitosa Filho[1], José Samuel Pereira Filgueira[1], Priscila Natiele Mauricio Alves[1], Imille Maria Alves Prazeres[1], Vitória de Melo Jerônimo[1]

[1] Universidade de Fortaleza, Fortaleza, CE, Brasil

Case presentation: Thyroid cancer is the most common head and neck neoplasm. Nodules with suspicious characteristics require biopsy. With the appearance of bone metaplasia in thyroid cancer, this paper aims to show a clinical case of this variant and discuss it. This is a case report about a 39-year-old woman underwent thyroid biopsy after identifying a tumor in the organ. The collected fragment showed a brown and firm parenchyma at macroscopy with two brownish well-delimited nodular lesions in the right lobe and one well-delimited heterogeneous (whitish portions and brownish portions) nodular lesion with calcification areas in the left lobe. **Discussion:** Histopathological evaluation allowed the identification of follicles of varying sizes and without cell atypia in non-encapsulated nodules. The presence of a focus of bone metaplasia consisting of well-differentiated trabecular bone and without cell atypia was also identified. The morphological picture was therefore compatible with the diagnosis of thyroid bone metaplasia associated with multinodular colloid goiter. This disease, as well as others, such as thyroid hyperplasia, follicular adenoma, papillary thyroid carcinoma and anaplastic thyroid carcinoma, has been reported with histopathological findings of bone metaplasia (BMM), bone marrow metaplasia (BMM), ectopic bone formation (EBF), ossification and extramedullary lesion and finally hematopoiesis (EMH). **Final comments:** Bone metaplasia can occur in papillary carcinoma variants, but maturation of bone in thyroid tumor is rare. According to studies, a common theory is that basic fibroblast growth factor (bFGF) and bone morphogenetic protein 2 play a key role in cell proliferation, bone formation and induction of the local bone process. Considering the exceptionality of this pathogenesis, the present case becomes worthy of attention in order to collaborate with future studies that elucidate the rarity of this manifestation.

BASIC/THYROID CANCER BASIC

117084 WASF3 PROTEIN IS OVEREXPRESSED IN PAPILLARY THYROID CARCINOMA

Lourenço Proença Ruivo[1], Kelly Cristina Saito[1], Victor Piana de Andrade[2], Katia Sakimi Nakadaira[1], Cesar Seigi Fuziwara[1], Edna Teruko Kimura[1]

[1] Department of Cell and Developmental Biology, Institute of Biomedical Sciences, University of São Paulo, São Paulo, SP, Brazil.
[2] A.C.Camargo Cancer Center, São Paulo, SP, Brazil

Introduction: Papillary thyroid carcinoma (PTC) is the most common histotype of thyroid cancer and can be further classified in variants such as: classical, follicular and tall cell variants. Despite showing a good prognosis, some cases may be more aggressive and refractory to conventional treatments. Therefore, finding molecules that can help in a better understanding of the thyroid cancer progression and/or be used as biomarkers is very important. The WASF3 protein participates in changes of cell morphology and cytoskeleton organization, and its overexpression is related to increased migration and invasion in different types of cancer such as ovarian and breast. Nevertheless, the role of WASF3 in thyroid tumorigenesis remains unexplored. **Objectives:** Investigate the expression of WASF3 protein in mice and human PTC tissue. **Methods:** Thyroid tissue was collected from BRAFT1799A transgenic (Tg-BRAF) and wild type (WT) mice at different ages (5, 12, 20, 22, 24, 30, 52, 60 weeks, n = 3 per group), and from PTC (n = 14) and non-tumoral (n = 9) human tissues, according to the animal and human ethics committees CEUA-ICB/USP 2023150720 and CEPSH-ICB/USP CAAE: 59053722.9.0000.5467. The tissues were fixed in 3.7% formaldehyde and embedded in paraffin. Histological sections were stained with H&E to analyze the tumor histopathology and were submitted to immunohistochemical reaction (IHC) to investigate the WASF3 expression. IHC was performed using anti-WASF3 antibody and biotinylated secondary antibody followed by streptoavidin-peroxidase-DAB incubation. The immunopositivity was analyzed under light microscopy as brown staining. **Results:** In mice, Tg-Braf and WT thyroid were positive for WASF3, nevertheless, WASF3 expression was higher in Tg-Braf PTC and increased with age evolution. The Tg-Braf PTC showed increase of WASF3 protein expression at 12 weeks of age, reaching a stronger positivity at 20 weeks. As the WASF3 expression increased in Tg-Braf PTC, a granular pattern of positivity was observed in the cytoplasm and accumulated as a strong expression in the apical region of the thyrocytes. On the other hand, in WT thyroid tissue, a weak and disperse cytoplasmatic staining was observed at all animal ages. In human, WASF3 was positive in PTC and non-tumoral tissues, however, in PTC tissues a higher expression could be observed. In PTC, the staining occurred throughout the cell cytoplasm and several cells show a stronger expression in the apical region. The non-tumoral tissues presented a weak staining and the tendency to form granules. **Conclusion:** The expression of WASF3 protein is detected in all evaluated tissues, however, enhanced expression is observed in human PTC and along PTC development in Tg-Braf mice thyroid. The high expression of WASF3 in thyroid malignancy suggests its participation in the thyroid cancer oncogenesis.

BASIC/THYROID EPIDEMIOLOGY

117110 EPIDEMIOLOGICAL ANALYSIS OF HOSPITALIZATIONS OWED TO TOTAL THYROIDECTOMY IN BRAZIL (PRE AND PANDEMIC PERIODS): ECOLOGICAL STUDY

Helvécio Neves Feitosa Filho[1], Stella Maria Macêdo[1], Júlia Silva Pinheiro Firmino[1], Amanda de Carvalho Assunção[1], Wilson Sanches Sanches Galas[1], Juliana Carneiro Melo[1], Denise Nunes Oliveira[1]

[1] Universidade de Fortaleza, Fortaleza, CE, Brasil

Introduction: Total thyroidectomy is the name of the surgery in which the thyroid is completely removed due to the presence of malignant tumors. The parameters of this surgery may have changed by COVID-19 pandemic in Brazil. This context makes it necessary to carry out an epidemiological analysis of hospitalizations due to the clinical condition in question as a resource to better understand the pre- and post-pandemic scenario, enabling debates to guide the conduct of health professionals in view of the highlighted conclusions. **Objective:** Analyze the impact of the pre- and post-pandemic period on hospitalization for total thyroidectomy and mortality in the Brazilian population. **Methods:** This is an ecological time-series study, in which use was made of the database of the Health Information System (TABNET), made available by the Department of Informatics of the Unified Health System (Datasus). In the Hospital Information System of SUS (SIH/SUS) of MS information was collected on hospitalization for total thyroidectomy. hospitalization, mean value per hospitalization, average days of stay, deaths and mortality rate and covering the pre- and post-pandemic period. The data obtained were analyzed quantitatively, with the aid of software "Microsoft Excel". This work used secondary data from the public domain, thus dispensing with ethical review. **Results:** There was a statistically significant reduction ($p < 0.001$), measured by the independent t-test, in the number of hospitalizations in the pre-pandemic period (22,046), compared to the pandemic period (13,895). Despite the decrease in hospitalizations, the average amount spent per hospitalization increased by 4.6%, being R$ 575.57 in the pre-pandemic period and R$ 602.25 in the pandemic period. Hospitalizations in the pandemic period had a shorter average stay (1.75 days) than those in the previous period (1.92 days). Despite the lower number of hospitalizations, the pandemic period registered 19 deaths, an increase of 11.7% in relation to the previous period, which registered 17. The highest mortality rate ($p < 0.001$) was found in the pandemic (0.14 x 0.09). **Conclusion:** There was evidence of a reduction in the number of hospitalizations and the average length of stay for these hospitalizations due to thyroidectomy, which can be explained by the pandemic period. Despite this, there was an increase in spending per hospitalization and an increase in the number of deaths. It is necessary to carry out further studies on the subject.

BASIC/THYROID EPIDEMIOLOGY

117111 EXPENSES OF BRAZILIAN HEALTH SYSTEM WITH TREATMENTS OF DISORDERS OF THE THYROID GLAND: WHAT CHANGED WITH PANDEMIC?

Helvécio Neves Feitosa Filho[1], Stella Maria Macêdo[1], Maria Vanessa Pereira dos Santos[1], Amanda de Carvalho Assunção[1], Mariana Macêdo Militão Mendonça[1], Juliana Carneiro Melo[1], Denise Nunes Oliveira[1]

[1] Universidade de Fortaleza, Fortaleza, CE, Brasil

Introduction: Thyroid disorders occur when there is some imbalance in the hormonal production of the gland, and can be divided more broadly into two categories: hypothyroidism and hyperthyroidism, without excluding Hashimoto's disease, Graves' disease, goiter and nodules. These disorders are a public health problem that is difficult to detect, since they can easily be confused with other pathologies. This issue often delays the accurate diagnosis and can consequently generate a higher financial cost in treatments and considering how much the pandemic affected the care of the Unified Health System (SUS), the therapy for thyroid-related pathologies may also have undergone changes. **Objective:** Analyze the impact on the expenses of the pre- and post-pandemic period of treatments of disorders of the thyroid gland in the Brazilian Health System. **Methods:** This is a descriptive quantitative study about the expenses of Brazilian Health System with disorders from the thyroid gland and the impact of the COVID-19 pandemic on investment in performing surgical procedures on thyroid based on data obtained by DATASUS from 2017 to 2022. **Results:** Pre-Pandemic Period: in the North, there was a spending peak (SGP) on 10/18, standard deviation (SD) was approximately (apx) R$ 4,262 with an average of R$ 4,927 and, overall, a trend line descending (TLD); in the Northeast there was a SGP on 06/19, SD of R$ 6,474.4, average of R$ 17679 and showing an increasing trend line (ITL); in the Southeast, there was a SGP on 07/18, SD was apx R$ 13,500, with an average of R$ 35,414 and TLD; in the South, there was a SGP on 12/18, the SD was 7,218.8, with an average of R$ 1,2143 and TLD; in the Midwest, there was a SGP on 01/18, the SD of 14,396 with an average of apx R$ 77,800 and TLD. In the pandemic period: in the North, there was a SGP on 01/20, SD was R$ 3,110,4 with an average of R$ 3,909 and ITL; in the Northeast there was a SGP on 07/22, SD was R$ 9,393,1 with an average of R$ 16,213 and ITL; in the Southeast, there was a SGP on 02/21, SD of R$ 16,433, average of R$ 32,200 and showing ITL; in the South there was a SGP on 12/21, SD of R$ 7,303,3, average of R$ 11,801 and showing ITL and in the Midwest, there was a SGP on 05/22, SD was 4,738,6, average of R$ 4,413 and showing TLD. **Conclusion:** The evaluated data allow inferring a decrease in expenses with treatments for thyroid gland disorders with variation between the five main regions of the State. The Midwest was the region with the greatest reduction in spending, equivalent to more than 94% of pre-pandemic values. On the other hand, the South region had the lowest percentage reduction in expenses, equivalent to around 2.8%. It is possible to attribute such differences to different government strategies in each region, as well as to different population health demands. Investigations of this type require greater emphasis, in view of their importance for a better understanding of the impacts of the pandemic in the context of national health.

BASIC/THYROID GENETICS

117120 GENETIC VARIANT INTERPRETATION OVER PROTEIN CHANGES MASKS SPLICING DEFECTS IN THE SODIUM IODIDE SYMPORTER-CODING PRE-MESSENGER RNA

María Celeste Abregú[1], Claudio David Schuster[2], Mariano Martín[1], Romina Celeste Geysels[1], Gerardo Hernán Carro[1], Ana María Masini-Repiso[1], Juan Pablo Nicola[1]

[1] Departamento de Bioquímica Clínica (CIBICI-CONICET), Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina. [2] Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales (IQUIBICEN-CONICET), Universidad de Buenos Aires, Buenos Aires, Argentina

Introduction: The interpretation of disease-causing genetic variants frequently ignores that either exonic or intronic variants can potentially lead to mRNA splicing defect. Exonic variants – including synonyms, missense or nonsense variants based on protein-coding sequence – can affect or create cryptic motifs recognized by the splicing machinery. The prediction of splicing defects is particularly relevant because, if present, a single nucleotide substitution can lead to a very significant effect on the protein, and they can be masked as synonymous or small effect variants if only interpreted at the protein level. **Objective:** To investigate the effect of congenital hypothyroidism-causing SLC5A5 gene variant on sodium iodide symporter (NIS) pre-mRNA splicing. **Methods:** Bibliographic compilation of congenital hypothyroidism-causing SLC5A5 gene variants. Bioinformatic prediction of the effect of variants on central and auxiliary elements involved in NIS pre-mRNA splicing. **Results:** Central elements involved in NIS pre-mRNA splicing, including donor and acceptor splicing sites, branch points, and poly-pyrimidine tracts) were identified. The variants c.970-3C>A and c.1315_1329del were predicted to affect donor and acceptor splicing sites, respectively. Complementary, the variants c.572A>G and c.749G>T, and the variants c.809T>A, c.859_864del, c.1157T>G and c.1593C>G were predicted to generate cryptic donor and acceptor splicing sites, respectively. In line, the variant c.1593C>G was reported to cause a deleterious NIS pre-mRNA splicing defect due to a cryptic acceptor site. Moreover, the variants c.816C>A, c.1106A>T, c.1628G>A, and c.1679C>T were predicted to affect auxiliary elements involved in NIS-pre-mRNA splicing. In line with high performance functional splicing assays, bioinformatic predictions indicated that the variants c.371G>A and c.1183G>A do not affect NIS pre-mRNA splicing. **Conclusions:** Although most disease-causing exonic variants causes changes in the protein-coding sequence, approximately 30% of disease-causing variants lead to pre-mRNA splicing defects. The present study predicted that 36% of congenital hypothyroidism-causing SLC5A5 gene variants, many of them experimentally tested at the protein level, are predicted to be deleterious for NIS pre-mRNA splicing. The results highlight the importance to assess the pathogenicity of novel variants on pre-mRNA splicing, before consider a potential effect on the protein.

BASIC/THYROID GENETICS

117107 IDENTIFICATION OF SELL GENE POLYMORPHISMS THAT MAY AID IN THE DIAGNOSIS AND/OR PROGNOSIS OF THYROID CANCER

Larissa Teodoro Rabi[1], Davi Zanoni Valente[2], Elisangela de Souza Teixeira[1], Karina Colombera Peres[1], Natassia Elena Bufalo[1], Laura Sterian Ward[1]

[1] Laboratory of Cancer Molecular Genetics, Faculty of Medical Sciences, University of Campinas (Unicamp), Campinas, SP, Brazil. [2] Department of Biomedicine, Nossa Senhora do Patrocínio University Center, Itu, SP, Brazil

Introduction: L-selectin is a transmembrane molecule encoded by the SELL gene located on the long arm of chromosome 1 (1q24.2) and has a cleavage site that allows its molecule to exist in soluble form. The cleavage of its structure occurs after its activation and this process may help regulate the inflammatory response. We previously described greater expression of SELL mRNA in malignant than benign thyroid tissues, but we were unable to associate the expression of this gene or the immunohistochemical expression of L-selectin with any characteristic of tumor aggressiveness or patient evolution. However, the expression of L-selectin in thyroid neoplastic cells has been related to a more aggressive behavior of tumors by others. Several DNA polymorphisms are known to have a relationship with disease development, diagnosis and/or prognosis. The SELL gene has 2 missense polymorphisms registered in NCBI polymorphism databank (dbSNP) with minor allele frequency (MAF) higher than 0.1: rs11311498 and rs2229569. **Objective:** To evaluate possible morpho functional, stability and protein flexibility modifications induced by SELL's polymorphisms on L-selectin protein. Methods. We used 11 bioinformatics tools including PredictSNP1.0, MAPP, PhDSNP, PolyPhen-1, PolyPhen-2, SIFT, SNAP, PANTHER, MutPRed2, MuPRO and Dynamut2.0. **Results:** The rs1131498 (F193L) was shown to be neutral in all structural or functional assessment tools. However, decreased protein stability (DeltaDeltaG:-0.3545) and increased protein flexibility (DeltaDeltaSvibENCoM: 0.005 kcal.mol-1.K-1) were observed. The rs2229569 (P213S) was shown to be deleterious in MAPP tool, thus demonstrating to possess a higher probability of structural alterations of the L-selectin protein. In addition, decreased stability (DeltaDeltaG:-0.6147) and rigidification of the molecule (DeltaDeltaSvibENCoM: -0.019 kcal.mol-1.K-1) were observed. So far, there is no literature data correlating the presence of rs1131498 or rs2229569 with characteristics of aggressiveness or any other feature of thyroid tumors. However, our data indicate that these polymorphisms are worth further investigation since they may contribute to thyroid cell dedifferentiation and tumor progression. **Conclusion:** Although our bioinformatics analysis indicate that the SELL gene may contribute to thyroid tumorigenic process, data in the literature are conflicting. Further functional assays and studies in patients with thyroid cancer should confirm the pathophysiological role and clinical utility of the 2 identified polymorphisms as diagnostic and/or prognostic markers.

BASIC/THYROID GENETICS

117165 OVEREXPRESSION OF CLDN1 AND TIMP1 GENE IS ASSOCIATED WITH THE PRESENCE OF PUNCTATE ECHOGENIC FOCI IN THYROID NODULES

Noemi Garcia Magallanes[1], Andrea Ross Orozco[1], Eliakym Arámbula Meraz[2], Anette Roxana Gastelum Quiroz[1], Fred Luque Ortega[2], Marco Antonio Alvarez Arrazola[3]

[1] Universidad Politécnica de Sinaloa, Sinaloa, México. [2] Universidad Autónoma de Sinaloa, Sinaloa, México. [3] Alvarez & Arrazola Radiólogos, Sinaloa, México

Introduction: Ultrasound is the imaging method of choice for assessing thyroid disease. This non-invasive technique, without ionizing radiation, provides information about thyroid nodules, such as the presence of punctiform echogenic foci. This sonographic finding has high sensitivity and specificity for diagnosing thyroid carcinoma. Furthermore, combining this sonographic characteristic and its association with molecular biomarkers, such as the expression of the CLDN1 and TIMP1 genes, may provide more excellent diagnostic value and support clinical-surgical decision-making. CLDN1 is a fundamental gene in the maintenance of epithelial and endothelial junctions, and it also plays a vital role in the maintenance of the cytoskeleton and cell signaling. In addition, TIMP1 exhibits metalloproteinase inhibitory functions and has important implications for physiological processes such as cell growth, survival, apoptosis, cell proliferation, and differentiation. **Objectives:** To analyze the expression of the CLDN1 and TIMP1 genes in thyroid nodules and their association with the presence of punctiform echogenic foci. **Methods:** CLDN1 and TIMP1 gene expression were analyzed in 42 thyroid nodules (malignant = 29, benign = 13) by qPCR-RT. Ultrasound images were obtained with a Siemens Antares ultrasound machine with a high-frequency linear transducer operated by a radiologist with dedicated expertise in thyroid pathology. **Results:** 42 samples of thyroid nodules were analyzed, of which 41 belonged to a female and 1 to male patients. The mean age among the patients was 48.94 ± 2.273. It was found that the CLDN1 gene is expressed 3.68 ± 0.759 times ($p = 0.02$, $N = 42$), and TIMP1 is expressed 1.77 ± 0.422 times in nodules with punctate echogenic foci ($p = 0.042$). **Conclusion:** These findings suggest a relationship between CLDN1 and TIMP1 overexpression and the presence of punctiform echogenic foci in thyroid nodules. The study of biomarkers in thyroid nodules represents an active area of research, and the identification of associations between biomarkers and sonographic findings suggestive of malignancy could contribute to better precision in managing thyroid nodules.

BASIC/THYROID GENETICS

117043 WOULD AUTOPHAGY EXPLAIN BOTH THE CYTOTOXIC EFFECTS OF BPA EXPOSURE ON THYROID CELLS AND THYROID PROLIFERATION?

Elisangela de Souza Teixeira[1], Larissa Teodoro Rabi[1], Karina Colombera Peres[1], Izabela Fernanda Dal'Bó[1], Natassia Elena Bufalo[1], Laura Sterian Ward[1]

[1] Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, SP, Brazil

We previously demonstrated that Bisphenol-A (BPA) causes important cytotoxic effects in thyroid cells, even at concentrations considered tolerable by Anvisa. This endocrine disruptor has also been linked to cell proliferation, may be associated with thyroid nodules and increased cancer incidence rate, but the mechanisms involved in its effect are still unknown. There is evidence that BPA induces autophagy, a biological process that eliminates damaged organelles to maintain intracellular homeostasis in both physiological and pathological processes. The modulation of autophagy plays dual roles in tumor suppression and promotion in many cancers. In addition, autophagy regulates the properties of cancer stem-cells by contributing to the maintenance of stemness, the induction of recurrence, and the development of resistance to anticancer reagents. The human Beclin-1 protein, encoded by the BECN1 gene is a key molecule involved in the initiation of autophagy. Previous studies considered that loss of expression or point mutation may serve as a mechanism of loss of suppressor function in cancers. Furthermore, scarcity of the encoded protein, beclin-1, is often associated with p53 deficiency, suggesting that the function of these two proteins is interrelated. In order to verify whether exposure to BPA could influence autophagy, we developed an interaction network with the main proteins associated with this process and function, starting with beclin-1. Using several *in silico* tools, we analyzed the possible morphofunctional impacts caused by punctual alterations in the maintenance of autophagy and in the proliferation of thyroid cells. A suite of *in silico* STRING interaction network tools, including SIFT, PredictSNP, SNPs&GO, PMut, I-Mutant v3.0 and HOPE, were used to predict and evaluate the functional and structural effects of beclin-1 alterations. Five proteins were selected from this interaction network: PIK3C3, BCL2, BCL2L1, mTOR and p53, which were further submitted to polymorphic analysis of their respective genes. In total, 19 high-risk SNPs sheltering highly deleterious mutations were prioritized, including one in BECN1 (A306S), 9 in PIK3C3 (R799P, D644E, L367S, Y405C, R705W, R768W, G185R, F64S, S12G), 3 in BCL2 (M166T, T122M, G233D), 4 in BCL2L1 (L226P, L108R, R6Q, R6W), one in MTOR (A1513D) and one in P53 (R335C). We found 12 variants (A306S, R799P, D644E, L367S, Y405C, G185R, F64S, S12G, M166T, G233D, L226P and R335C) presenting high probability of being pathogenic and cause structural and functional changes in proteins. These variants presented changes in amino acid size and hydrophobicity which could affect contact with the lipid membrane, affect hydrogen bond formation, and result in the loss of external interactions with amino acids or substances. We suggest that these variants may have a biological effect and may help explain exposure to BPA effects, deserving further investigation.

BASIC/THYROID HORMONE ACTION

117034 DENDRITIC CELL METABOLISM IS TARGETED BY THYROID HORMONE ACTION

Antonella Blanco[1], Dana María Negretti-Borga[1], Elida Nahir Puentes[1], Mariana Pires Teixeira[1], Ana Carolina Donadio[1], María del Mar Montesinos[1], Claudia Gabriela Pellizas[1]

[1] Centro de Investigaciones en Bioquímica Clínica e Inmunología (CIBICI-CONICET), Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

The adaptive immune response is initiated after antigens (Ag) recognition by professional Ag presenting cells, like Dendritic Cells (DC), which integrate these signals and activate T lymphocytes to different effector profiles. The differentiation of DC from murine bone marrow precursors (BMP) with granulocyte and macrophages colony stimulating factor (GM-DC) is one of the *in vitro* models most used to study DC's biology. Our group demonstrated that Triiodothyronine (T3) induced GM-DC's maturation and activation, directing pro-inflammatory and cytotoxic T cells responses, restraining regulatory signals. These results were successfully exploited in T3-stimulated GM-DC (T3-GM-DC)-based antitumor vaccines against melanoma and colon carcinoma in mice. In recent years, it became clear that DC's function in response to stimulus is highly dependent on its cellular metabolism. Maturation signals induce a metabolic reprograming in GM-DC, favoring glycolytic metabolism over oxidative phosphorylation (OXPHOS). Sustained commitment to glycolysis relays on OXPHOS inhibition caused by nitric oxide (NO) produced by inducible NO Synthase (iNOS). On this basis, considering the potential of T3-GM-DC vaccines on cancer immunotherapy, and given the well-known role of T3 as a metabolic regulator, our aim was to assess T3 effects on GM-DC's metabolic programming. GM-DC were differentiated from C57BL/6 mice BMP and stimulated (or not) with T3 (10 nM, T3-GM-DC) for different time points. Glucose and lactate were measured in culture's supernatants (SN) with commercial kits. Glucose uptake was evaluated using the glucose analog fluorescent dye 2-NBDG by Flow Cytometry. Glucose transporter 1 (Glut1) and iNOS expression were analyzed by Western Blot. Nitrite levels were measured in SN by the Griess reaction. Statistics: ANOVA, t test, t test with Welch's correction or Mann Whitney test, $p < 0.05$ was considered statistically significant. Results showed a significant increase in glucose consumption in a time dependent manner after T3 stimulus of GM-DC. This process was accompanied by a higher lactate production in T3-GM-DC ($p < 0.01$), indicating an anaerobic use of the glucose. In addition, T3-GM-DC exhibited a significant increase in both glucose uptake and Glut1 expression ($p < 0.05$) when compared to GM-DC. Besides, T3-GM-DC expressed high levels of iNOS ($p < 0.01$), not detected in GM-DC. In accordance, nitrite levels, indicative of NO production, were significantly increased in T3-GM-DC ($p < 0.05$) compared to GM-DC. This study gives the first insights into the impact of T3 on DC's metabolism, focusing on the glycolytic pathway. In this regard, the increase in the glycolysis may be the consequence of OXPHOS' inhibition caused by NO. Further research under course will help elucidating the DC's metabolic reprogramming induced by T3 and its impact on DC's functionality, giving the basis to develop new strategies to improve immunotherapies by manipulating the immunogenic potential of DC.

BASIC/THYROID HORMONE ACTION

117041 THYROID GLAND DYSFUNCTION AND LIVER MITOCHONDRIAL FUNCTION: AN INTEGRATED APPROACH

Ana Caroline Rippi Moreno[1], Yago Carvalho Lima[1], Érique de Castro[1], Maria Tereza Nunes[1]

[1] University of São Paulo (USP), São Paulo, SP, Brazil

Thyroid hormones (TH) are essential for the regulation of numerous body functions, including energy metabolism, in which their mitochondrial action on liver was one of the first described. Although many studies investigated the effect of T3 on the hepatic mitochondrial function, little is known about the mitochondrial function in TH deficiency condition. The present study investigated important markers of mitochondrial function in liver tissue of hypothyroid, euthyroid and thyrotoxic rats. The study was approved by the ethics committee nº 92/2017 and included 40 Wistar rats weighing ± 250 g, randomly divided into the following groups: (1) Control (C); (2) Hypothyroid (Hypo), which received Methimazole (MMI), 0.03%, dissolved in drinking water, and (3) Thyrotoxic (T3), which received ip injections of 1.5 µg/100g BW of T3. After two weeks, they were euthanized and the pituitary and liver were collected and stored at -80 °C. Pituitary Gh and βTsh gene expression (RT-qPCR) and liver protein content of respiratory chain (NDUFV8, SDHB, CORE2, MTC01, ATP5A and CYCSC), mitochondrial function (UCP2, SOD1, NRF2 and PINK1), fusion (OPA1, MFN1, MFN2) and fission (DRP1) were evaluated by Western Blotting. Citrate synthase activity (Epoch Spectrophotometer) and mitochondrial respiration (Oroboros) were also analyzed. The effectiveness of the interventions was evidenced by βTsh reduction in T3 ($p < 0{,}0001$ *vs.* C and Hypo) and increase in Hypo group ($p < 0{,}0001$ *vs.* C and T3) and by reduced Gh gene expression in Hypo group ($p < 0{,}0001$ *vs.* C and T3). Increased oxygen consumption was observed in T3 group in states two ($p = 0{,}02$ *vs.* Hypo), three ($p = 0{,}03$ *vs.* Hypo and C) and four ($p = 0{,}02$ *vs.* Hypo), suggesting increased ATP synthesis (state 3) and thermogenesis (state 2 and 4). Citrate synthase activity was also increased in T3 group compared to others ($p = 0{,}04$ *vs.* C and $p = 0{,}0004$ *vs.* Hypo), suggesting that T3 enhances mitochondrial mass in hepatocytes. In the Hypo group, we noticed a reduction in CYCS ($p = 0{,}01$ *vs.* T3), and increase in NRF2 ($p = 0{,}01$ *vs.* C and $p = 0{,}04$ *vs.* T3) and PINK1 ($p = 0{,}04$ *vs.* T3) content. The other evaluated proteins showed no statistical difference. NRF2 is an antioxidant transcription factor that upregulates the expression of cytoprotective genes. Under conditions of oxidative stress, NRF2 increases and translocates to the nucleus, inducing the expression of its target genes such as PINK1, which acts by promoting mitophagy and reversing cellular degeneration phenotypes. In conclusion, T3 treatment, even in doses 10 times lower that those usually used to induce thyrotoxicosis, promotes an increase in mitochondrial mass, thermogenesis and ATP synthesis. Interestingly in TH deficiency state (14 days) there is an increase in NRF2-PINK1 signaling pathway, suggesting an adaptive strategy for hepatocyte survival, by protecting them against oxidative stress.

BASIC/THYROID NODULE

117162 BRAF V600E MUTATION AND OVEREXPRESSION OF CLDN1 AND KRT19 GENES ARE ASSOCIATED WITH THE ELASTOGRAPHIC APPEARANCE OF THYROID NODULES

Noemi Garcia Magallanes[1], Anette Roxana Gastelum Quiroz[2], Eliakym Arámbula Meraz[3], Andrea Ross Orozco[2], Fred Luque Ortega[3], Hector Daniel Brito Rojas[2], Marco Antonio Alvarez Arrazola[4]

[1] Universidad Autónoma de Occidente, Valle del Cauca, Colômbia. [2] Universidad Politécnica de Sinaloa, Sinaloa, México. [3] Universidad Autónoma de Sinaloa, Sinaloa, México. [4] Alvarez & Arrazola Radiólogos, Sinaloa, México

Introduction: Ultrasound elastography has been described as a predictor of malignancy, which assesses tissue elasticity. Although ultrasound is a sensitive technique for diagnosing thyroid lesions, it generally lacks specificity in differentiating a benign from a malignant nodule. Elastography can improve its accuracy if combined with tools such as molecular biomarkers. The BRAF V600E gene mutation is the most frequent genetic alteration in papillary thyroid cancer. This mutation activates the mitogen-activated protein kinase (MAPK) signaling pathway, inducing abnormal growth and resistance to pro-apoptotic signals. CLDN1 is a crucial gene in the maintenance of epithelial and endothelial junctions and also plays an essential role in cytoskeletal maintenance and cell signaling. KRT19 has a role in providing epithelial cell structural integrity and tissue markers, as well as cell proliferation, survival, invasion, migration, and apoptosis. **Objectives:** Analyze the relationship between the BRAF V600E mutation, the overexpression of CLDN1 and KRT19, and the elastographic appearance of thyroid nodules. **Methods:** Forty-four thyroid nodules (malignant = 25, benign = 19) were analyzed for expression and mutational analysis using qPCR-RT. Images were obtained with an Antares Siemens ultrasound machine with a high-frequency linear transducer by an experienced radiologist dedicated to thyroid pathology. **Results:** 43 samples of thyroid nodules were analyzed, of which 42 were from female patients and one from male patients. The age average of the patients was 48.94 ± 2.273. We found 29 BRAF V600E negative and 15 BRAF V600E positive. BRAF V600E mutation was associated with the elastographic appearance of thyroid nodules and a significant difference in the expression of the CLDN1 ($p = 0.008$, $N = 43$) and KRT19 ($p = 0.011$) genes based on their elastographic appearance. Expression differences were found between the nodules with a rigid and mosaic appearance, finding an expression factor of 3.43±0.568 in the CLDN1 gene ($p = 0.0238$) and 4.97 ± 0.526 in the KRT19 gene ($p = 0.0143$) in the rigid nodules, and an expression factor of 2.94 ± 0.706 in the CLDN1 gene and 2.25 ± 0.468 in the KRT19 gene in nodules with a mosaic appearance. Also, a difference was found between the nodules with a rigid and soft appearance in which an expression factor of 1.46 ± 0.232 was found in the CLDN1 gene ($p = 0.044$) and -0.21 ± 0.368 in the KRT19 gene ($p = 0.0393$). **Conclusion:** An association was found between the BRAF V600E mutation and the elastographic appearance of thyroid nodules. Furthermore, it was found that the expression of CLDN1 and KRT19 differs between nodules with different aspects of elasticity. Therefore, ultrasound elastography combined with molecular biomarkers may improve accuracy in diagnosing malignant thyroid nodules.

BASIC/THYROID PHYSIOLOGY

117057 SHORT-TERM THYROID HORMONES TREATMENT DO NOT MODULATE INSULIN SIGNALLING PROTEINS IN THE HIPPOCAMPAL FORMATION OF HEALTHY RATS

Johnatas Maldonado Campos[1], Ana Caroline Rippi Moreno[1], Maria Tereza Nunes[1]

[1] Universidade de São Paulo, São Paulo, SP, Brasil

Cognitive performance mediated by the hippocampal formation in the brain depends, among others, of the adequate glucose supply provided by insulin. Thyroid hormones are known to regulate systemic glucose metabolism and may also be involved with this process in the brain. The present study investigated the content of four important proteins in the glucose metabolism (IR, pIRS-1, GSK3 and pGS3) in the hippocampal formation of hypothyroid, euthyroid and thyrotoxic rats (those two latter proteins being involved not only in the insulin signalling pathway, but also hallmarks of neurodegeneration). The study was approved by the ethics committee nº 92/2017 and included 40 Wistar rats weighing ± 250 g, randomly divided into groups: (1) control (C); (2) hypothyroid (Hypo), which received methimazole (MMI), 0.03%, dissolved in drinking water; and (3) thyrotoxic (T3), which received intraperitoneal injections of 1.5 µg/100 g body weight (BW) of T3. The animals weight and feed consumption were measured weekly. After two weeks, they were euthanised and the hippocampal formation was collected and stored at -80 °C. The investigated proteins were analysed by western blotting. Any alteration was observed in the BW among groups. In the literature is reported that hypothyroidism can result in weight gain, due to the accumulation of mucopolysaccharides, which leads to greater water retention, as well as a reduction in basal metabolism and that hyperthyroidism leads to a decrease in BW. However, in addition to the controversy regarding the issue of weight gain in the condition of hypothyroidism, and the increased basal metabolic rate in hyperthyroidism the present study analysed this parameter in animals with only 14 days of MMI/T3 treatment, which is a relatively short period to observe alterations in BW. Regarding the investigated proteins, no significant difference was observed in their content among groups, indicating that short-term period of thyroid dysfunction does not alter insulin signalling pathway and possibly cognitive function. This is very interesting, because we have shown that diabetic rats induced by alloxan presented reduction of insulin signalling and increased expression of GSK3 (protein that leads to tau protein phosphorylation, hallmark of Alzheimer's disease), and that both parameters are recovered to control levels when rats were treated with T3. This is one more indication that thyroid hormone action may differ between healthy and unhealthy individuals, like diabetes, in which thyroid hormones imbalance is often found in combination with other metabolic disturbances. Acknowledging it, ongoing studies from our group are currently investigating the effects of T3, alone and associated with insulin, in the brain of alloxan-induced diabetic rats, aiming to evaluate parameters such as: glucose metabolism/insulin signalling, behaviour and cognitive performance.

BASIC/THYROID SURGERY

117130 RADIOFREQUENCY ABLATION TREATMENT FOR THYROID NODULES AND PRIMARY HYPERPARATHYROIDISM: OUR EXPERIENCE IN THE ARGENTINIAN PUBLIC HEALTH SYSTEM

Gabriel Damiano[1], Jaime Guarin[1], Dante Ovejero[1], Roberto Santoro[1], Mariano Slimel[1], Florencia Rezzonico[1]

[1] Hospital Pirovano, Buenos Aires, Argentina

Introduction: Thyroid nodules are a common pathology in the adult population. Most of these nodules are of a benign nature which depending on their evolution can be treated with multiple interventions or can be followed in time. Surgery has been a to go option when other treatments fail but it has several deterrents mainly a cosmetic concern and the possibility of a for life medication after surgery. RFA is new type of treatment ideal for benign nodules, it can be done as an ambulatory procedure and can provide solutions for the unwanted effects of surgery. **Objectives:** To show our experience using RFA for the first time in the public health system of Buenos Aires City. **Methods:** Since August 2022 until January 2023 we have performed 7 procedures of RFA, 5 thyroid nodules, and 2 patients with primary hiperparathyroidism. The patients had to be over 18 years old, no gender distinction. Thyroid nodules had to have 2 FNA with a result of Bethesda II, we did our own ultrasonography and calculated our own TIRADS and Chamas scores and volume for the nodules. Patients with primary hiperparathyroidsm needed ultrasonography and a sestamibi scintigraphy to locate the adenoma and discard ectopic glands. Every patient had a preoperative rinofibroscopy. All the procedures were done with mild sedation and local anesthesia, we recorded the time of the procedure and the time of ablation. Patients stayed overnight and were discharged 24 hours later. **Results:** Of the 7 procedures we performed none had intra or postoperative complications. Every patient was discharged 24 hours after the procedure. In thyroid nodules we observed that decrease in size (evidenced by the patient) and volume (ultrasonography) was evident after 2 months of the procedure. At the time of this report our oldest patient had 6 months postoperatory and had a reduction of more than 50% of the total volume of the thyroid nodule. Hyperparathyroidism patients underwent Intraoperative PTH measurements and (10 and 30 minutes after ablation) and a postoperative PTH measurement 24 hours later. The descent in PTH values was observed mainly in the measurement done 24 hours later, these patients are still being followed monthly ad haven't showed an increase in PTH values. **Conclusions:** RFA for benign nodules is a new tool that can be offered to patients. There is a worldwide tendency of minimally invasive procedures that can benefit the patient and replace more morbid classic procedures. There is still evidence needed for the use of this method in patients with thyroid carcinoma, but multiple studies are being conducted. Until new evidence can be gathered this is a new secure tool that can benefit patients and give new treatment options to a common pathology.

BASIC/THYROID SURGERY

117132 THYROID GLAND AND TRACHEAL METASTASIS OF RENAL CLEAR CELL CARCINOMA

Gabriel Damiano[1], Jaime Guarin[1], Dante Ovejero[1], Roberto Santoro[1], Mariano Slimel[1], Florencia Rezzonico[1]

[1] Hospital Pirovano, Buenos Aires, Argentina

Case presentation: We present a case report of a female patient, 36 years old, that had a medical history of a total left nephrectomy, 1 year prior to our consult, with a diagnosis of renal clear cell carcinoma and had been admitted several times in the Emergency Room for episodes of shortness of breath. The patient provided ultrasonography studies which showed a right thyroid nodule augmented in size (77 x 29 x 29 mm) with multiple hypoechoic nodules that merge with one another, a left thyroid nodule with multiple images of similar characteristics, and several right side lymphatic nodules at levels III-IV. Tomography showed an enlarged thyroid gland by multiple nodular formations which extended through the anterior wall of the trachea, multiple nodules in both lungs, and a FNA, of a thyroid nodule and lymphatic nodule, that reported a result of Bethesda VI. Thyroid profile showed no alterations in thyroid hormones and a negative result for Calcitonin. Rinofibroscopy showed below the cricoid cartilage an exophytic mass in the anterior wall of the trachea. We performed a total thyroidectomy with a modified lymphadenectomy of levels II through VII, a tracheal resection of the second, third and fourth tracheal rings with an end to end anastomosis and a tracheostomy inferior to this resection. The patient had a 5 day postoperatory without any complications, was decannulated on the sixth day and started oral intake and was discharged on the seventh day. Later the results from pathology were given revealing a right and left thyroid lobe with clear cell carcinoma infiltration, 0/10 lymph nodes with metastases (Group VI), 1/14 lymph nodes with metastases by clear cell carcinoma (Groups II-V), 3 tracheal rings with clear cell carcinoma infiltration on the anterior wall (free margins). **Discussion:** Thyroid nodules are a common among the adult population. Most are of a benign and can be studied with different minimally invasive methods. Metastasic tumors to the thyroid gland are unusual, being reported in some series with less than 1% incidence and are most of the times not synchronous often arising several years after the initial tumor was treated. In this case we see a rare metastatic tumor arising from a previous kidney carcinoma. This type of carcinoma has also been associated with a majority of FNA diagnostic error. Genetic markers have shown to be helpful when trying to identify the origin of this tumors but unfortunately it is not available for all institutions. Multiple imaging studies must be made in case of suspecting a metastasic tumor to the thyroid, to evaluate were the primary tumor or if other interventions will be needed part from treating the thyroid and neck. **Final comments:** Although rare, metastatic tumors in the thyroid gland can pose a difficult diagnostic task even for experienced medical crews. Correct evaluation of this tumors must be made to secure correct treatment of patients and prevent undertreating metastatic disease.

BASIC/THYROID SURGERY

117131 VIDEO ASSISTED TRANSORAL RESECTION OF RETROPHARYNGEAL LYMPH NODE METASTASIS OF PAPILLARY THYROID CARCINOMA

Gabriel Damiano[1], Jaime Guarin[1], Dante Ovejero[1], Roberto Santoro[1], Mariano Slimel[1], Florencia Rezzonico[1]

[1] Hospital Pirovano, Buenos Aires, Argentina

Case presentation: We present a female patient, 56 years old, with a medical history of a total thyroidectomy (2017) because of a papillary thyroid carcinoma. She had no evidence of neck disease at the moment of surgery. After surgery she received iodine treatment (100 mci) and kept close follow-up with her endocrinologist with ultrasonography and thyroglobulin levels. 3 years after surgery there was an elevation in her thyroglobulin levels with no evidence of nodules in the surgical site or lateral compartments of the neck, rinofibroscopy was normal. A PET-CT was conducted that showed a 1cm lymph node in the retropharyngeal space with an SUV of 4.3. The patient was admitted for surgery. We performed a video assisted transoral approach in which we opened the posterior pharyngeal wall finding a single nodule with was excised completely. Introperatory frozen section confirmed papillary inclusions. The patient had a postoperatory without complications and was discharged 72 hours later tolerating oral intake. Afterwards the histological result confirmed fibroadipous tissue with papillary carcinoma infiltration. After surgery the patients thyroglobulin levels were undetectable and have remained this way a year after surgery. **Discussion:** Papillary thyroid carcinoma is the most common malignant tumor of the thyroid gland. Its spread to cervical lymph nodes can vary from 30 to 70%. The most common site of spread is the central compartment (VI) and after this the lateral compartment of the neck, mainly levels III-IV. Retropharyngeal metastasis are unusual, less than 1%, are more related with patients with extensive lateral metastases. They are often asymptomatic and are often found with a persistent or recurring disease. In this case the patient had no evidence of lateral metastasis at the moment of her initial surgery which makes this presentation of retropharyngeal involvement rarer. Ultrasonography usually is limited to help diagnose this lymph nodes, and tomography is limited to the size of the nodule. In this cases PET-CT is very helpful to determine its location. There are multiple ways to approach this lymph nodes varying from traditional cervicotomy all the way to robotic surgery. The decision of which approach must be used depending on the exact location, experience and resources that the surgeon has on his workplace. **Final comments:** This case showed us a rare metastatic site of the most common malignant tumor of the thyroid gland. We could observe the various limitations that exist with the usual tools commonly used to study this pathology, and other diagnostic methods not commonly used in thyroid carcinoma stadification. The various surgical approaches must be individualized to each patient to ensure a correct treatment with the least amount of complications, but are often limited because of the surgeon experience or the resources available.

CLINICAL/HYPERTHYROIDISM

117155 CASE REPORT: THE DIAGNOSTIC CHALLENGE OF PRETIBIAL MYXEDEMA

Rosita Fontes[1], Clarisse Ponte[1], Maria Helane Costa Gurgel Castelo[1], Tamara Cristina Silva Sousa[1]

[1] Diagnósticos da América S.A. (DASA), São Paulo, SP, Brasil

Case report: We report the case of a 75-year-old female patient who presented symptoms of thyrotoxicosis with a five-year evolution. Two years ago, she underwent her first appointment at the clinic. She had a diffuse goiter, and there was no evidence of ophthalmopathy or acropachy. Past medical history was not relevant. Thyroid-stimulating hormone (TSH) was < 0.01 mUI/L (reference interval: 0.4-4.3), and free thyroxine (freeT4) was 5.03 ng/dL (reference interval: 0.7-1.8). The patient was referred for treatment with radioiodine, which was not performed due to the COVID-19 pandemic. Since then, she has been treated with carbimazole. She developed an asymmetric hyperchromatic lesion with an irregular surface and associated stiff edema on both legs, especially on the left. Consultations with several specialists did not clarify the diagnosis. The goiter has been growing, and when she was re-evaluated, using 20 mg/day of carbimazole (CBZ), complementary exams were requested: TSH was < 0.01 mUI/L, and free T4 was 0.5 ng/dL. On thyroid ultrasound (US), was observed a diffuse goiter with heterogeneous texture and a thyroid volume of 217.5 cm^3. After fifteen days without CBZ, 24 hours of radioactive iodine uptake by the thyroid was 20%, and the scintigraphy showed diffuse marker uptake. The US of soft tissues of the pretibial region showed thickened subcutaneous tissue intercalated to hypoechogenic areas, representing edema and loss of interface with the skin, which, in the context of thyroid disease, suggests myxedema related to thyroid disease. **Discussion:** Graves' dermopathy was described in the literature as a complication of Graves' disease. Pretibial myxedema is a rare feature, affecting less than 1.5%-1.7% of hyperthyroid patients. Often it presents as irregular nodular hyperpigmented, indurated, non-pitting edema on bilateral legs. The authors presented a case of pretibial myxedema whose diagnosis was delayed due to the complex asymmetrical presentation. **Final comments:** Due to its rare occurrence, pretibial myxedema differential diagnosis is often difficult. When the presentation is asymmetrical, the diagnosis is even more difficult. However, in the context of autoimmune thyroid disease, it is a diagnosis that should always be kept in mind.

CLINICAL/HYPERTHYROIDISM

117125 CLINICAL AND BIOCHEMICAL PHENOTYPE IN NEWLY DIAGNOSED GRAVES' DISEASE DURING THE SARS-COV-2 PANDEMIC

Jessica Paola Urrutia Miranda[1], Gimena González Buján[1], Ana Gabriela Fernández de Córdova[1], Ana Laura Marchesse[1], Sofia Lanzilotti[1], Patricia Otero[1], Marcos Sergio Abalovich[1], Graciela Nélida AlcaraZ[1], Adriana Marcela Vázquez[1]

[1] Hospital Carlos Durand, Buenos Aires, Argentina

Introduction: Graves' disease (GD) accounts for 80% of thyrotoxicosis in iodine-sufficient areas. Recently, it was reported that its phenotype at diagnosis is becoming milder in these first decades of the 21st century compared to the 20th century. We wonder if stress caused by the SARS-CoV-2 pandemic and the delay in accessing to health centers due to confinement, could have led to more severe clinical features at diagnosis. **Objectives:** To assess whether clinical and biochemical features in newly diagnosed patients with Graves' disease hyperthyroidism differed between the SARS-CoV-2 pandemic period and the previous decade. **Material and methods:** Observational retrospective cohort study of patients with GD. We included 115 patients > 18 years old, with 1st. episode of clinical hyperthyroidism (H+): TSH < 0.1 uIU/mL; FT4 > 1.8 ng/dL and/or T3 > 200 ng/dL, diagnosed at our hospital. Patients were divided in 2 groups: Group 1 (G1; pandemic) diagnosed since 03/2020 to 05/2022 (n = 31) and Group 2 (G2) diagnosed since 1/2010 to 12/2018 (n = 84). G2 patients were selected from a study carried out previously to assess response to antithyroid drugs, which included only patients with good compliance, who had more than 2 years of follow-up. G1 included all the patients who consulted during the pandemic. We analyzed: age, F/M ratio, smoking prevalence, presence of clinical infiltrative ophthalmopathy, estimate of thyroid size by palpation and 131I uptake % at 24 hours, T4, FT4 and T3 measured by QL and TRAb, times increased above the upper limit of the normal range. Statistical analysis: variables were described and analyzed with tests according to their distribution. A $p < 0.05$ was considered significant. **Results:** Thirty one patients diagnosed during the pandemic period (G1) were compared to 84 patients diagnosed from 2010 to 2018 (G2). No significant statistical differences were observed in age at diagnosis, F/M ratio, prevalence of clinical infiltrative ophthalmopathy, thyroid size, 131I uptake at 24 hours, thyroid hormone levels and TRAb titles between both groups. A non-significant increase in the prevalence of smoking during the pandemic was observed (G1 = 41.3% *vs.* G2 = 24%; p = 0.121). **Conclusion:** We did not observe significant changes in Graves' disease phenotype at presentation, between patients who consulted in SARS-CoV-2 pandemic period and those diagnosed during the second decade of the 21st century. Although, a priori, the pandemic could have been associated with more severe clinical and/or biochemical features at time of diagnosis, it has not happened in patients evaluated at our center.

CLINICAL/HYPERTHYROIDISM

117045 FIVE DIAGNOSTIC TESTS FOR DRY EYE DISEASE EVALUATION ON GRAVES ORBITOPATHY PATIENTS: A CROSS-SECTIONAL STUDY

Alana Almeida Rôxo de Carvalho[1], Iane Gusmão[2], Fabyan Esberard de Lima Beltrão[3], Mariluze Sardinha[4], Helton Estrela Ramos[5]

[1] Serviço de Oftalmologia e Oculoplástica do Hospital Santo Antônio, Obras Sociais Irmã Dulce (OSID), Salvador, BA, Brasil. [2] Endocrinology Department, University Hospital, Federal University of Bahia (UFBA), Salvador, BA, Brazil. [3] Lauro Wanderley University Hospital, Federal University of Paraíba, João Pessoa, PB, Brazil. [4] Serviço de Plástica Ocular e Doenças da Órbita, Hospital Universitário Professor Edgard Santos (HUPES)/Empresa Brasileira de Serviços Hospitalares (EBSERH)/UFBA, Salvador, BA, Brazil. [5] Bioregulation Department, Health and Science Institut, UFBA, Salvador, BA, Brazil

Introduction: Graves orbitopathy (GO) is commonly associated with dry eye disease (DED). The GO-DED is multifatorial: (i) increased palpebral fissure with greater exposure of the ocular surface, (ii) instability of the tear film and (iii) tears evaporation and high osmolarity. In addition, lacrimal gland involvement may also occur. However, GO-DED diagnosis is often challenging and tests currently used are far from being perfect because their poor association with subjective symptoms. **Objectives:** To evaluate the characteristics, symptoms related to GO-DED and five standardized diagnostic tests of DED in patients followed up at the Ophthalmology Service/University Hospital/Federal University of Bahia. **Methods:** Demographic and socioeconomic characteristics were collected. The patients underwent clinical investigation: (i) anamnesis, (ii) complete ophthalmological examination (including exophthalmometry and clinical activity score evaluation). Data regarding thyroid disease, treatment, and thyroid function tests (TSH, freeT4 and Anti TSH receptor antibody) were obtained. DED evaluation was performed by: (i) tear film break-up time (BUT), (ii) Schirmer's test, (iii) fluorescein and lissamine staining and (iv) Ocular Surface Disease Questionnaire (OSDI). **Results:** 29 participants with GO were included. The average age of participants was 48.7 ± 10.5 years, with a predominance of females (65.5%). 18/29 (62%) were smokers. Hypertension (55.2%) and *diabetes mellitus* (13.8%) were the most prevalent comorbidities. 23/29 (79.3%) were considered as GO inactive phase (CAS < 3). As for the symptomatology associated with DED: 18/29 (62%) with foreign body sensation, photophobia (16/29, 55.1%), visual blurring (15/29, 51.7%), tearing (14/29, 48.3%). All patients had at least one of the positive diagnostic tests used to DED diagnosis. Schirmer test results. 22/29 (75.9%) had normal values, 4/29 (13.8%) patients had moderate DED and 3/29 (10.3%) had severe DED. The Schirmer test showed a lower median value in patients who were in inflammatory activity [15.2 (9-31.6) mm] *vs.* inactive phase GO patients [17 (10-28) mm]. BUT results. 24/29 (82.7%) patients had severe DED and 5/29 (17.2%) had moderate DED. Among all variables: Corneal fluorescein staining scale (CFSS) had a negative correlation with tonometry (-0.393, p = 0.03), positive correlation between total margin-reflex distance and CAS (0.447, p = 0.02) and between age and CAS (0.569, p = 0.01). OSDI ≥ 20 was associated with tearing (p = 0.01) and low visual activity (p = 0.04). **Conclusion:** Most GO-DED diagnostic tests are still poorly standardized and, in our hands BUT, CFSS and OSDI tools were particularly usefull to identify patients with advanced GO-DED disease.

CLINICAL/HYPERTHYROIDISM

116502 LONG TERM TREATMENT WITH METHIMAZOLE OF OLDER ADULTS WITH THYROTOXICOSIS – RETROSPECTIVE OBSERVATIONAL STUDY

Carina Parisi[1], Martina Laner[1], Lucía Selvaggio[1], Ayelén Ridolfo[1], Vittorio Falco[1], Yessica Ortiz[1], Yanina Morosan Allo[1], Cristina Faingold[1], Gabriela Brenta[1]

[1] Hospital C. Milstein, CABA, Argentina

Introduction: Thyrotoxicosis in older adults can have cardiovascular and bone impacts without appropriate intervention. Although surgery or radioiodine are the alternatives to the conventional 18 months of methimazole (MMI), older adults may be limited by their clinical status to endure surgery or have difficult access to radioiodine administration. Long-term MMI treatment has been proposed in younger patients, but its use has not yet been proven in older adults. **Objectives:** 1) To assess the efficacy of long-term MMI treatment in older adults with thyrotoxicosis. 2) To identify if there are better responders according to the etiology of thyrotoxicosis. **Methods:** A cohort of hyperthyroid patients older than 60 referred to our Endocrine center was retrospectively evaluated. Inclusion criteria were treatment with MMI for more than 18 months after the initial diagnosis, Patients with incomplete information were excluded. Age, gender, body mass index (BMI), etiology (Graves' disease (GD) and toxic nodular goiter (TNG), severity (subclinical or clinical) and symptoms of thyrotoxicosis were assessed at baseline. Thyroid function tests (TSH, Free T4 and T3), thyroid antibodies (TRAB and TPOab) and MMI doses were recorded at baseline and at 24, 36, 48 and ≥60 months of follow-up. The proportion of euthyroidism (TSH 0.3-5 mU/L and FT4 0.8-1,9 ng/dL), subclinical hyperthyroidism (ScH) (TSH < 0.3 mU/L and FT4 0.8-1.9 ng/dL), overt hyperthyroidism (OH) (TSH < 0.3 mU/L and FT4 > 1.9 ng/dL or T3 > 190 ng/dL) and hypothyroidism (TSH > 5 mU/L) was calculated. CHI2 and logistic regression were used to assess the proportion of Euthyroidism during treatment. **Results:** Out of 64 patients aged 81 ± 8.7 years, 84% were females, BMI 25.6 ± 5, 25% were asymptomatic, 29% had weight loss, 19% had palpitations, 5% had nervousness/insomnia, and 5% had tremors. Thirty-nine percent were ScH, and 61% OH. TNG was present in 42%, while 58% were GD. The initial dose of MMI was 17 ± 12 mg and reduced progressively to 7.5 ± 5.5 mg at ≥60 months of follow-up It was found that 64, 53, 62, and 54% of patients were Euthyroid at 24, 36, 48 and ≥60 months under MMI. The proportion of Euthyroidism was higher in the TNG *vs.* GD group in most of the time periods: 84 *vs.* 51% ($p < 0.001$), 75 *vs.* 37% ($p < 0.05$) and 85 *vs.* 33% ($p < 0.001$) at 24, 36 and ≥60 months. The calculated odds ratio for achieving euthyroidism in TNG patients adjusted for age was OR = 4.8 (IC95% 1.3-17) $p = 0.016$; OR = 4.6 (IC95% 1.2-16) $p = 0.019$; OR = 5.3 (IC95% 1.2-22) $p = 0.024$ and OR = 9.3 (IC95% 2.1-41) $p = 0.003$ at 24, 36, 48 and ≥60 months. **Conclusion:** Treatment of thyrotoxic older adults with long-term MMI normalized thyroid function tests in more than half of the patients during all the follow-up period. The dose of MMI required decreased significantly during the study. Patients with TND were the most benefited with this kind of intervention.

CLINICAL/HYPERTHYROIDISM

117085 MANAGEMENT OF GRAVES' DISEASE IN CHILE – RESULTS OF A NATIONAL SURVEY

Alejandra Lanas[1], Nicole Lustig[2], Barbara Zuñiga[1], Varsha Vaswani[1], María Francisca Gajardo[1], Francisco Cordero[1], Katherine Contreras[1], Hernan Tala[3], Pedro Pineda[1]

[1] Hospital Clínico de la Universidad de Chile, Santiago, Chile. [2] Pontificia Universidad Católica de Chile, Santiago, Chile.[3] Clínica Alemana de Santiago, Santiago, Chile

Introduction: Graves' disease (GD) is the most common cause of hyperthyroidism. Geographical differences in the management of this disease have been described in clinical surveys. The choice of diagnostic methods as well as therapy options may vary according to different circumstances. Local availability, costs and patient choice may influence these decisions. There are no studies in our country that allow us to know our local reality. **Methods:** A survey was applied to endocrinologists who manage patients with GD in Chile. Clinical preferences were consulted regarding an index clinical case of GD. The case corresponded to a 42-year-old woman with hyperthyroidism, tachycardia and diffuse goiter. Then we consulted about 2 sub variants: a patient with active Thyroid Orbitopathy (CAS score = 3) and a patient with fertility planning. The survey was sent electronically to endocrinologists who manage patients with hyperthyroidism. Results are expressed as frequencies and average with standard deviations. **Results:** A total of 62 endocrinologist answered the survey. 50.8% worked in a tertiary care center, 29.5% in university clinic, 13.1% in private clinic, and 6.6% in a private practice. Index case. The most frequently requested diagnostic tool was Ac. Anti-TSH receptor (TRAb) (88.7%) followed by thyroid ultrasound (40.3), radioiodine uptake 14.5% and thyroid scintigram 8.1%. All of the participants responded that they would start a beta-blocker drug. 93.5% selected thiamazole as initial therapy and the remaining 6.5% radioiodine. 72.6% indicate the first medical control at 4-6 weeks. Regarding the duration of pharmacological therapy to consider a definitive therapy such as radioiodine or surgery, 29% indicated 12-18 months, 25.8% 6-12 months and 21% 12-18 months. Orbitopathy variant 74% answer intravenous methylprednisolone as treatment of choice, 53.2% would use selenium and 22.6% prednisone. When consulting which therapy is chosen in case of a reactivation of the ocular disease after 6 months of evolution, 66.1% indicate an immunosuppressant, being tocilizumab the main choice, and 37.3% would have indicated a new course of methylprednisolone. In this case, 42.6% chose thiamazole, 9.8% propylthiouracil, 26.2% surgery, and 21.3% radioiodine. In the case of selectin thiamazole, 87.5% switch to propylthiouracil in the first trimester. The vast majority turned to thiamazole in the second trimester (92.9%). **Conclusions:** We present the results of the first survey applied in Chile on the management of GD. The most used therapy was anti-thyroid drugs. This is similar as described for Latin America, but in a higher percentage. The most requested tests are TRAb followed by thyroid ultrasound, which is different from what was reported a decade ago in other regions.

CLINICAL/HYPERTHYROIDISM

117152 RHEUMATIC CARDIOPATHY AND GRAVES'S DISEASE – POSSIBLE LINKS: A CASE SERIES

Laura da Silva Girão Lopes[1], Tamara Cristina Silva Sousa[1], Maria Helane Costa Gurgel Castelo[1]

[1] Diagnósticos da América S.A. (DASA), São Paulo, SP, Brasil

Case presentations: We present nine patients from Brazil who presented with hyperthyroidism after they suffered from rheumatic cardiopathy in a secondary hospital for cardiovascular and pulmonary diseases. All of them had hyperthyroidism due to Graves's disease. In addition, in all patients the rheumatic cardiopathy was diagnosed lately in adulthood. The specific valve lesions are described in Table 1. The clinical diagnosis of hyperthyroidism was confirmed by laboratory studies and the rheumatic disease by echocardiographic findings (Table 1). In four patients, the diagnosis of Grave's disease and cardiopathy were done at the same time. In one patient, there was one year between those diagnoses. Finally, in four patients, hyperthyroidism was diagnosed in less than ten years after the cardiopathy. The clinical treatment for cardiopathy was started immediately, and seven patients underwent surgical repair after discussion with the expert staff. About the hyperthyroidism, all the patients were initially treated with thionamides, and three of them were submitted to radioiodine ablation. Five patients developed pulmonary arterial hypertension (echocardiographic parameters in Table 1). All the patients have been followed focusing on the cardiovascular outcomes. **Discussion:** Rheumatic heart disease remains an important cause of cardiovascular disease in developing countries. Its pathogenesis is incompletely understood, but the activation of the innate immune system is a key element. Graves's disease is the most common cause of hyperthyroidism. In addition, the cardiovascular dysfunction is the major cause for morbimortality in hyperthyroidism. Our case series highlights the need for a deeper knowledge of the cardiovascular consequences of hyperthyroidism in different contexts, including a previous cardiac disease. The hyperthyroidism is considered a reversible cause of pulmonary hypertension. However, the patient's progress when there is another cardiopathy is incompletely known. **Conclusion:** According to the current literature, there is not a causal link between rheumatic heart disease and Grave's disease. On the other hand, the possibility of common elements related to the immune system should be considered.

CLINICAL/HYPERTHYROIDISM

117149 RHEUMATIC CARDIOPATHY AND HYPERTHYROIDISM: REFLECTIONS OF A REPORT OF CASES IN SIBLINGS

Tamara Cristina Silva Sousa[1], Laura da Silva Girão Lopes[1], Maria Helane Costa Gurgel Castelo[1]

[1] Diagnósticos da América S.A. (DASA), São Paulo, SP, Brasil

Case 1: Male, age 44. Rheumatic fever at 12 years old, with polyarthritis and fever. Rheumatic carditis diagnosis at 28 years old. He underwent an aortic biological valve change and a mitral repair at age 32. In November 2008 (age 39), a calcified biological prosthesis with significant stenosis was detected. It was then performed another aortic valve change for a biological bioprosthesis. After the procedure, he presented with delirium, weight loss, goiter and palpitations, having then received the diagnosis of thyrotoxicosis during hospitalization (lab reports on Table 1). The diagnosis was confirmed by another exams: thyroid ultrasound: diffuse and heterogenic goiter; thyroid scintigraphy with a gland sharply hypercaptant. The development of the echocardiographic parameters is also described in Table 1. It is possible to observe a significant increment of the left atrium, in addition to hypertension in the pulmonary artery, with improvement after valve surgery. The patient was treated with thionamides and radiotherapy. **Case 2:** Female, age 44. Mentions frequent odynophagia in childhood, however, denies rheumatic fever diagnosis in that period. A rheumatic cardiopathy was detected at the age of 29, and she underwent a biologic mitral valve change at 36 years old. The diagnosis of hyperthyroidism was confirmed in 2016 (age 38) with weight loss and diarrhea (lab results in Table 1). Another exams: thyroid ultrasound shows heterogenic goiter, with a small nodule. Thyroid scintigraphy: diffuse goiter with hypercaptant gland. Echocardiogram shows a slight systolic dysfunction. The patient was treated with thionamides. **Discussion:** Several evidences suggest a cardiovascular dysfunction as the major cause for morbimortality in hyperthyroidism, manifested mainly by pulmonary hypertension, dilated cardiomyopathy and heart failure. Nevertheless, there is no description of a causal link between the Graves' disease and rheumatic carditis. However, an autoimmune component between those two conditions can be suggested due to the cases described here, especially with siblings. The cardiac dysfunction associated to previous rheumatic cardiopathy probably increased the deleterious consequences of hyperthyroidism over the cardiovascular system. Therefore, it is expected that the reversibility of cardiac dysfunction related a return to euthyroidism, as described in the literature, after the thyroid disease treatment does not occur completely in those patients. **Conclusion:** The reversibility of cardiac alterations after the management of hyperthyroidism is viable and depends on the gravity and degree of the cardiovascular dysfunction's compromise. These cases highlight that rheumatic fever and its complications are still a public health problem in Brazil, especially when associated to the cardiac dysfunction related to hyperthyroidism

CLINICAL/HYPERTHYROIDISM

116907 THYROTOXIC CRISIS AND SARS-COV-2 INFECTION: A CASE REPORT AND LITERATURE REVIEW

Natália Guedes Conte[1], Paula Milena Cavalli[1], Letícia Casagrande[1], Millena Raquel Schiavini[1], Valéria Giacomelli Pansera[1]

[1] Universidade de Caxias do Sul, Caxias do Sul, RS, Brasil

Case presentation: Thyrotoxic crisis (TC) or thyroid storm is a condition there is clinical exacerbation of hyperthyroidism, with a mortality rate of around 10%. We report a 56-year-old Brazilian woman with a history of irregularly treated hyperthyroidism who sought medical attention due to disorientation, tachycardia, anasarca and abdominal pain. The initial physical examination revealed a heart rate of 197 beats per minute with an electrocardiogram showing atrial fibrillation with high ventricular response, a respiratory rate of 22 breaths per minute, oxygen saturation at 98%, blood pressure at 119 x 90 mmHg and temperature body of 37.9 °C. She was initially managed with intravenous metoprolol, methimazole, hydrocortisone, oral atenolol, empiric antibiotic therapy and diuretic therapy with furosemide. Initial thyroid function tests showed: serum free thyroxine (free T4) 3.10 ng/dL (0.7 to 1.48), triiodothyronine (T3) 3.69 ng/mL (0.35 to 1.93), thyrotropin (TSH) < 0.01 mIU/L (0.4 to 4.5), anti-TSH receptor antibody (TRAb) positive at 40 IU/L (up to 0.55 IU/L) and antigen screening for SARS-CoV-2 positive. The patient evolved with mixed circulatory shock, refractory pleural effusion and anasarca, which had a multifactorial component of hypoalbuminemia and heart failure secondary to the thyrotoxic crisis. Following the mentioned clinical management, in addition to thoracentesis, after 21 days of hospitalization, the patient evolved with adequate control of thyroid hormone levels, improvement of systemic congestion and hemodynamic. She was discharged on methimazole and referred to the endocrinology outpatient service. **Discussion:** The main causes of TC are infections and abrupt withdrawal of antithyroid medication. The most common clinical manifestations are tremors, vomiting, diarrhea, dehydration, agitation, delirium, fever and peripheral edema. Furthermore, individuals with TC may experience more severe complications from SARS-CoV-2 infection. The diagnosis is clinical and laboratory findings are elevation of T4 and T3 associated with suppressed TSH levels, which may be associated with hyperglycemia, mild leukocytosis, and altered liver function. Control of thyrotoxicosis must be obtained with the use of beta-blockers, glucocorticoids and thionamides. **Conclusion:** Thyrotoxic crisis is a rare clinical condition that, if not diagnosed and treated early, can be potentially fatal. In the reported case, there is a clinical presentation of Graves' disease with irregular treatment associated with SARS-CoV-2 infection leading to thyrotoxic crisis.

CLINICAL/HYPERTHYROIDISM

117154 TWO UNDIAGNOSED CASES OF COMPLETE AV BLOCK IN HYPERTHYROIDISM

Rosita Fontes[1], Clarisse Ponte[1], Maria Helane Costa Gurgel Castelo[1], Tamara Cristina Silva Sousa[1]

[1] Diagnósticos da América S.A. (DASA), São Paulo, SP, Brasil

Background: Complete atrioventricular (AV) block is an infrequent complication of hyperthyroidism, usually presenting with syncope. We report two cases of patients with hyperthyroidism due to Graves' disease presenting with complete AV block without syncope. **Case reports:** Case 1: MFA, 65 years old, presented at the hospital after falling from a standing height in the bathroom. The fall resulted in a femoral fracture three days before being attended to in an emergency service, and she had a surgical indication. She did not complain about signs and symptoms such as dyspnea, chest pain, or syncope. In the preoperative exams, previously undiagnosed complete AV block and hyperthyroidism were evidenced. Thyroid-stimulating hormone (TSH) < 0.001 mUI/L (Reference interval 0.4-4.3), and free thyroxine (FT4) was 4.09 ng/dL (reference interval 0.7-1.7). A temporary transvenous pacemaker was placed in the right femoral, and treatment with carbimazole (CBZ) and enoxaparin was started. She was discharged without further complications. Case 2: FB, 83 years. Five days before she has seen in the emergency, she presented non-specific malaise, dizziness, nausea, drowsiness, and muscle weakness. She denied chest pain. She was on carbimazole and beta block. TSH was <0.001 mIU/mL, and FT4 was 1.86 ng/dL. In the complementary exams, she presented a complete AV block and was also diagnosed with pneumonia. A definitive pacemaker PPM was installed, antibiotics were administered, and the CBZ dose was adjusted. She was discharged without further complications. **Discussion:** We describe two cases of complete AV block associated with hyperthyroidism: the first one was a previously undiagnosed case of both hyperthyroidism and complete AV block, and the second, with previously diagnosed hyperthyroidism treated still not euthyroid, despite undergoing treatment, and no diagnosed complete AV block. Both were diagnosed when they were seen at the hospital emergency room for reasons other than hyperthyroidism or syncope complaints. The diagnosis provided the installation of a permanent pacemaker and adequate treatment of hyperthyroidism. **Conclusion:** Because a lack of awareness of atypical presentation in patients with hyperthyroidism may delay diagnosis and treatment, recognizing that hyperthyroidism can be one of the reversible causes of complete AV block is essential.

CLINICAL/HYPERTHYROIDISM

117138 USE OF RADIOFREQUENCY ABLATION FOR THE TREATMENT OF AUTONOMOUSLY FUNCTIONING THYROID NODULES

Hugo Fontan Köhler[1], Alex Dufloth Santin[1], Lizieux Matos Fernandes[1], Luiz Henrique de Oliveira Schiavon[1], José Guilherme Vartanian[1], Luiz Paulo Kowalski[1]

[1] A.C.Camargo Cancer Center, São Paulo, SP, Brasil

Introduction: Treatment for autonomously functioning thyroid nodules (AFTN) may be indicated due to compressive symptoms, cosmesis or symptoms of hyperthyroidism. The traditional treatment options are radioiodine therapy or surgery, but, in recent years, radiofrequency ablation (RFA) is gaining ground for benign and malignant thyroid disease treatment. Our objective is to report a case series of patients treated for AFTN using RFA. **Materials and methods:** We report five consecutive patients treated with RFA for AFTN. All patients were submitted to preoperative ultrasonography (USG), thyroid scintigraphy, laboratory evaluation (TSH, fT4, T3, anti-TPOAb, anti-TGAb) and fine needle aspiration cytology. Follow-up strategy consisted of laboratory hormonal evaluation (TSH and fT4) after 30 days with subsequent reevaluation after 180 days or earlier if necessary. Postoperative USG was performed after 180 days for all patients. **Results:** Three patients were females and two males with ages ranging from 22 to 67 years at diagnosis. The size of the nodule ranged from 2.1 to 5.5 centimeters in maximal dimension with mean nodule volume of 20.5 milliliters and three nodules were classified as solid (solid area > 90%) and two as predominantly solid (solid area > 50% and <90%). There was concordance of USG image and thyroid scintigraphy regarding localization in all patients. RFA was performed under USG guidance with sedation with ablation needles with 10 mm active tips. Time of ablation ranged from 14 to 32 minutes. The time of follow-up ranged from 122 to 911 days and post-ablative hormonal evaluation was performed in all patients. At the first evaluation (29 to 42 days), four patients had normal hormonal levels and one patient presented an elevation of TSH (5.24 mU/L). After 60 days, this patient presented a TSH level of 13.15 mU/L and levothyroxine was introduced. All other patients remained with normal thyroid function for, at least, 180 days after ablation. The nodule volume after RFA had a shrinkage ranging from 45% to 82%. No post-ablative complications were recorded. **Conclusion:** RFA for Graves' disease presents an alternative to iodine therapy or surgery. Its morbidity profile is favorable with high probability of disease control and conservation of thyroid function, eliminating the need for hormonal reposition in most patients.

CLINICAL/HYPOTHYROIDISM

117126 CHANGES IN THE DOSE OF LEVOTHYROXINE IN HYPOTHYROID PATIENTS FOLLOWING BARIATRIC SURGERY

María Paz Martinez[1], Maria Victoria Ortuño[1], Antonio Marmo[1], Rudolf Baron Buxhoeveden[1], Francisco Schlottmann[1], María Pía Lozano Bullrich[1]

[1] Hospital Alemán, Buenos Aires, Argentina

Introduction: In previously hypothyroid patients who underwent bariatric surgery with the gastric bypass technique (GBP) for obesity, it is postulated that, due to weight loss, there is a decrease in levothyroxine (LT4) requirements. LT4 dissolves at the gastric level and it is absorbed mainly in the jejunum and upper ileum, therefore, after GBP there would be LT4 malabsorption. Recent studies show that after a GBP, although the LT4 doses in ug per day (ug/d) decrease, the doses in ug per kilogram of body weight (ug/kg) are higher. **Objectives:** 1) To evaluate in previously hypothyroid patients the changes in LT4 doses expressed in ug/kg after undergoing GBP 2) To evaluate in previously hypothyroid patients the changes in the LT4 doses expressed in ug/d after undergoing GBP. **Methods:** Retrospective, descriptive study of previously hypothyroid patients who underwent GBP between April 2010 and October 2020. Data was collected by reviewing medical records. All surgeries were performed in our hospital and by the same surgeon. **Results:** Eleven previously hypothyroid patients who underwent GBP were included, 100% were women, with a mean age of 42.7 years. The most frequent cause of hypothyroidism was Hashimoto's thyroiditis (6 patients). The mean LT4 doses expressed in ug/kg at baseline was 1.2 ug/kg, at 3-6 months it was 1.61 ug/kg and at one year 1.89 ug/kg, with an increase from baseline of 34.2% (p 0.0689) at 3-6 months and 57.5% (p 0.0051) at one year. The mean LT4 doses expressed in ug/day at baseline was 136.2 ug/d, at 3-6 months it was 130.64 ug/d and at one year 131.4 ug/d, with a decrease from baseline of 4.1% (p 0.644) at 3-6 months and 3.5% (p 0.6858) at one year. All patients presented at one year, an increase in LT4 doses expressed in ug/kg, unlike the doses expressed in ug/d in which only 18.18% showed an increase, 54.55% continued with the same doses and 27.27% decreased it. After one year, 4 patients (36.36%) presented LT4 doses expressed in ug/kg greater than 1.9 ug/kg. The mean weight at baseline was 118.3 kg, at 3-6 months it was 83.67 kg and 72.17 kg at one year, with a decrease from baseline of 29.27 % at 3-6 months and 38.99% at one year. **Conclusion:** 1) Although our work is limited by a low number of patients, we were able to detect the greater LT4 requirement expressed in ug/kg one year after the GBP was performed. 2) Despite the fact that GBP is described as one of the causes of refractory hypothyroidism, only one third of the patients developed it after one year of follow-up. 3) We conclude that due to the fact that all patients required higher LT4 doses expressed in ug/kg at one year of follow-up compared to baseline, malabsorption secondary to GBP exceeds the lower LT4 requirements due to the weight loss. 4) We stress the importance of monitoring patients undergoing GBP due to the malabsorption of drugs and nutrients that can develop over time.

CLINICAL/HYPOTHYROIDISM

117167 COGNITIVE LEVEL IN CHILDREN AND ADOLESCENTS WITH CONGENITAL HYPOTHYROIDISM: THE IMPACT OF MATERNAL SCHOOLING

Juliana Cristina Romero Rojas Ramos[1], Julita Maria Pelaez[1], Torquato Domingos[1], Gabriela de Carvalho Kraemer[1], Fernanda Bora Moleta[2], Adriane André Cardoso-Demartini[2], Julienne Ângela Ramires de Carvalho[2], Cássio Slompo Ramos[3], Rosana Marques Pereira[2], Luiz de Lacerda[2], Suzana Nesi França[2]

[1] Fundação Ecumênica de Proteção ao Excepcional, Curitiba, PR, Brasil.[2] Complexo Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, PR, Brasil.[3] Pontifícia Universidade Católica do Paraná, Curitiba, PR, Brasil

Introduction: Early and adequate levothyroxine replacement greatly improves neurodevelopment in children with congenital hypothyroidism, however subtle deficiencies have been reported, mainly related to disease severity and treatment variables. Environmental stimuli, partially represented by mother schooling, have rarely been considered in previous studies, particularly in low socioeconomic status populations. **Objectives:** To evaluate the cognitive level of children and adolescents with congenital hypothyroidism detected by neonatal screening in a reference center in Southern Brazil, followed under the same treatment protocol. To correlate intelligence quotient (IQ) scores with age at start of treatment, disease severity (pretreatment thyroxine and free thyroxine values) and maternal schooling. **Methods:** Review of medical records for data collection, and psychometric assessment of patients with the Brazilian version of the Wechsler Abbreviated Scale of Intelligence, from which estimate Verbal IQ scores (VIQ), Performance IQ scores (PIQ) and Full-scale IQ scores (FSIQ) were obtained. Scores were correlated with neurocognitive determinant variables, such as age at start of treatment, initial thyroxine (T4) and free thyroxine (fT4) levels and maternal schooling. **Results:** Eighty-six patients (65.1% females), aged 6-17 years, detected between 2002 and 2015 were evaluated. Thyroid dysgenesis was the most prevalent etiology (71.2%), with 37.5% ectopy and 12.5% athyreosis. Median T4 and fT4 at diagnosis were 3.6 µg/dL (0.0 - 16.0) and 0.53 ng/dL (0.0 - 1.95), respectively; median age at start of treatment was 15.0 days (3-30). Maternal schooling (n = 80): 1.3% of illiteracy, 63.7% with basic education and/or incomplete secondary level. Mean VIQ and PIQ scores were 85.5 (±10.7) and 84.8 (±10.7), respectively, with no significant difference between them. Mean FSIQ scores was 83.0 (±9.9) and intellectual deficit (FSIQ < 70) was identified in 5.8%. FSIQ scores showed no correlation with age at start of treatment or pretreatment T4 and fT4, but correlated significantly with maternal schooling level ($p = 0.006$). **Conclusions:** Treatment provided by neonatal screening programs is essential for preventing intellectual disability, however, better IQ scores depend mainly on the socioeconomic status of the population, which is represented by maternal schooling.

CLINICAL/HYPOTHYROIDISM

117143 DIAGNOSIS OF CENTRAL HYPOTHYROIDISM IN A PATIENT WITH PAPILLARY THYROID CARCINOMA

Luciana Sant'Ana Leone de Souza[1], Erika Ferreira Rodrigues Tesa[1], Ayla Loranne Rebelo Canário Santiago[1], Rebeca Valentim Casar[1], Rebecca Souza Sessa Dantas[1], Geisa Barreto Santos de Souza[1], Adriana Silva Andrade[1], Aimée Teieira dos Santos Meira[1], Fabiana Freire Almeida Silva[1], Jeane Meire Sales de Macedo[1], Ana Luísa Castro Nascimento de Aguiar[1], Gabriela Silveira Teixeira Dantas Mathias[1], Gabriel Fernando Dultra Bastos[1]

[1] Centro de Referência Estadual para Assistência ao Diabetes e Endocrinologia (Cedeba), Salvador, BA, Brasil

Case presentation: We present the case of a female patient, 51 years old, diagnosed with papillary thyroid carcinoma who during follow-up discovered to have central hypothyroidism. The patient underwent a total thyroidectomy in 2014, with anatomopathological study presenting single lesion of 1.1 cm on its longest axis. Initial thyroglobulin (Tg) was 0.38 with TSH 26.8.TNM staging T1BN0M0, with low initial risk of recurrence. Then, radioiodine (RAI) therapy dose of 100 mCi was administered in 2015. Whole-body imaging performed after RAI indicated absence of regional or distant metastases. In 2013, restaging was carried out by levothyroxine T4 (LT4) interruption. Blood tests showed Tg of 0.18, no anti-thyroglobulin antibody and TSH 10.98. Due to excellent response, it was decided to reduce LT4 dose gradually: from 150 mcg to 75 mcg. However, TSH remained suppressed: between 0.02 and 0.07 mU/L, at six different dosages. This condition led to suspicion of central hypothyroidism and pituitary MRI was requested, with an image suggestive of partially empty sella. Other pituitary axes were evaluated: FSH 12.7 mUI/mL, LH 22.8 mUI/mL, estradiol 232 pg/mL, IGF-1 175 µg/L (94-252); Prolactin: 9.3 ng/mL; morning serum cortisol 5.5 ug/dL. Clinically, patient's menstrual cycles was regular, with report of dizziness and an episode of syncope. For better evaluation of corticotrophic axis, an insulin tolerance test was performed, which was negative for deficiency of this axis. Glycemia and serum cortisol were measured at times 0, 15', 30', 45', 60' and 90' with the respective **Results:** 85 mg/dL and 6.46 ug/dL ; 59 mg/dL and 6.15 ug/dL; 35 mg/dL and 8.66 ug/dL; 37 mg/dL and 13.62 ug/dL; 40 mg/dL and 23.44 ug/dL; 93 mg/dL and 30.75 ug/dL. Therefore, it was concluded that it was isolated central hypothyroidism. **Discussion:** The central hypothyroidism usually occurs sporadically, at any age, but it is rare, with an estimated prevalence of 1:20,000 in the general population. In most cases, it is accompanied by deficiency in other pituitary axes. Central lesions such as macroadenomas are the main cause, but it is also associated with empty sella. Isolated idiopathic TSH or TRH deficiency are rare causes of central hypothyroidism. Previous reports reveal that empty sella was present in 50% of patients with isolated idiopathic deficit of TSH secretion. Rarely, it was associated with pituitary microadenoma. **Conclusions:** In case presented, identification of persistently suppressed TSH, despite reduction in LT4 dose, allowed suspecting of central hormone deficiency, as well as evaluation of other pituitary axes. Impaired TSH secretion is often associated with secretion of other pituitary hormones. It has been reported, however, that isolated idiopathic TSH deficiency is rare.

CLINICAL/HYPOTHYROIDISM

117068 PITUITARY HYPERPLASIA SECONDARY TO PRIMARY HYPOTHYROIDISM

Salma Ali El Chab Parolin[1], Cássio Slompo Ramos[1], Julia Machado do Carmo Kneip Lopes[1], Julia Faversani Barreiros Cruz[1]

[1] Pontifícia Universidade Católica do Paraná (PUC-PR), Curitiba, PR, Brasil

Case presentation: A 29-year-old man, with a history of gastritis and paresthesia in left upper limb and asthenia. Physical examination: acromegalic facies, BMI = 21,7 kg/m², normotensive status, without thyroid, visual and muscle strength abnormalities. Admission tests: Brain magnetic resonance image (MRI) = increased volume of adenohypophysis with extension to suprasellar cistern, discreetly compressing the optical chiasm and homogeneous enhancement by contrast material, dimension: 11 x 13 x 11 mm. Diagnostic suspicion was GH-producing hypothalamic adenoma. Laboratorial tests: TSH > 500 mIU/mL (RV 0,38-5,33 mIU/mL), free-T4 = 0,5 ng/dL (RV 0,54-1,50 ng/dL); antiperoxidase antibody = 32 UI/mL (RV < 5 UI/mL); FSH = 2,50 mIU/mL (RV 1,27-19,26); LH = 2,83 mUI/mL (RV 1,24-8,62 mUI/mL); prolactin = 12,27 ng/mL (RV 2,64-13,13 ng/mL); testosterone = 357,60 ng/dL (RV 175-781 ng/dL); 24 hours urinary cortisol = 126,9 ug/24 h (RV 58-403 ug/24 h) e IGF-1 = 173 ng/mL (RV 83-271 ng/mL). The final diagnosis was primary hypothyroidism. Levothyroxine (LT4) 200 ug/day was performed. New hormonal tests were obtained after 4 months: TSH 0,08 mIU/mL and free-T4 1,51 ng/dL. The LT4 dose has been changed to 175 ug/day and another tests were done after 4 months: TSH 1,49 mIU/mL and free-T4 livre 0,95 ng/dL. MRI after hypothyroidism control: normal volume and small hypocaptant image on the right wing of the adenohypophysis after contrast administration, measures = 4 mm x 4 mm. The good levothyroxine treatment evolution led to the diagnosis pituitary hyperplasia due to primary hypothyroidism. **Discussion:** Pituitary hyperplasia (PH) is defined as a non-neoplastic increase in the number of one of the cell types present in the pituitary gland. Prolonged primary hypothyroidism is one of the pathological causes of this condition and occurs due to the lack of negative feedback. It occurs more usually in young and females' gender, otherwise our patient was male. Only 25% of patients with pituitary hyperplasia due to primary hypothyroidism present compression signals of increase pituitary volume, our patient did present anyone. The paresthesia could an unspecific hypothyroidism symptom that can occur int this case. The acromegalic facies was due to hypothyroidism causes deposition and accumulation of mucopolysaccharides in the dermis and other tissues and may rarely lead to acromegalic changes in extremities and face this signal lead to hypothesis of GH-producing hypothalamic adenoma. The objective of this report was to demonstrate the presence of pituitary hyperplasia in a male patient with body characteristics suggestive of acromegaly. Laboratory investigation confirmed the presence of primary hypothyroidism and ruled out acromegaly. Treatment with LT4 was instituted, leading to regression of pituitary hyperplasia. **Final comments:** This case illustrates the importance of an appropriate investigation in patients with PH, as well as discussing the pathophysiology and treatment of this disease.

CLINICAL/HYPOTHYROIDISM

116920 USE OF THYROID HORMONES IN HYPOTHYROID AND EUTHYROID PATIENTS: A 2022 THESIS QUESTIONNAIRE SURVEY OF MEMBERS OF THE LATIN AMERICAN THYROID SOCIETY (LATS)

Jessica Fernanda Cassemiro[1], Veronica Ilera[2], Stella Batalles[3], Adriana Reyes[2], Endre V. Nagy[4], Enrico Papini[5], Petros Perros[6], Laszlo Hegedüs[7], Helton Estrela Ramos[1]

[1] Department of Bioregulation, Health & Science Institute, Federal University of Bahia, Salvador, BA, Brazil.[2] Department of Endocrinology, Hospital Ramos Mejía, CABA, Argentina.[3] Cardiovascular Institute of Rosario, Santa Fé, Argentina.[4] Division of Endocrinology, Department of Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary.[5] Department of Endocrinology and Metabolism, Regina Apostolorum Hospital, Rome, Italy.[6] Department of Endocrinology, Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom.[7] Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark

Introduction: Inconsistencies in the medical management of hypothyroidism have been reported between endocrinologists in different countries. THESIS surveys (Treatment of Hypothyroidism in Europe by Specialists: an International Survey) have explored this issue among European physicians. **Objective:** To identify the attitudes of Latin American (LA) thyroid specialists towards the use of thyroid hormones in hypothyroid and euthyroid individuals. **Methods:** An e-mail with an invitation to participate in an online survey investigating practices use of thyroid hormones was sent to members of LATS. **Results:** 81/446 (18,2%) individuals completed the questionnaire. All were clinically active and 70.4% treated > 100 patients/year. Levothyroxine (LT4) was the treatment of choice for hypothyroidism for all respondents. A low number (9/81) prescribed LT4+LT3 or LT3. More than half of the respondents would consider LT4 use in biochemically euthyroid patients: infertile women with elevated anti-thyroid antibodies (46.9%, resistant depression (17.3%), growing goiter (12.0%). Female more frequently than male physicians would favor use of thyroid hormones in infertile women ($p = 0.003$), as would participants treating more than 50 patients/year ($p = 0.02$). In various conditions that might interfere with the absorption of LT4, most participants preferred tablets over liquid formulations or soft gel capsules, and would not consider switching formulations in patients with persistent symptoms. 71.6% of respondents would never use supplementation with selenium or iodine in addition to LT4. Although 39.5% would never use LT4+LT3 combination therapy in symptomatic biochemically euthyroid patients due to low quality evidence for benefit, almost half of physicians would favor this indication. Most respondents (61.7%) reported that persistence of symptoms despite normal TSH is rare and that the prevalence has remained stable over the last five years. Psychosocial factors, comorbidities and the burden of chronic disease were considered the top three explanations for this phenomenon. 16/81 participants (19.8%) declared having a diagnosis of hypothyroidism. Among them, 3 (18.8%) experienced excessive tiredness under treatment. Only 13.9% of physicians would consider L4+LT3 therapy for themselves in case they were diagnosed with hypothyroidism **Conclusion:** For LA thyroid specialists, LT4 tablets are the treatment of choice for hypothyroidism, even in the presence of conditions affecting bioavailability. A significant proportion would use LT4 in some groups of euthyroid individuals, contrasting local practice guideline indications. Although recognizing low evidence for benefits of LT4+LT3 in euthyroid symptomatic patients, almost half of specialists would consider this indication. In contrast to a number of European countries, LA respondents report a low and unchanged proportion of dissatisfaction among their patients over the last five years however.

CLINICAL/IODINE DEFICIENCY

117095 IODINE SUFFICIENCY EVALUATION IN PREGNANT WOMEN ASSISTED BY THE PUBLIC HEALTH SYSTEM IN CURITIBA, SOUTH OF BRAZIL

Paulo Cesar Zimmermann Felchner[1], Tatiane Mendes Boutin Bartneck Telles[2], Leonardo Ivantes Mesa[1], Thyago Proença de Moraes[1], Cleo Otaviano Mesa Júnior [1]

[1] Pontifícia Universidade Católica do Paraná (PUC-PR), Curitiba, PR, Brasil.[2] Universidade Federal do Paraná (UFPR), Curitiba, PR, Brasil

Introduction: Iodine is essential for the production of thyroid hormones and its deficiency during pregnancy may be associated with unfavorable obstetric outcomes, including fetal neurodevelopmental disorders. The median urinary iodine concentration (UIC) is an indicator of the iodine intake of a given population. Iodine intake in Brazil is considered adequate or even above adequate in some populational studies, however there are few studies in the pregnant population. **Objectives:** To determine the iodine status in a pregnant women population assisted by the public health system in Curitiba, South Brazil. **Methods:** Urine samples were collected from women beginning antenatal care in each one of the ten health districts in the city. The pregnant population attended by the public health system was selected proportionally to the number of pregnant women in each health district. The samples were collected in the morning, between 5 and 8 a.m. The iodine urinary concentration was measured using inductively coupled plasma mass spectrophotometry. Classification of the iodine status was made according to the World Health Organization. **Results:** Of the 225 women studied, 47 % (n = 108) has urinary iodine concentration indicating iodine deficiency. 7 (3.11%) patients has UIC < 50 µg/L, 46 (20.44%) 50-99 µg/L, 55 (24.44%) 100 to 149 µg/L. Sufficiency of iodine, 150 to 249 µg/L, was found in 64 (28,44%) pregnant women, 47 (20.89%) had iodine status classified as more than adequate with urinary iodine concentration 250 to 499 µg/L and 6 (2.67%) UIC > or = 500 µg/L. The median urinary iodine concentration of the study population was 158,2 µg/L. **Conclusion:** The pregnant population in this study had normal median urinary iodine concentration. Almost half of the pregnant women had UIC classified as insufficiency.

CLINICAL/THYROID AND COVID-19

117078 CONVERTED TO GRAVES' DISEASE WITH ORBITOPATHY FROM HYPOTHYROIDISM AFTER VACCINATION AGAINST COVID-19: A CASE REPORT

Lenara Golbert[1], Ana Carolina Falck de Almeida[2], Gabriel Mesquita[2], Giovana Bissaco Brancalione[2], Izadora Meira Rogério[2], Ismael Cavalheiro Carvalho[2]

[1] Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Santa Casa de Porto Alegre, Porto Alegre, RS, Brasil. [2] UFCSPA, Porto Alegre, RS, Brasil

Case presentation: Female, 31 years old, white, diagnosed with subclinical hypothyroidism due to Hashimoto's Thyroiditis in 2015 on treatment with Levothyroxine. On July 30th and September 24th of 2021, she received the mRNA COVID-19 vaccine. Approximately 10 days after that, she started with thyrotoxicosis manifestations and laboratory analysis demonstrated thyroid stimulating hormone (TSH) < 0.05mUI/L (reference 0.45-4.5 mUI/L) and free T4 of 2.0 ng/dL (reference 0.9-1.7 ng/dL). The levothyroxine was withdrawn, but the patient continued with thyrotoxicosis and presented Graves' orbitopathy. Repeat laboratory investigation showed TSH suppression, normal levels of T3 and free T4, with positive thyrotropin receptor antibody (TRAb 5.9U/L, reference inferior to 1.0U/L). Methimazole treatment was used for 6 months, euthyroidism was achieved after 2 months, but there was no regression of the orbitopathy. **Discussion:** Case reports of new onset or relapse of Graves' disease occurring after receiving the SARS-CoV-2 vaccines, predominantly RNA-based, had been published. It is noted that the symptoms appear generally a few days after the first or second dose of vaccination, as the case presented here with thyrotoxicosis started 10 days after the second vaccine dose. Also, our case is a young female, similar to the background epidemiology of Graves' disease and reported cases developed after the COVID-19 vaccination. Interestingly, we showed a case who converted to hyperthyroidism from hypothyroidism after vaccination and presented with moderate Graves' Orbitopathy, which has few cases related to the literature. Although a recent population-based Study in Hong Kong didn't demonstrate an association of COVID-19 vaccination with CoronaVac or BNT162b2 with instability in thyroid status or an increased risk of adverse outcomes, this topic is still under investigation, and studies from Latin America are needed. **Final comments:** Although Graves' disease is not commonly associated with COVID-19 vaccination, it is important to be vigilant of precipitation or exacerbation of autoimmune thyroid disease after vaccine administration. Further studies are needed to clarify the epidemiological and pathological association between COVID-19 vaccines and thyroid autoimmunity.

CLINICAL/THYROID AND COVID-19

117166 LABORATORY EVALUATION IF THYROID FUNCTION IN PATIENTS WITH COVID-19: A VALUABLE TOOL FOR PROGNOSTIC EVALUATION OVERLOOKED IN THE REAL WORD

Nicole Mesquita Model[1], Nicolle Moreira[1], Anne Beatriz da Cruz[1], Larissa Teodoro Rabi[2], Karina Colombera Peres[1], Natassia Elena Bufalo[1]

[1] School of Medicine, Max Planck University Center (UNIMAX), Indaiatuba, SP, Brazil. [2] Department of Biomedicine, Nossa Senhora do Patrocínio University Center, Itu, SP, Brazil

Patients with COVID-19 exhibit an exacerbation of the inflammatory response, including high levels of cytokines and glucocorticoids. As a result, the entire hypothalamus-pituitary-thyroid (HPT) axis is profoundly affected, resulting in changes in serum thyroid hormones (TH) levels. In mild-to-moderate illness, the most typical laboratory finding is a reduction in serum T3 and, remarkably, no concomitant increase in TSH. Accordingly, this condition has been named "low T3 syndrome". A series of studies indicated the prognostic value of this condition in various pathologies. Recent prospective studies confirmed a tight correlation between the TH levels during hospital admission and disease severity and mortality also among COVID-19 patients. To verify the use of serum TSH levels, FT4 and T3 in patients with COVID-19 and its correlation with prognostic evaluation. Data collection and analysis was retrospectively performed employing medical records of patients admitted to the intensive care unit (ICU) and in the hospital wards of Indaiatuba Hospital between 03/2020 and 12/2022. This descriptive, longitudinal study involved a cohort of 2,016 patients diagnosed with COVID-19. Only 60 out of the 2,016 patients had thyroid function data requested at admission and during the hospitalization and were included in this study. Demographical and clinical information on all patients were obtained by their charts, including age, gender, serum TSH, FT4, T3, and antithyroid antibodies. Of those 60 (30 women and 30 men, 58.75 ± 14.4 years old) medical records analyzed, a total of 10 patients (16.3%) had previous thyroid dysfunction: 9 cases presented hypothyroidism and 1 had hyperthyroidism. Of those, 4 had elevated TSH levels, 1 evolving to death, and 1 had decreased TSH levels and had a good evolution. In those patients with hypothyroidism, 4 had elevated FT4 and evolved to a critical state, requiring mechanical ventilation, and 2 patients evolved to death. Only 3 patients had serum T3 data described, of which 1 patient presented low level of T3 and needed to be transferred to the ICU, evolving with desaturation, need for mechanical ventilation and use of vasoactive drugs, and subsequently death. Therefore, characterization of low T3 syndrome was difficult since serum T3 levels were not requested in those patients. In contrast, of the 50 patients who did not have thyroid dysfunctions, 6 presented high TSH levels, 2 of whom died, and 12 had low TSH levels, 4 of whom died. Nineteen patients had elevated FT4 and 8 died. The patients with TH normal levels were admitted only to the hospital wards, with a good evolution and were discharged. Although serum TH levels are associated with illness severity and mortality, thyroid function utility as a valuable tool for prognostic evaluation has been largely overlooked in the real world, suggesting the need for awareness of its importance among health professionals, especially those who work with critically ill patients.

CLINICAL/THYROID AND COVID-19

117140 OUTCOMES OF ELECTIVE THYROIDECTOMIES IMPACTED BY THE COVID-19 PANDEMIC: A RETROSPECTIVE COHORT STUDY

Ana Luiza Gomes Sgarbi[1], Yasmin Abrahão[2], Barbara Klyslie Kato[3], Lara Hossepian Hojaij[4], Giovana Irikura Cardoso[1], Flávio Carneiro Hojaij[2]

[1] Faculdade de Medicina de Marília (FAMEMA), Marília, SP, Brasil. [2] Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo, SP, Brasil. [3] Universidade Municipal de São Caetano do Sul (USCS), São Caetano do Sul, SP, Brasil. [4] Faculdade de Ciências Médicas da Santa Casa de São Paulo (FCMSCSP), São Paulo, SP, Brasil

Introduction: On March 11th, 2020, the World Health Organization (WHO) declared the COVID-19 pandemic. In Brazil, the first case was confirmed in São Paulo on February 26th, 2020, followed by another case confirmed in Rio de Janeiro on March 5th. By March 17th, community transmission was already evident in the country. Given this emergency scenario, there was a decrease in the number of elective surgeries, as the material and human resources of the health system were largely reallocated to meet the demands of patients affected by COVID-19. **Objectives:** The purpose of this research is to assess the incidence of the SARS-CoV-2 virus in patients who underwent elective thyroidectomies during the COVID-19 pandemic. Given this consideration, we included the test results of patients pre-operatively, including the prognosis of these cases. This analysis will provide relevant information for the management of patients who undergo thyroidectomy and SARS-CoV-2 infection, as well as promote prevention measures for safer surgeries during the pandemic. **Methods**: This retrospective, descriptive cohort study was conducted using the analysis of electronic medical records of patients undergoing thyroidectomy from April 2020 to October 2021, corroborating the time of the pandemic, with surgeries performed by a single Head and Neck surgeon. Out of 152 patients with elective surgeries analyzed, only thyroidectomy procedures were included, without gender distinction and with the widest age range. Thus, 80 patients were selected and evaluated regarding the pre, intra, and postoperative outcomes. **Results:** From April of 2020 to October of 2021, 80 thyroidectomies were performed. All patients consented to undergo a COVID-19 PCR test before the surgery to decrease contamination risk, respecting hospital guidelines. Out of the 80 patients, 35 (43.75%) had papillary carcinoma, 6 (7.5%) had goiter, 6 (7.5%) had a combination of goiter and papillary carcinoma, and 1 (1.25%) had medullary carcinoma, finally, 32 patients (40%) had benign adenomatous goiter (Bethesda III and IV). Out of 80 thyroidectomy procedures (either total or partial), only 2 (2.5%) were postponed due to a positive COVID-19 test result before hospital admission. The surgery was later completed without any issues. One patient had a positive COVID-19 PCR 8 days after operation. None of the patients experienced any complications or infections during their hospital stay. **Conclusion:** The findings of this study highlight the safety of thyroidectomy as a surgical procedure during the COVID-19 pandemic, once hospitals, healthcare professionals, and patients adhered to Personal Protective Equipment (PPE) guidelines. This is especially important as most of the Brazilian population was not yet vaccinated during the study period. Adherence to hospital protocols, including COVID-19 pre-surgery testing, inpatient care and proper use of PPE, has proven effective in reducing virus exposure for both patients and staff.

CLINICAL/THYROID AND COVID-19

117046 THR92ALA TYPE II DEIODINASE POLYMORPHISM HETEROZYGOSITY PREVENTS MYOSTEATOSIS IN HOSPITALIZED PATIENTS WITH MODERATE TO SEVERE COVID-19

Fabyan Esberard de Lima Beltrão[1], Daniele Carvalhal de Almeida Beltrão[2], Giulia Carvalhal de Almeida Cordeiro[3], Fabyo Napoleão de Lima Beltrão[4], Jair de Souza Braga Filho[5], Jocyel de Brito Oliveira[5], Joice dos Santos de Jesus[5], Gabriel Jeferson Rodríguez Machado[5], Hatilla dos Santos Silva[5], Helena Mariana Pitangueira Teixeira[5], Juliana Lopes Rodrigues[5], Camila Alexandrina Viana de Figueiredo[5], Ryan dos Santos Costa[5], Fabio Hecht[6], Maria da Conceição Rodrigues Gonçalves[7], Helton Estrela Ramos[5]

[1] Federal University of Paraíba (UFPB), Lauro Wanderley University Hospital, Department of Endocrinology, João Pessoa, PB, Brazil. [2] University Centre of João Pessoa (UNIPE), João Pessoa, PB, Brazil. [3] Federal University of Campina Grande (UFCG), Campina Grande, PB, Brazil. [4] Center for Biological and Health Science (FCM-PB), João Pessoa, PB, Brazil. [5] Department of Bioregulation, Federal University of Bahia, Salvador, BA, Brazil. [6] Instituto de Biofísica Carlos Chagas Filho, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil. [7] UFPB, João Pessoa, PB, Brazil

Introduction: Recently, a published study demonstrated a protective role played by Thr92Ala-DIO2 heterozygosity in patients with COVID-19. Thyroid hormones and deiodinases (DIO) (mainly DIO2 and DIO3) are also crucial for metabolic processes, plasticity, and signaling in skeletal muscle. **Methods:** We conducted an observational, longitudinal, and prospective cohort study to investigate a possible association between the Thr92Ala-DIO2 polymorphism and thyroid function with body composition (appendicular muscle mass, myosteatosis, and fat distribution) from chest CT in consecutive patients with SARS-CoV-2. The patients were admitted between June and August 2020 to a tertiary hospital specializing in COVID-19. According to Thr92Ala-DIO2 polymorphism we analyzed blood biochemistry, cumulative mortality, comorbidities, complications, and severity scores. **Results:** 172 consecutive patients [median age: 61 (49 –72) years] were stratified into three subgroups: Thr/Thr (n = 61), Thr/Ala (n = 92), and Ala/Ala (n = 19). The patients had a prevalence of low muscle mass of 52.3 % (90/172). Low muscle mass [(muscle area (MA) < 92 cm^2] was lower in Ala/Thr patients (44.6%) than in Thr/Thr (60.7%) or Ala/Ala patients (63.2%) (p = 0.043). The heterozygous genotype (Thr/Ala) was associated with reduced risk at low muscle mass (between 47 to 70%) and myosteatosis (between 64 to 74%), whereas the univariate and multivariate logistic regression adjusted for multiple 14 covariates. The mortality rate was higher in the homozygotic sarcopenic group (MA < 92 cm^2) than in the heterozygous without sarcopenia (30.6% *vs.* 3.9%, p = 0.001). Regarding Kaplan-Meier curves, the group with the best survival rate was patients with MA ≥ 92 cm^2 and heterozygous. **Conclusion:** We provide evidence of a protective role played by Thr92Ala-DIO2 heterozygosity in patients with COVID-19, possibly preventing muscle mass wasting and developing myosteatosis. More studies are needed to verify these preliminary results.

CLINICAL/THYROID AND METABOLISM

117146 CHANGES IN THYROID MORPHOLOGY AND FUNCTION AFTER BARIATRIC SURGERY AND IT RELATIONSHIP WITH INFLAMMATORY AND METABOLIC PARAMETERS

Priscila Aves Medeiros de Sousa[1], Joana Rodrigues Dantas[1], João Regis Ivar Carneiro[1], Rodrigo Soares Fortunato[1], Andressa Lima de Vasconcelos[1], Denise P. Carvalho[1], Patrícia de Fátima dos Santos Teixeira[1]

[1] Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brasil

Introduction: Until now there are few studies evaluating the impact of bariatric surgery (BS) in thyroid function, morphology; as well how it correlates with changes in inflammatory markers and insulin resistance. We aimed to evaluate all those parameters at the same population in a prospective study. **Methods:** A cohort included 70 patients with severe obesity, that were divided into two groups. The experimental group was composed of 40 patients submitted to (BS) and the control group was composed of 30 patients submitted to a clinical treatment. Both were submitted (at the beginning and in the second year of follow-up) to thyroid US and laboratory analyses to determine levels of serum TSH, free T4,TPO-Ab, leptin, glucose, insulin (for HOMA- IR calculation),glycosylated hemoglobin (A1c), IL 6 and TNF-α. **Results:** Regarding the thyroid volume, there was a reduction after BS (-1,5 cm^3) that differed significantly from the control group (+0,6 cm^3; p = 0,003). We observed that the variation in thyroid volume was positively correlated with the variation in BMI (rs = 0,356; p = 0,002), leptin (rs = 0,583; p = 0,007) and insulin (rs = 0,285; p = 0,060). The final volume correlated positively with the final values of glycemia (Rs = 0,354; p = 0,002), insulin (Rs = 0,383; p = 0,005), HOMA-IR (Rs = 0,415; p = 0,003) and with TNF-α (rs = 0,519; p = 0,051). In relation to TSH the reduction was borderline (-0,3872 *vs.* -0,2483; p = 0,128) and we also observed after BS a significant increase in the conversion of T4 to T3 demonstrated by the T3/T4 ratio (+5.5; p = 0,01). Despite an increase in the prevalence of thyroid nodules in the experimental group, it did not reach statistical significance (p = 0,340). **Conclusion:** Bariatric surgery was associated with a reduction in the thyroid volume, a borderline reduction in TSH and no impact on nodular disease. The variations in thyroid volume were related to changes in metabolic parameters and the final thyroid volume was also related to inflammatory markers. It was detected an augment in the conversion of T4 to T3 with BS.

CLINICAL/THYROID AND METABOLISM

117021 INFLUENCE OF THE DEGREE OF OBESITY IN OBESE EUTHYROID INDIVIDUALS: CORRELATION BETWEEN BODY MASS INDEX (BMI) AND THYROID STIMULATING HORMONE (TSH) IN PATIENTS UNDERGOING BARIATRIC SURGERY

Adriano Francisco de Marchi Junior[1], Victor Rocha Pinheiro[1], Miriane de Oliveira[1], Maria Teresa de Sibio[1], Gláucia Maria Ferreira da Silva Mazeto[1], Paula Barreto da Rocha[1], Célia Regina Nogueira[1]

[1] Faculdade de Medicina de Botucatu, Universidade Estadual Paulista (Unesp), Botucatu, SP, Brasil

Objective: Although controversial, there may be a positive correlation between the body mass index (BMI) of individuals with obesity in euthyroidism and serum levels of thyroid stimulating hormone (TSH). This study aimed to evaluate the correlation between BMI and serum levels of TSH in individuals with morbid obesity undergoing bariatric surgery. **Patients and methods:** The medical records of patients treated between the years 2012 and 2016 were used. A total of 96 patients with obesity, pre-surgery BMI ≥ 40 kg/m^2, being followed up in the endocrinology unit, with mean age of 50 years, were evaluated pre and post operatively. In addition to the plasma TSH dosage by IRMA and plasma free T4 by RIE, age, BMI and biochemical parameters (fasting glucose, total cholesterol and triglycerides) were analyzed. **Results:** Patients with BMI > 40 kg/m^2 prior to surgery showed higher serum TSH than subjects with a BMI < 40 kg/m after surgery (2.48 ± 0.2 *vs.* 1.81 ± 0.25, p < 0.001). The decrease in BMI was accompanied by an improvement in the glycemic and lipid profiles, as well as free T4 and TSH levels are shown to accompany BMI. **Conclusion:** Bariatric surgery was efficient in controlling obesity, since 100% of the patients had their degree of obesity decreased with concomitant metabolic improvement. We found that BMI and TSH are positively related, as post-surgical patients had both BMI and TSH decreased.

CLINICAL/THYROID AND PEDIATRIC DISEASE

117168 APPLICABILITY OF INITIAL RISK STAGING AND DYNAMIC RISK STRATIFICATION APPLIED TO ADULTS THYROID CANCER PATIENTS IN THE PEDIATRIC GROUP- 50 YEARS OF EXPERIENCE

Mariana Mazeu Barbosa de Oliveira[1], Marilia Martins Silveira Marone[2], Cristiane Kochi[1], Osmar Monte[1], Carlos Alberto Longui[1], Nilza Maria Scalissi[1], Adriano Namo Cury[1], Carolina Ferraz da Silva[1], Rosália Padovani[1]

[1] Santa Casa de São Paulo, São Paulo, SP, Brasil. [2] Medicina Nuclear da Santa Casa de São Paulo – Nuclimagem, São Paulo, SP, Brasil

Introduction: Thyroid cancer corresponds to more than 6% of all cancers in childhood. Despite of the 10 years disease specific survival is close to 100%, patients with advanced initial disease present high morbidity. The objective of the initial recurrence risk classification (IRRC) proposed by ATA 2015 for adults is to assess the risk of recurrence of the disease and to identify patients who will benefit from a more aggressive treatment and a closer follow-up. In childhood, the 2015 ATA guidelines acknowledge that there isn't a prospective study to validate a risk-based stratified approach. Furthermore, the dynamic risk stratification (DRS) is not a stablished approach for them. **Objective:** Assess the applicability of the IRRC and DRS used for adults in the pediatric population and evaluate if the initial stratification could be a predictor of a long-term response. **Methods:** 125 differentiated thyroid cancer (DTC) patients aged ≤ 18 years that were following in the endocrinology or in the nuclear medicine service of a tertiary hospital of São Paulo, from 1970 to 2020 were evaluated retrospectively. Patients were stratified according to the IRRC proposed by both, the ATA Children and Adults DTC Guidelines 2015. Subsequently, the patients were re-staged by the DRS and classified as excellent response, indeterminate, incomplete biochemical and incomplete structural. Finally, the initial responses were correlated with the late responses (1, 3, 5, 10 and >10 years). **Results:** From 125 patients, barely one received a different initial staging from the two classifications. The initial stratification was correlated with the long-term responses (p: 0.001), so that, patients with low initial risk had, in their greatest majority, an excellent/indeterminate response over the long follow-up. Also, most of the high risk group had an unfavorable response. Furthermore, 86.11% of the patients remained with the same response of the first reestaging throughout all the follow-up (p: 0.074). When calculating the OR, we observed that the low and intermediate risk patients presented the same possibility of evolving with a complete/indeterminate response OR: 0.379 (0.092-1.556). On the other hand, the high risk ones had a lower chance of a favorable response OR: 0.082 (0.019-0.359). **Conclusion:** The initial risk stratification proposed for the pediatric age group corresponds to the risk classification proposed for adults and can be considered a good predictor of recurrence and persistence disease. Furthermore, the initial DRS response was considered a good predictor of long-term response. We suggest that DRS could be implemented to the children's guideline as a new tool to improve children's follow up strategy and to guide the TSG goals.

CLINICAL/THYROID AND PEDIATRIC DISEASE

117067 PEDIATRIC THYROID CANCER – STARTING POINT REVIEW AT HOSPITAL UNIVERSITARIO AUSTRAL

Jorgelina Luz Guerra[1], Ana Inés Voogd[1], Nicolás Seffino[1], Martina Musumeci[1], Guido Cragnolino[1], Sofia Marchionatti[1], Alejandro Begueri Buquet[1], Malena Berger[1], María del Carmen Negueruela[1], Andrea Forrester[1]

[1] Hospital Universitario Austral, Buenos Aires, Argentina

Introduction: The incidence of thyroid cancer in the pediatric population appears to be increasing. The most common subtype is papillary thyroid carcinoma (PTC) which represents more than 90% of cases. Despite a good prognosis, at the time of diagnosis lymph node metastases are present in 78% of all cases and lung metastases in about 9% to 30%. **Objective:** The aim is to analyze our experience in the management of thyroid cancer (TC) in the pediatric population treated in our hospital by a multidisciplinary team and their oncological outcomes in order to promote our best practice standards to manage children TC. **Methods:** This is a retrospective communication of 11 pediatric differentiated thyroid carcinoma (DTC) treated from December 2017 to January 2023. **Results:** We included 7 men and 4 women; the median diagnosed age was 15 years old (8-18). All but one presented a rapid growing neck mass at the time of diagnosis; 3/11 had lung metastases. Most of them showed hypoechoic with microcalcifications nodules (8/11); 5/11 patients had confirmed lateral neck lymph node metastases. All patients underwent total thyroidectomy with intraoperative neuromonitoring system, 4 patients had both central and lateral compartment lymph node dissection. Median hospitalization days were 4 (1-6). Regarding post-surgical complications, 9 patients presented transient hypoparathyroidism with calcium and vitamin D supplementation, 1 had unilateral vocal cord paralyses because the laryngeal nerve was involved, 4 patients were high-risk, 6 low-risk and 1 patient was considered intermediate risk. All patients received radioactive iodine (RAI) after surgery, 4 of them received dosimetry prescribe activity of 131I. Median follow-up period was 14 months (3-60). At the time of last evaluation, 6 patients are free of disease, 2 have biochemical incomplete and 2 indeterminate responses to treatment; one patient cannot be evaluated because less than twelve months of follow-up. No one had lymph node relapse. **Conclusions:** In our daily practice, we carry out and individualized multidisciplinary treatment based on pre- and postoperative staging and risk stratification because pediatric population exhibits differences in clinical presentation and long-term outcomes. Pediatric DTC treatment needs to be addressed in a hospital with the full spectrum of pediatric specialty care as well as thyroid surgery should ideally be performed by a high-volume surgeon for lower complications rates and better oncological outcomes. Complete and meticulous first surgery in our population showed an excellent response without neck relapse. Based on the lack of data comparing empiric prescribe and dosimetry-based activity of 131I, we are unable to recommend for or against either approach in most patients. It is recommended that all activities of 131I should be calculated by experts with experience in dosing children. Well-designed long term, multicenter studies in pediatric DTC are needed.

CLINICAL/THYROID AND PEDIATRIC DISEASE

116544 SONOGRAPHIC FEATURES OF INTRATHYROIDAL THYMUS: REPORT OF THREE CASES

Pablo Morikawa[1], Natalia Ortega[2], Claudia Neves de Souza[3], Hugo Boggino[4], Miguel Calvo[5]

[1] Asunción Medical Center, Asunción, Paraguay. [2] Instituto Privado del Nino, Asunción, Paraguay. [3] Instituto de Previsión Social (IPS), Asunción, Paraguay. [4] PATLAB, Asunción, Paraguay. [5] Instituto Radiológico Calvo, Asunción, Paraguay

We report three cases of intrathyroidal thymus in children, two male and one female, aged 3, 4 and 14 years old. The diagnosis was made upon sonographic features of visualized cervical extension of the thymus. In one case, a complementary histopathologic analysis was obtained by fine needle aspiration biopsy (FNAB). The cases were compared with their own cervical extension of the thymus present in all cases and the ultrasound features of 27 cervical extension of thymus cases found during thyroid ultrasound studies in children aged 3 to 10 years old. In a case confirmed by FNAB, pathology reported benign lymphocytic tissue compatible with thymus. All three cases of intrathyroidal thymus showed similar ultrasonographic features as the ones seen in cervical thymus extension. Presence of fine echogenic strips and multiple scattered echogenic focuses, some with comet-like echo patterns resembling starry sky appearance over solid hypoechogenic background. The size ranged from 7 to 13 mm in its largest diameter and were all located on the middle to inferior portion of the right lobe. The borders were smooth and all cases showed small, thin paratracheal caudal projection. Doppler mapping showed poor vascularization, similar or less than the normal thyroid gland. In conclusion, all cases of intrathyroidal thymus showed the same sonographic appearances of the cervical extension of the thymus, differentiating this diagnosis from other thyroid nodules. The small, thin caudal projection present in our cases could represent the structure of the remnant pathway, reinforcing the diagnosis. A remnant ectopic thymus tissue can occur in any level of the descending cervical pathway from the angle of the mandible to the mediastinum. Persistence of cervical portion of thymus is a common anatomic variation sonographically detected in around two third of children. On the other hand, Intrathyroidal thymus is a rare case which is seen occasionally during thyroid ultrasound examinations. Considering its rarity, cases of intrathyroidal thymus may not be easily recognizable by radiologists who do not regularly perform thyroid ultrasound in children, which poses the risk of misdiagnosis. Therefore, in order to avoid unnecessary procedures, it is crucial to acknowledge the importance of recognizing the unique sonographic features of thymic tissue when performing thyroid ultrasound in children.

CLINICAL/THYROID AND PEDIATRIC DISEASE

117144 THE NATURAL COURSE OF IDIOPATHIC SUBCLINICAL HYPOTHYROIDISM IN CHILDREN AND ADOLESCENTS

Gil Kruppa Vieira[1], Célia Regina Nogueira[1]

[1] Faculdade de Medicina de Botucatu, Universidade Estadual Paulista "Júlio de Mesquita Filho" (Unesp), Botucatu, SP, Brasil

Objectives: Subclinical hypothyroidism (SCH) is biochemically characterized by a persistent elevation in plasma levels of TSH, normal levels of thyroid hormones (free T3 and T4), and the absence of clinical manifestations. Although it is common in the adult population, its real prevalence in the pediatric population is unknown. Likewise, the clinical significance and natural history of SCH in the pediatric age group remain unclear. This study was aimed at analyzing the clinical and laboratory characteristics of children with idiopathic SCH by the time of diagnosis and their natural course. **Subjects and methods:** We retrospectively evaluated 131 children with increased TSH levels found by chance during routine exams. Out of the total, 29 (15 females) were included. Their ages ranged from 3 to 15 years, and they underwent follow-up with our service for at least 24 months. The presence of clinical manifestations, anthropometric data, and thyroid function were assessed at each visit. **Results:** At baseline, the mean age of was 7.5 ± 3.5 years; 20 patients (68.9%) were prepubertal, and none had clinical manifestations of hypothyroidism, history of abnormal neonatal screening test for congenital hypothyroidism and transient congenital hypothyroidism and 22 patients (75.8%) had a family history of thyroid disease. Twenty-one patients (72.4%) presented at least one altered lipid profile variable. In 10 patients (34.5%), a decrease in HDL-cholesterol levels was identified, and in 11 (37.9%), an increase in triglyceride levels was observed. Five patients (17.2%) had both alterations and no patient had elevated LDL-cholesterol. No patient had impaired fasting glycemia or insulin resistance. After 24 months of follow-up, the TSH levels of 17 patients (58.6%) normalized (Group A), 12 patients (41.4%) persisted with SCH (Group B), and no patient developed overt hypothyroidism. All patients maintained free T4 levels within the normal range, and no patient developed thyroid antibodies. When comparing Groups A and B, we identified no statistically significant differences in clinical and laboratory findings at baseline. After 24 months of follow-up, the Group A had TSH levels significantly lower than Group B ($p < 0.01$), as expected. We found no statistically significant differences in the patients' anthropometric data, family history of thyroid disease, TSH and FT4 levels at baseline and FT4 levels at 24 months between groups. **Conclusions:** The thyroid function of the majority of children with SCH normalized and no impairment was observed in anthropometric parameters such as height or BMI.

CLINICAL/THYROID AND PEDIATRIC DISEASE

117141 THE NATURAL HISTORY OF THE MILD NON-AUTOIMMUNE SUBCLINICAL HYPOTHYROIDISM IN CHILDREN AND ADOLESCENTS: A 2-YEAR FOLLOW-UP

Gil Kruppa Vieira[1], Célia Regina Nogueira[1]

[1] Faculdade de Medicina de Botucatu, Universidade Estadual Paulista "Júlio de Mesquita Filho" (Unesp), Botucatu, SP, Brasil

Objectives: Subclinical hypothyroidism (SCH) is characterized by a persistent elevation in plasma levels of the thyrotrophic hormone (TSH), normal levels of thyroid hormones, and the absence of clinical manifestations. Its clinical significance and natural history in the pediatric age group remain unclear. This study was aimed at analyzing the clinical and laboratory characteristics of children with idiopathic SCH by the time of diagnosis and their natural course. **Subjects and methods:** We prospectively evaluated 25 (7 females) children with non-autoimmune SCH aged from 3 to 15 years for 24 months. We excluded patients with any chronic illness such as obesity, type 1 *diabetes mellitus*, celiac disease, and Hashimoto's thyroiditis, defined as positive for anti-thyroid peroxidase and/or anti-thyroglobulin and those who received levothyroxine (LT4), medications containing iodine, or drugs known to affect thyroid hormonal secretion or TSH effect. The presence of clinical manifestations of hypothyroidism, anthropometric data and thyroid function were assessed at each visit. Lipids and glucose profile and bone age were assessed annually. Thyroid ultrasonography was performed in all patients. **Results:** At baseline, the mean age of was 7.6 ± 2.7 years; 23 patients (92%) were prepubertal, and none had clinical manifestations of hypothyroidism. Two patients (8%) had history of abnormal neonatal screening test for congenital hypothyroidism and transient congenital hypothyroidism and 12 patients (48%) had a family history of thyroid disease. Thirteen patients (52%) presented at least one altered lipid profile variable. In 7 patients (28%), a decrease in HDL-cholesterol levels was identified, and in 8 (32%), an increase in triglyceride levels was observed and 6 patient (24%) had elevated LDL-cholesterol. No patient had impaired fasting glycemia or insulin resistance. After 24 months of follow-up, 19 patients (76%) were euthyroid (group A), 5 patients (20%) maintained SCH (group B) and one patient (4%) progressed to overt hypothyroidism (group C). Fourteen patients (56%) normalized thyroid function in the first year of follow-up. Thyroid hypoplasia was found in 10 (40%) of the patients. Seven of them returned to euthyroidal state during the follow-up period and 3 maintained SCH. No impairment in linear growth and bone maturation was observed in groups A and B. We found no statistically significant differences in the patients' anthropometric data, family history of thyroid disease, initial TSH levels or presence of dyslipidemia at baseline and after the follow-up period between groups neither correlation between the improvement in thyroid function and normalization in any lipid profile variable. **Conclusions:** Subclinical hypothyroidism evolved benignly, with normalization of thyroid function in most patients, with no impact in growth, bone maturation or BMI.

CLINICAL/THYROID AND PREGNANCY

117050 REFERENCE INTERVALS FOR SERUM T4 AND FT4 AMONG PREGNANT WOMEN LINKED TO THE MÃE CURITIBANA PROGRAM

Tatiane Mendes Boutin Bartneck Telles[1], Paulo Cesar Zimmermann Felchner[2], Maria Eduarda Amaral de Carvalho[2], Leonardo Ivantes Mesa[2], Thyago Proença de Moraes[2], Cleo Otaviano Mesa Júnior[3], Gisah Amaral de Carvalho[3]

[1] Universidade Federal do Paraná (UFPR), Curitiba, PR, Brasil. [2] Pontifícia Universidade Católica do Paraná (PUC-PR), Curitiba, PR, Brasil. [3] Complexo Hospital de Clínicas da UFPR, Curitiba, PR, Brasil.

Introduction: Thyroid diseases are frequent in women of childbearing age and can have negative maternal and fetal repercussions when not identified and properly treated. Physiological changes during pregnancy cause changes in thyroid function tests, which is why they must be interpreted with caution and, whenever possible, based on local and specific reference values for pregnant women. Determining the serum level of total (T4T) or free (FT4) T4 is fundamental for defining the diagnosis of thyroid dysfunctions between clinical or subclinical. This definition modifies the treatment recommendations for thyroid disorders in the various published guidelines. **Objectives:** To determine the reference intervals for FT4 and T4T of pregnant women, in the first trimester of pregnancy. **Methods:** A longitudinal study using a sample of the population of pregnant women, aged > 18 years old, with up to 14 weeks of gestation. Pregnant women were selected proportionally to each health district in the city of Curitiba so that they represented the entire population of the city served by the public health system. Pregnant women who had TSH outside the reference range, positive ATPO, family history of thyroid disease, use of antithyroid drugs, use of medications that could interfere with the measurement of the markers under study were excluded. The studied population had a median urinary iodine concentration considered adequate for pregnant women (158 mcg/L). Serum FT4 and T4T were measured by ECLIA method. Continuous variables were expressed as mean and standard deviation (SD). Percentiles were determined and variations between 2.5 and 97.5 percentiles were considered as the normal reference interval. The results were analyzed and compared with the reference interval provided by the manufacturer for non-pregnant women. **Results:** Of the 225 pregnant women (with mean ± SD of gestational age 8 weeks ± 2.3; with mean ± SD of age 27 years ± 5.9) the FT4 values of the pregnant women ranged between 0.83 and 1.68 ng/dL, with mean ± SD of 1.23 ± 0.15. The 2.5th and 97.5th percentiles were 0.94 and 1.64 ng/dL. Compared with the kit manufacturer's reference values for non-pregnant women (0.95 to 1.47 ng/dL), we would have 08 pregnant women with a high FT4 result. The T4T values of the pregnant women varied between 9.2 and 12.2 ng/dL, with a mean ± SD of 10.9 ± 2.48. The 2.5th and 97.5th percentiles were 9.2 and 12.2 ng/dL. Compared with the kit manufacturer's reference values for non-pregnant women (4.87 and 11.72 ng/dL), we would have 25 pregnant women with high T4T results. **Conclusion:** The FT4 and T4T reference intervals of first trimester pregnant women are different from the non-pregnant population, however this difference is less relevant in FT4. In total T4, the lower limit of normal in pregnant women is much higher than in the normal population, which makes it less sensitive for the definition of clinical hypothyroidism in first trimester pregnant women.

CLINICAL/THYROID AND PREGNANCY

117121 TREATMENT WITH POTASSIUM IODIDE IN PATIENTS WITH HYPERTHYROIDISM DUE TO GRAVES' DISEASE IN THE 1ST TRIMESTER OF PREGNANCY: REPORT OF 6 CASES

Diana Liset Saucedo[1], Gimena González Buján[2], Paola Urrutia[2], Julieta Tkatch[2], Laura Beatriz Ramos[2], Marcos Sergio Abalovich[2], Adriana Marcela Vázquez[2], Graciela Nélida Alcaraz[2]

[1] Hospital Carlos Durand, Buenos Aires, Argentina. [2] Hospital Carlos Durand, Buenos Aires, Argentina

Introduction: Hyperthyroidism (H+T) due to Graves' disease occurs in 0.2% of pregnant women, being thionamides the treatment of choice. Observational studies showed a higher prevalence of teratogenic effects when used in early stages of pregnancy. Thionamides increase the usual risk of congenital malformations, by nearly 2%-4%. "Methimazole embryopathy (MMI)" is the result of maternal exposure to this drug during the 1st trimester (T). For this reason, different therapeutic alternatives have been proposed to avoid its use. International guidelines recommend withdrawing MMI in selected cases with mild hyperthyroidism. In patients with moderate to severe H+T, switching MMI to propylthiouracil (PTU) has been proposed, although the latter has been also associated to a lesser extent birth defects. In Japan there is experience with the replacement of MMI by potassium iodide (KI), without deleterious effects for mothers and neonates. To date, its efficacy in regions with lower iodine intake is unknown. In our opinion, it could be a viable strategy in countries, where PTU is not available. **Objective:** To assess if treatment with IK as the only drug is efficient in reducing FT4 levels in women with moderate to severe H+T due to Graves' disease in the 1st T of pregnancy. **Materials and methods:** 6 patients with H+T due to Graves' disease, on 1st T of pregnancy. In 4 patients MMI was withdrawed between weeks 4 and 7 of gestational age. One patient discontinued MMI 6 months prior to pregnancy before undergoing *in vitro* fertilization, being subclinical hyperthyroid at that time. The remaining patient was newly diagnosed with H+T during early pregnancy. All the patients were treated with IK (3% Lugol's oral solution), initial dose: 3-5 drops/day, until the end of the1st T. In 5 patients, the KI was started between week 5 and 7 and one patient at week 10. TSH (QL; VR: 0.39-3.48 mUI/L) and FT4 (QL; VR: 0.82-1.1 ng/dL) were measured weekly. TRAb was measured at least once during 1st T. **Results:** Median (X) age = 32.5 years (r = 27-42), X baseline FT4 = 3.82 ng/dL (r = 2.4-5.16). TSH remained suppressed throughout the follow-up (<0.01-0.13). A promptly dropping in FT4 levels between 49 and 77% (r = 0.71-1.88 ng/dL) compared to baseline was evidenced post starting KI. None had escape phenomenon from the Wolff-Chaikoff effect prior to week 12. One patient increased FT4 when Lugol was reduced on week 11 from 3 to 2 drops/day, concomitantly with a remarkable increase in TRAb levels. Five patients required MMI in the 2nd T. **Conclusion:** In our initial experience, with a still limited number of cases, potassium iodide in patients with moderate to severe Graves' disease hyperthyroidism, was effective and safe at early pregnancy. As PTU is not available in some countries, we believe that potassium iodide allows us to promptly decrease in FT4 levels, achieving the therapeutic aim and avoiding MMI exposure during the organogenesis period.

CLINICAL/THYROID AND PREGNANCY

117094 TSH REFERENCE RANGE IN THE FIRST TRIMESTER IN A IODINE SUFFICIENT POPULATION OF PREGNANT WOMEN ATTENDED BY THE PUBLIC HEALTH SYSTEM IN CURITIBA – SOUTH OF BRAZIL

Paulo Cesar Zimmermann Felchner[1], Tatiane Mendes Boutin Bartneck Telles[2], Maria Eduarda Amaral de Carvalho[1], Thyago Proença de Moraes[1], Cleo Otaviano Mesa Júnior [1]

[1] Pontifícia Universidade Católica do Paraná (PUC-PR), Curitiba, PR, Brasil.[2] Universidade Federal do Paraná (UFPR), Curitiba, PR, Brasil

Introduction: Thyroid diseases are common among women of reproductive age, and the serum concentration of thyroid-stimulating hormone (TSH) is the most used index to assess thyroid function during pregnancy. During pregnancy, there are changes in thyroid function that can have a clinical impact on the woman's health and on the outcome of pregnancy, as well as interfere with fetal health and child development, and adequate thyroid function is essential for normal intrauterine development. When comparing the levels of TSH between pregnant and non-pregnant women, TSH levels are lower in pregnancy, mainly in the first trimester, with gradual growth during pregnancy. Although some guidelines propose fixed TSH reference values in pregnancy according to the gestational trimester, the main recommendation is to carry out a study of their local population due to the significant variation in TSH reference range levels in different populations and different essays. Therefore, it is necessary to determine the values of a reference interval for TSH for the local population of pregnant women. **Objectives:** Our objective is to determine the normal reference range of TSH in the first trimester of gestation in the public health system of pregnant women from Curitiba. **Methods:** This is an ongoing prospective cohort study, with the population sample from pregnant women using the public health system, with an age > 18 years old in Curitiba, South Brazil. 383 pregnant women were invited to participate. After evaluating the exclusion criteria (gestational age more than 13 weeks, twin pregnancy, thyroid disease, iodine ingestion, identification of the samples in the laboratory), 225 pregnant women had the TSH studied using. TSH was measured using Chemiluminescence with the ADVIA Centaur XPT (Siemens Healthineers). The TPO-ab presence, FreeT4, and Total T4 were also measured. The 2.5, 50 e 97,5 TSH percentiles were estimated for the normal pregnant population. **Results:** The mean gestational age was 8,6 weeks (standard deviation 2.33). From 225 pregnant women, 22 (9.8%) had TPO-ab positive. The 2.5 and 97.5 percentiles of TSH were 0.12 and 5.28 µIU/mL after using the exclusion criteria. The populational iodine status was sufficient. In the TPO-ab positive population was found a higher level of TSH. The proportion of TPO-ab positive was significantly higher in the population with TSH > 2.5 µg/mL. **Conclusion:** This preliminary data shows the TSH reference range with levels higher than other regions, reinforcing does not use of fixed values of TSH from other populations to evaluate the thyroid function in pregnancy. Comparing the laboratory reference for non-pregnant adults (0.48 to 5.60 µIU/mL), the recommended reduction on the upper limit of 0.5 mU/L and 0.4 on the lower limit found similar values to our findings.

CLINICAL/THYROID AND REPRODUCTION

117081 IS THERE A CORRELATION BETWEEN THYROID FUNCTION AND OVARIAN RESERVE IN SUBFERTILE WOMEN?

Yuri Ian Lima Alves de Oliveira[1], Paulo Gallo de Sá[1], Lenora Maria Camarate Silveira Martins Leão[2], Ana Beatriz Winter Tavares[2]

[1] Universidade do Estado do Rio de Janeiro (UERJ), Vida – Centro de Fertilidade, Rio de Janeiro, RJ, Brasil. [2] UERJ, Rio de Janeiro, RJ, Brasil

Introduction: Decreased ovarian reserve represents 25% of the female population with subfertility. Anti-Mullerian hormone (AMH) is the most reliable marker of ovarian reserve. Studies on the association between AMH and thyroid function and autoimmunity are discordant in the literature, with some studies suggesting a positive association. There is data suggestive of thyroid dysfunction resulting in abnormal folliculogenesis, alterations in the ovulatory cycle and lower fertilization rate. **Objective:** To correlate thyroid function and autoimmunity with AMH levels and antral follicle count (AFC) in subfertile women being evaluated for ovarian stimulation during assisted reproduction treatment. **Methods:** We evaluated 370 patients who underwent controlled ovarian stimulation for oocyte cryopreservation and/or *in vitro* fertilization (IVF) at an Assisted Human Reproduction center in Rio de Janeiro ("Vida – Centro de Fertilidade"). The following laboratory data were registered: 1) assessment of ovarian reserve through prestimulation FSH, AMH and AFC; and 2) thyroid function through TSH, free T4 and autoantibodies (antithyroperoxidase and antithyroglobulin). Thyroid autoimmunity was identified with 1 or both positive antibodies. AMH cutoff values < 1.1 ng/mL and/or AFC < 6 follicles were considered low ovarian reserve, according to the consensus of the Brazilian Society of Human Reproduction (SBRH). The reference ranges for TSH and free T4 were, respectively, 0.4-4.3 µUI/mL and 0.7-1.9 ng/dL. **Results:** The median age was 38 years (25-41), TSH 1.63 µUI/mL (0.37-6.2), free T4 1.26 ng/dL (0.18-10.2), AMH 1.51 ng/mL (0.01-18.3), and AFC 11 follicles (1-89). 17% of patients had positive autoimmunity. In the evaluation of the 370 patients, there was no statistically significant correlation between TSH and AMH, TSH and AFC, or TSH and FSH. 156 patients (42.1%) had low ovarian reserve according to one or both criteria. 145 patients (39.1%) had AMH < 1,1 ng/mL; in this group, there was no statistically significant correlation between AMH and TSH, or TSH and AFC. The already known positive statistical correlation between FSH and AMH was corroborated in our study ($r = 0.19$ and $p = 0.02$). The low ovarian reserve group identified by AMH values with positive autoimmunity (18/145 patients) showed no statistically significant correlation between TSH and AMH, or TSH and CFA, despite a tendency toward negative correlation between TSH and AFC ($r = -0.44$, $p = 0.06$). **Conclusion:** The results evidenced a lack of correlation between ovarian reserve assessed by AMH and AFC and thyroid function in the population of subfertile women undergoing assisted reproduction, demonstrating that thyroid function has no impact on ovarian reserve.

CLINICAL/THYROID AUTOIMMUNITY

117077 DETECTABLE LEVELS OF THYROID PEROXIDASE ANTIBODIES DETECTABILITY, BUT NOT ITS POSITIVITY, ARE ASSOCIATED WITH INCREASED CAROTID INTIMA-MEDIA THICKNESS: ELSA-BRASIL STUDY

Vandrize Meneghini[1], William R. Tebar[1], Itamar Souza Santos[1], Carolina Castro Porto Silva Janovsky[1], Paulo A. Lotufo[1], Alessandra C. Goulart[1], Isabela M. Bensenor[1]

[1] Universidade de São Paulo, São Paulo, SP, Brasil

Introduction: Increased carotid intima-media thickness (cIMT) is an important indicator of atherosclerosis and a strong predictor of future cardiovascular events. There is an association between thyroid autoimmunity and the cardiovascular system. However, it remains unclear whether detectability and positivity of thyroid peroxidase antibodies (TPOAb) could contribute to the development of atherosclerosis. **Objective:** To explore the association of multiple categories of TPOAb with increased cIMT in participants from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). **Methods:** This is a cross-sectional study using baseline data of 9651 participants (mean age of 51.5 years-old, 55.8% women), without a history of cardiovascular disease. Fasting serum TPOAb levels were determined (Roche Diagnostics) and categorized as undetectable (≤5.00 IU/mL), low detectable (5.01-14.99 IU/mL), high detectable (15.00-33.99 IU/mL), and positive (34.00-600.00 IU/mL). Values of cIMT equals or above 1 deviation standard of the sample's mean were classified as increased cIMT (IMT ≥ 0.74 mm). We performed logistic regression to determine odds ratio (OR) and 95% confidence intervals (CI) of the univariate and adjusted (for sex, age, BMI, smoking, alcohol consumption, diabetes, hypertension, dyslipidemia, and family history of cardiovascular disease) models. Sensitivity analyses were performed for euthyroid individuals that were not using medication that interferes on thyroid function (n = 7,253). **Results:** Increased cIMT was prevalent in 14,2% of our sample, with statistically significant difference among the categories of TPOAb (p = 0.011). Compared to the group with undetectable TPOAb, participants in the low (OR = 1.37, CI = 1.04-1.82) and high (OR = 1.37, CI = 1.04-1.82) detectable categories were associated with higher odds of having increased cIMT in the univariate analyses. Both categories remained associated with increased cIMT after adjustment for sex, age and BMI (Low: OR = 1.42, CI = 1.02-1.97, High: OR = 1.42, CI = 1.02-1.97) and for the other covariates (Low: OR = 1.42, CI = 1.02-1.97, High: OR = 1.42, CI = 1.02-1.97). In the sensitivity analyses, the associations have not changed. **Conclusions:** In conclusion, detectable levels of TPOAb were associated with a higher risk of increased cIMT, even in euthyroid individuals. These findings may suggest a role of TPOAb in the atherosclerotic process.

CLINICAL/THYROID AUTOIMMUNITY

117104 ORBITAL SURGERY IN MODERATE-TO-SEVERE GRAVES' OPHTHALMOPATHY: INSTITUTIONAL EXPERIENCE

Laura Carolina Delfino[1], Anabela Zunino[1], Veronica Ilera[1], Valeria García Roel[1], Adriana Reyes[1], Alicia Gauna[1]

[1] Hospital Ramos Mejía, CABA, Argentina

Introduction: Management of moderate-to-severe Graves' ophthalmopathy (GO) depends mainly on the degree of soft tissue inflammation. While immunosuppressive therapy is indicated in the active phase, orbital surgery (OS) is reserved for sequelae disease. Indication of OS during active phase is sight-threatening GO not responding to steroids. Although not a common practice, OS during active disease has been performed in our institution as a second-line therapy. We aim to describe our experience with patients that underwent OS for active and inactive GO. **Methods:** Retrospective study. Activity and severity were defined according to 2021 EUGOG guidelines. Response to OS was classified as: adequate (improvement of GO), partial (stabilization without progression) and poor (progression of GO). **Results:** 32 patients underwent OS, 59.4% were women, median age 47 years (25-67), 48.4% smokers. Management of hyperthyroidism comprised antithyroid drugs in 19 cases (59.3%), radioiodine in 11 (34.4%) and thyroidectomy in 2. At the time of surgery 27 patients (84.4%) were euthyroid, 4 (12.5%) subclinical hyperthyroid and 1 (3.1%) hypothyroid. GO was inactive in 18 (56.3%) of cases and active in 14 (43.7%). All patients with active GO and 6 patients with inactive GO had been treated with weekly intravenous steroids as proposed by Kahaly or with 1 g methylprednisolone/d for 3 days. Indications for OS were rehabilitation for aesthetic/functional sequelae in53.1%, dysthyroid optic neuropathy in 15.6%, poor response to steroids in 15.6% and others (optic nerve elongation, exposure keratopathy, ocular subluxation) in 15.6% of cases. At the time of OS 16 patients received concomitant steroids, 10 with active and 6 with inactive GO but positive anti-TSH receptor antibodies (TRAb) and risk factors. Response to treatment was considered adequate in 81.3%, stable in 12.5% and poor in 6.3% (one active and one inactive GO). Before OS TRAb was positive in 90.6% of patients. After surgery TRAb decreased in 64.3%, remained stable in 10.7% and were negative in 25% of cases. No patient with negative TRAb before OS presented positive levels after procedure. The percentage of patients with negative TRAb was significantly higher post-surgery [90.6% *vs.* 65.6%, X2(1) = 5, p = 0.025]. Evolution of TRAb was not related with concomitant use of steroids for OS. **Conclusions:** In our experience, response to OS was satisfactory in more than 90% of cases. In patients with active GO and inadequate response to previous intravenous steroids treatment, OS achieved favorable results in more than 80%. TRAb levels decreased or became negative in most cases, with no increments after surgery. We consider that OS can be an appropriate second-line treatment option in cases of unfavorable response to steroids and inaccessibility to other treatment modalities, and that positivity of TRAb should not be a condition to preclude OS.

CLINICAL/THYROID AUTOIMMUNITY

117076 POTENTIAL DETERMINANTS OF THYROID PEROXIDASE ANTIBODIES TITERS AND MORTALITY RISK IN MIDDLE-AGED MEN AND WOMEN PARTICIPANTS OF THE ELSA-BRASIL STUDY

Vandrize Meneghini[1], William R. Tebar[1], Itamar Souza Santos[1], Carolina Castro Porto Silva Janovsky[1], Bianca de Almeida-Pititto[2], Marina G. Birck[1], Paulo A. Lotufo[1], Alessandra C. Goulart[1], José Sgarbi[3], Patrícia de Fátima dos Santos Teixeira[4], Gisela Tunes da Silva[1], Isabela M. Bensenor[1]

[1] Universidade de São Paulo, São Paulo, SP, Brasil. [2] Universidade Federal de São Paulo, São Paulo, SP, Brasil. [3] Faculdade de Medicina de Marília, Marília, SP, Brasil. [4] Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brasil

Introduction: Thyroid peroxidase antibodies (TPOAb) has been considered an indicator of low-grade inflammation, associated with a higher risk of cardiovascular diseases and mortality. **Objective:** To investigate, according to sex, the potential determinants of thyroid peroxidase antibodies levels and analyze the association of baseline TPOAb levels, its detectability and positivity with the risk of all-cause, cardiovascular and cancer-related mortality. **Methods:** Baseline data of 6,066 men and 7,266 women (median age 50 years old), from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), were analyzed. Fasting serum TPOAb levels were determined and categorized as undetectable (≤5.00 IU/mL), low detectable (5.01-14.99 IU/mL), high detectable (15.00-33.99 IU/mL), and positive (≥34.00 IU/mL). Thyrotropin (TSH) and potential determinants (age, body mass index (BMI), self-reported race, education, smoking, alcohol intake, rheumatic diseases, and parity) were also assessed. All-cause, cardiovascular, and cancer-related mortality data up to December 2018 were confirmed by death certificate. Adjusted multinomial regression models (OR) were used to verify the association of TPOAb categories and potential determinants. The association of TPOAb levels, detectability and positivity with mortality was determined by Cox regression (HR) using an adjusted model (age, sex, TSH, smoking status, BMI, alcohol intake, *diabetes mellitus*, serum C-reactive protein, dyslipidemia, and hypertension). **Results:** Men with higher BMI levels and current smokers were associated with higher odds of having low and high detectable, and positive TPOAb (ORs from 1.03 to 5.06, all $p < 0.05$). For both sexes, Black and Mixed races and higher education, compared to Whites and lower education, were protective factors for low and high detectable, and positive TPOAb titers (ORs from 0.26 to 0.47, all $p < 0.05$). For women, higher BMI levels were positively associated with TPOAB positivity (OR = 1.03, CI = 1.00-1.06), and current smokers had a higher risk of having TPOAb low and high detectability, and positivity (ORs from 4.40 to 9.58, all $p < 0.05$). Women with intermediate education and heavy drinkers presented lower odds of having detectable and positive TPOAb titers (ORs from 0.45 to 0.54, all $p < 0.05$ except low detectability for alcohol intake). Age, rheumatic diseases and parity were not significantly associated with TPOAb categories. Regarding the association of TPOAb and mortality, higher levels of log-transformed TPOAb were significantly associated with a lower risk of cardiovascular mortality (HR = 0.67; CI = 0.46-0.99) and higher risk of cancer-related mortality (HR: 1.26; CI: 1.01-1.57), only for men. **Conclusions:** Our results suggest that sociodemographic, economic and lifestyle-related factors were determinants of TPOAb multiple categories and this indicator may impact on mortality risk. Therefore, we highlight the clinical importance of all TPOAb levels, not only its positivity.

CLINICAL/THYROID AUTOIMMUNITY

117106 SEVERE GRAVES' ORBITOPATHY YEARS POST-THYROIDECTOMY

Laura Carolina Delfino[1], Anabela Zunino[1], Alicia Gauna[1]

[1] Hospital Ramos Mejía, Buenos Aires, Argentina

Introduction: TSH receptor (TSH-R) is the main auto-antigen in Graves' disease (GD). Not limited to the thyroid gland; it is ubiquitous and especially present in the orbit and subcutaneous cellular tissue. This is essential for the physiopathology of extra-thyroid manifestations of GD. **Objectives:** Analyze 3 cases with de novo Graves Orbitopathy (GO) years after thyroidectomy. Materials and **Methods:** Retrospective analysis of demographics data, thyroidectomy cause, risk factors and disease evolution. **Results:** CASE 1: Ukrainian 53-year-old woman, hypertense, smoker with diagnosis of GD (hyperthyroidism without GO, TRAb 72% -NR < 15%-) and nodular goiter. Due to a history of exposure to ionizing radiation (Chernobyl nuclear accident), total thyroidectomy was indicated. Thirteen years later she presented bilateral exophthalmos, chemosis, conjunctival injection, and epiphora. She was euthyroid, ATPO negative and TRAb 70% (NR < 15%). With a diagnosis of moderate/severe active GO (CAS 4), glucocorticoid pulses were given with adequate response. CASE 2: Argentinian 51-year-old female patient, smoker, total thyroidectomy for goiter and hyperthyroidism 6 years before the consultation. She was on levothyroxine replacement therapy with poor compliance. On first evaluation, she was hypothyroid, ATPO 61 IU/mL (NR < 35 IU/mL), TSI 5.91 IU/L (NR < 0.55 IU/L), with moderate/severe active GO (CAS 4). Adjustment of levothyroxine and glucocorticoid pulses was performed with an adequate response, but reactivation of the disease post suspension. Decompressive surgery and treatment with azathioprine were indicated. CASE 3: Argentinian 60-year-old female, history of Chagas disease and total thyroidectomy for nodular goiter 5 years before first evaluation. She referred ocular discomfort (ocular pain, photophobia, proptosis) for 2 years. She was euthyroid under levothyroxine replacement, ATPO and AcTg negative, TRAb 14.3 IU/L (NR < 1.75 IU/L), TSI 9.92 IU/L (NR < 0.55 IU/L), GO moderate/severe inactive (CAS 2). Decompressive surgery was indicated, although the patient had inactive disease, given intermittent signs of inflammation, GC pulses were indicated pre- and post-surgery to minimize the inflammatory effects with satisfactory evolution. **Conclusions:** 1) We present three cases of patients with development of de novo GO after a long-time post- total thyroidectomy. 2) Age, high TRAb titers and smoking were the risk factors in these patients. 3) It is noteworthy the high TRAB titers several years after total thyroidectomy. We consider that glandular remains as well as the presence of TSH-R in other tissues might be the cause of the persistence or reappearance of antibodies to these membrane antigens and lead to the development of OG several years after surgery. This seems contrary to the choice of total thyroidectomy with the objective of negativizing antibodies postulated in pregnancy and GO.

CLINICAL/THYROID CANCER CLINICAL

117182 15 YEARS EXPERIENCE ON RET GENETIC SCREENING ON MEN2 IN A SINGLE CENTER: AN UPDATE ON THE PREVALENCE OF GERMLINE RET VARIANTS

Lucieli Ceolin[1], Flávia de Oliveira Facuri Valente[1], Ilda Sizue Kunii[1], Luiz Antonio de Jesus Rocha[1], Marthina Colchesqui[1], Maria Inez Caser França[1], Maria Cecília Martins-Costa[1], Marina Malta Letro Kizys[1], João Roberto Maciel Martins[1], Magnus Regios Dias-da-Silva[1], Susan Chow Lindsey[1], Cléber Pinto Camacho[1], Rui Monteiro de Barros Maciel[1]

[1] Laboratório de Endocrinologia Molecular e Translacional (LEMT), Universidade Federal de São Paulo (Unifesp), São Paulo, SP, Brasil

Introduction: Multiple endocrine neoplasia type 2 (MEN 2) is an autosomal dominant hereditary cancer syndrome caused by pathogenic germline variants in the REarranged during Transfection (RET) oncogene. MEN 2 comprises two distinct clinical entities: MEN 2A and MEN 2B, both involving a high risk for medullary thyroid carcinoma (MTC). Clinical recognition and accurate diagnosis of individuals and families who are at risk of harboring a pathogenic germline RET variant is critical since the earlier diagnosis and treatment increase the likelihood of cure of MTC. Here, we describe the prevalence of the pathogenic germline RET variant screened at a reference center for molecular analyzes in the RET gene. **Methods:** Genetic screening of 994 patients was performed. **Results:** From 2007 to 2022, 994 individuals were analyzed, and 329 of them carried germline pathogenic variants in the RET gene. In total, 25 distinct germline variants were found. The most frequent variants were p.Met918 [19.2%: p.Met918Val (17.6%), p.Met918Thr (1.6%)]; p.Cys634 [24.2%: [p.Cys634Tyr (11.8%), p.Cys634Arg (8.6%) p.Cys634Gly (3.5%), p.Cys634Ser (0.3%)], p.Val804 [23.6%: p.Val804Met (14.7%), p.Val804Leu (14.7%)]; p.Ser891Ala (8.9%) and p.Gly533Cys (7%), in exons 16, 11, 14, 15 and 8 of the RET gene, respectively. Less frequently, we also find the following alterations: p.Cys609Gly, p.Cys609Ser, p.Cys609Trp, p.Cys609Tyr, p.Cys611Arg, p.Cys618Arg, p.Cys620Arg, p.Cys620Phe, p.Cys620Tyr, p.Cys630Arg, p.Cys634Gly, p.Cys634Ser, p.Val648Ile, p.Lys666Asn, p.Glu768Asp, p.Leu790Phe, p.Arg886Trp. **Conclusions:** Genetic screening for RET is informative and helps in the clinical management of MTC patients. The prevalence of different mutations is variable, in our cohort the variants in exons 918, 634 and 804 were the most frequents, however p.Met918Val (17,6%), p.Val804Met (14.7%), p.C634Tyr (11.8%) were more frequent than usually reported.

CLINICAL/THYROID CANCER CLINICAL

117056 ACTIVE SURVEILLANCE VERSUS IMMEDIATE SURGERY IN THE MANAGEMENT OF LOW-RISK PAPILLARY THYROID MICROCARCINOMA: A LONG-TERM COMPARISON OF THE COSTS IN BRAZIL

Fernanda Nascimento Faro[1], Antonio Augusto Tupinambá Bertelli[1], Nilza Maria Scalissi[1], Adriano Namo Cury[1], Rosália do Prado Padovani[1], Carolina Ferraz[1]

[1] Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, Brasil

Introduction: Although active surveillance (AS) has been demonstrated as a safe strategy in the management of low-risk papillary thyroid microcarcinoma (PTMC), economic burden has been questioned as a barrier to its acceptance. Cost analyses have methodological limitations and vary based on clinical protocols, follow-up duration and countries. Therefore, cost-effectiveness should be considered individually for each region. **Objective:** This study aimed to compare the long-term medical costs of AS, partial thyroidectomy (PT) and total thyroidectomy (TT) for low-risk PTMC under the Brazilian Public Health System (*Sistema Único de Saúde* – SUS). **Methods:** We reviewed previous AS cohorts and our own data and created a model of the flow of AS, PT and TT for 10, 20 and 30 years of care per patient, following national and international guidelines and the clinical practices of our service. The medical costs included the step of diagnosis, surgery (type, anesthesia, pathological examination and hospital admission), prescription of medicine (levothyroxine, calcium and calcitriol), and expenses of the follow-up care (consultations, blood tests, ultrasound examinations). The cost of conversion surgery was included in the AS group. Based on studies of 2,802 patients with low-risk PTMC on AS, we considered that 13.3% of the patients on AS evaluate to surgery during follow-up, and that TT was the surgery of choice. The media time for conversion was 21.3 months after diagnosis. According to our review of literature, we considered that 4% of the patients in the TT group evaluate to permanent hypoparathyroidism, and, in the PT group, 43% evaluate to hypothyroidism. The values of the activities were stablished using the SUS table of costs. **Results:** The total cost of AS was more economic than both alternatives of immediate surgery. The 10, 20 and 30-year costs of TT were 18.3, 15.3 and 13.4 times higher than that of AS, respectively (R$ 4,247.74 *vs.* R$ 1,501,81/patient/10 years; R$ 5,015.91 *vs.* R$ 1,983.16/patient/20 years; R$ 5,784.08 *vs.* R$ 2,464.51/patient/30 years). Likewise, the 10, 20 and 30-year costs of PT were 1.6, 1,7 and 1.8 times higher than that of AS, respectively (R$ 1,742.71 *vs.* R$ 1,501,81/ patient/10 years; R$ 2,319.73 *vs.* R$ 1,983.16/patient/20 years; R$ 2,896.74 *vs.* R$ 2,464.51/patient/30 years). While the difference costs between TT and AS presented a trend to reduce during follow-up, the difference costs between PT and AS tend to increase, favoring AS. When conversion surgeries were not considered in the group of AS, the cost of TT was 29.4, 23.1 and 19.6 times the cost of AS, and the cost of PT was 6.2, 5.3 and 4.8 times the cost of AS in 10, 20 and 30 years, respectively. **Conclusion:** AS was more cost-effective than immediate surgery (PT or TT) for 10, 20 and 30 years of follow-up care. Thus, economic burden on public health should not be a barrier to the implementation of AS in our country.

CLINICAL/THYROID CANCER CLINICAL

117170 ANAPLASTIC THYROID CARCINOMA DURING PREGNANCY: CASE REPORT

Cássio Antonio Bezerra de Oliveira[1], Rudival Faial de Moraes Junior[1], Milena Coelho Fernandes Caldato[1], Vanessa Campos Couto da Rocha[1], Ana Augusta Motta Oliveira Valente[1], Natália Xavier Silva Chini[1], Carolina Tavares Carvalho[1], Samuel Sabbá Fadul[1], Fabiola de Arruda Bastos[1]

[1] Centro Universitário do Pará (Cesupa), Belém, PA, Brasil

Case presentation: Female, 22 years old, hospitalized in the Head and Neck Surgery ward due to multinodular goiter of onset and rapid growth (approximately one year), without ever having performed fine needle aspiration, with the proposal to undergo thyroidectomy total. However, due to the report of a 2-month menstrual delay, a serum β-HCG test was requested, which confirmed her 5th pregnancy. Thus, at approximately 10 weeks of gestational age, the patient was promptly discharged from the hospital. 13 days after vaginal delivery, the patient was re-admitted to the ward with a large pedunculated goiter and severe compressive symptoms. The surgery was performed – total thyroidectomy with neck dissection, and the histopathological and immunohistochemical reports confirmed an undifferentiated malignant neoplasm, measuring approximately 12 cm in the longest axis. **Discussion:** Anaplastic thyroid cancer (ATC) is the least common but the most lethal of thyroid cancers. It is more frequent in females in the proportion of 3:1, and is usually diagnosed in the 6th or 7th decade of life. It is believed that originates from differentiated thyroid cancers as a result of de-differentiation. The median survival is 5 months and the overall 1 year survival is 20%. It is the most aggressive solid tumor known to humans, and over seven decades there has been little progress in treating this malignancy. Despite this, multimodal treatment, which includes surgery, radio and chemotherapy and, recently, targeted molecular therapy, is considered the best strategy to mitigate the terrible prognosis. Regarding the association of ATC and pregnancy, there is only one record in the medical literature. In this case, a Ukrainian patient, probably contaminated by ionizing radiation at the age of 8 during the Chernobyl nuclear accident, was admitted to the hospital with a goiter and compressive symptoms at 27 years of age and 16 weeks of gestational age. The Ukrainian case differs from our report (Ukrainian case x Brazilian case, respectively), regarding exposure to ionizing radiation as a probable causal factor (present x absent), the type of surgery (hemithyroidectomy with ipsilateral dissection x total thyroidectomy with bilateral dissection), the decision to terminate the pregnancy (yes x no), survival after surgery (38 x 98 days). The two cases agree only in relation to the presentation in the 2nd decade of life (27 x 22 years), the presence of a long-lasting goiter/nodule (13 x 2 years), the involvement of the right thyroid lobe (left thyroid lobe apparently spared in both cases) and the inexorable prognosis (death at 1.2 x 3.5 months after surgery). **Final comments:** In the association between ATC and pregnancy, given the current context of poor prognosis regardless of whether or not any therapeutic modality is performed, conservative treatment until now childbirth seems to us to be the most appropriate management option for the mother-fetus binomial.

CLINICAL/THYROID CANCER CLINICAL

117089 CLINICAL AND ANATOMOPATHOLOGICAL CHARACTERIZATION OF DIFFERENTIATED THYROID CANCER WITH LOW-RISK OF RECURRENCE IN A TERTIARY SERVICE OF THE FEDERAL DISTRICT, BRAZIL

Alana Ferreira de Oliveira[1], Thamyris Vilar Correia[1], Kellen Karenine Pinho de Medeiros[1], Hiloma Rayssa Fernandes Siqueira[1], Cristiana Rocha Pinto de Abreu Pontes[1], Cicilia Luiza Rocha dos Santos Paiva[1], Cristiane Jeyce Gomes Lima[1]

[1] Instituto Hospital de Base do Distrito Federal, Brasília, DF, Brasil

Introduction: Thyroid carcinoma is the most common endocrine malignancy in the population and accounts for approximately 2.1% of cancer diagnoses worldwide. Among the types of thyroid cancer, approximately 90% are of the differentiated type (differentiated thyroid carcinoma – DTC). After surgical treatment, the DTC risk stratification may be either high, intermediate, or low, based on the chance of disease recurrence. **Objectives:** To characterize the clinical and anatomopathological behavior of DTC with low risk of recurrence with or without radioiodine therapy (RIT) in a tertiary service in the Federal District. **Methods:** Collection of data from medical records of patients in follow-up at the Endocrinology outpatient clinic of a tertiary service in the Federal District. **Results:** The mean age of this cohort was 44 ± 10.3 years with RIT and 49.3 ± 10.2 years without RIT. Among the 81 patients (50 in the RIT group and 31 in the non-RIT group) included, there was a female predominance (98.7%). The papillary histological type accounted for > 90% of cases. The mean follow-up time was 14.2 ± 4.1 years (RIT group) and 10.9 ± 2 years (non-RIT group) ($p < 0.001$). Total thyroidectomy with central dissection was performed in 98% of the RIT group ($p = 0.006$). There were no cases of recurrence in the RIT group. Disease recurrence or persistence occurred in one patient in the non-RIT group, who maintained a positive anti-thyroglobulin antibody for more than 10 years. Excellent treatment response occurred in 98% of the RIT group versus 83.9% of the non-RIT group ($p = 0.039$). **Conclusions:** This study corroborate data from the current literature, by showing that the absence of RIT does not increase recurrence/mortality nor decrease overall survival. Positive anti-thyroglobulin antibody levels for more than three years may justify the use of RIT.

CLINICAL/THYROID CANCER CLINICAL

116886 CLINICAL AND MOLECULAR CHARACTERIZATION OF PATIENTS WITH MEDULLARY THYROID CARCINOMA IN THE STATE OF BAHIA, BRAZIL

Rafael Reis Campos da Matta[1], Marli Viapiana Camelier[2], Taíse Lima de Oliveira Cerqueira[3], Juliana Lima Von Ammon[1], Ana Clara Telles[1], Gabriel Jeferson Rodríguez Machado[1], Gilberto Dauricio Silva Leite[3], Fabyan Esberard de Lima Beltrão[4], Ana Luiza Maia[2,5], Helton Estrela Ramos[3]

[1] Postgraduate Program in Interactive Processes of Organs and Systems, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil. [2] Clinical Hospital of Porto Alegre, Endocrinology Service, Porto Alegre, Rio Grande do Sul, Brazil. [3] Department of Bioregulation, Institute of Health Sciences, Federal University of Bahia, Bahia, Salvador, Bahia, Brazil. [4] Lauro Wanderley University Hospital, Federal University of Paraíba, João Pessoa, Paraíba, Brazil. [5] Department of Internal Medicine, Faculty of Medicine, Federal University of Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil

Introduction: Medullary thyroid carcinoma (MTC) is a rare cancer that originates from C cells. MTC can present as sporadic (75%) or hereditary (25%) as a component of multiple endocrine neoplasia type 2 syndromes (MEN2A and MEN2B). Both sporadic disease and hereditary disease are mainly caused by mutations in the RET proto-oncogene. The incidence of MTC and its molecular bases is still unknown and little investigated, especially in northeastern states of the country. Although the Northeast region is the second in number of registered cases of MTC, there are still few studies that investigate the behavior and characteristics of this disease in the region. There is also no record regarding the clinical presentation, research of polymorphisms and mutations of the RET proto-oncogene in patients affected by MTC in Bahia. **Objective:** To clinically and molecularly characterize patients with CMT in the state of Bahia. **Methods:** Cross-sectional and descriptive study involving patients with a histopathological diagnosis of MTC referred for the RET molecular test from 2020 to 2022. Clinical and pathological data were collected from the anatomopathological and immunohistochemical reports of the patients. Genomic DNA was extracted from peripheral blood. Exons 10, 11, 13, 14 and 15 of the RET were amplified by Polymerase Chain Reaction (PCR) and subsequently sequenced by the Sanger method. **Results:** Clinical data: 29 patients were included in the study (82.8% female). Mean age at diagnosis was 46.5 ± 13.1 years and mean tumor size 2.1 ± 1.4 cm. According to the tumor, node, metastasis (TNM) classification, 38% of the tumors were staged as T1a, 27.6% T1b, 24.1% T2 and 10.3% T3. Regional lymph node metastasis (N1) was present in 44.8% of cases. Presence of distant metastasis (M1) to the mediastinum was observed in one case (3.4%). RET proto-oncogene sequencing: the germline mutation C634R (TGC→CGC), located in RET exon 11, was identified in one patient (3.4%). RET proto-oncogene polymorphisms were identified in 51.7% of patients. The L769L polymorphism (CTT→CTG, exon 13) was the most frequent (80%). It occurred in isolation in 53.3% of patients and in 6.7% of patients it co-occurred with the variant of uncertain significance Y791N (TAT→AAT, exon 13). L769L/S836S and G691S/S904S cosegregation were observed in 13.3% and 20% of cases, respectively. In one case (6.7%) the cosegregation G691S/L769L/S904S was identified. **Conclusion:** This study described, for the first time, the clinical and molecular profile of patients with CMT in Bahia. A germline RET mutation was identified confirming the diagnosis of MEN2A in one patient. The absence of germline mutations in the other patients is suggestive of sporadic disease. Polymorphisms of the RET proto-oncogene were identified in 51.7% of the patients, with L769L being the most frequent in our sample (80%). Founding: PAPERGRS/CNPq.

CLINICAL/THYROID CANCER CLINICAL

117163 CLINICAL PROFILE OF PATIENTS DIAGNOSED WITH DIFFERENTIATED THYROID MICROCARCINOMA IN A SPECIALIZED CENTER IN BELÉM DO PARÁ

Natália Xavier Silva Chini[1], Cássio Antonio Bezerra de Oliveira[1], Carolina Tavares Carvalho[1], Ana Augusta Motta Oliveira Valente[1], Vanessa Campos Couto da Rocha[1], Milena Coelho Fernandes Caldato[1], Samuel Sabbá Fadul[1]

[1] Centro Universitário do Pará (Cesupa), Belém, PA, Brasil

Introduction: Advances in imaging device resolutions and access to exams such as Fine Needle Aspiration (FNA) have increased the diagnosis of differentiated thyroid microcarcinomas (MCDT), which by definition are lesions measuring 1 cm or less, at its largest diameter. The biological behavior of these tumors can be atypical, with cases of distant metastases and even death. Multifocality and lymph node metastasis at the time of diagnosis were positively associated with an increased risk of recurrence. According to the American Thyroid Association Guideline (ATA) 2015, an adequate way to assess the prognosis is through the classification according to the risk of recurrence of the disease and on the type of response after the initial treatment. **Objectives:** To identify the clinical profile of patients diagnosed with differentiated thyroid microcarcinoma in a specialized center. **Methods:** The study was observational, cross-sectional and retrospective by collecting data from the medical records of 20 patients with a histopathological diagnosis of thyroid microcarcinoma in specialized center, monitored from January 2016 to December 2021. We collected for the construction of the clinical profile and data collection of preoperative and histopathological tests, evaluation of laboratory test results and postoperative imaging to establish recurrence risk criteria and treatment response profile, based on the ATA 2015 criteria. **Results:** The clinical profile of patients with microcarcinomas are individuals with a mean age of 43.7 years, from female gender (90%), with complete high school (75%), who sought initial care with a complaint of cervical nodulation. The mean size of the nodules was 1.6 cm on the initial ultrasound. This is the most frequently found characteristic of hypoechogenicity. The most used initial treatment was total thyroidectomy, with all patients with papilliferous histological classification. The variant with the highest proportion was classic and with size at histopathology equal to or greater than 5 mm. In the ATA risk stratification, there was statistical significance in the proportion of cases at low risk of recurrence. Regarding the response to the initial treatment, the favorable response was statistically significant, that is, with an excellent response. Regarding the variables that could increase evolution with an unfavorable response, multifocality was observed in 25% of the cases. The presence of lymph node metastasis and the presence of lymphatic/perineural/vascular invasion reached the same proportion, being both 30%. **Conclusion:** Although patients with MCDT are considered to be at low risk and, in general, with an excellent response, there is a group of individuals who may evolve with an unfavorable response and, therefore, benefit from intensive therapy and follow-up. Complementary studies, with a larger population group, are needed to delimit and estimate possible prognostic factors dependent on the clinical profile.

CLINICAL/THYROID CANCER CLINICAL

117054 CUSTOMIZED MULTIGENIC PANEL OF 100 TUMOR SAMPLES SHOWS 7 NOVEL BRAF NO-V600E MUTATIONS IN THYROID CANCER

Juliana Lima Von Ammon[1], Gabriel Jeferson Rodríguez Machado[1], Rafael Reis Campos da Matta[1], Ana Clara Telles[1], Fabiane Carrijo[1], Bruno Alexsander França dos Santos[1], Jessica Fernanda Cassemiro[1], Beatriz Oliveira Almeida[1], Thiago Magalhães da Silva[2], Gustavo Cancela Penna[3], Juliana Cabral[4], Helton Estrela Ramos[1]

[1] Universidade Federal da Bahia (UFBA), Salvador, BA, Brasil. [2] Universidade Estadual do Sudoeste da Bahia (UESB), Vitória da Conquista, BA, Brasil. [3] Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brasil. [4] Hospital Agamenon Magalhães (HAM), Recife, PE, Brasil

Introduction: Follicular cell-derived thyroid carcinoma (FCDTC) constitutes the majority of thyroid neoplasms, corresponding to almost 90% of cases. The analysis of tumor molecular profile, through the technique of next generation sequencing (NGS) in patients from Latin America is still little studied. **Objectives:** To correlate clinicopathological aspects of FCDTC in adult patients with mutations through a customized mutigenic panel. **Material and methods:** Retrospective, cross-sectional, unicentric study, involving tumor samples from 100 adult patients diagnosed with FCDTC, between 2010 and 2019, at Hospital Aristides Maltez in Salvador, Bahia. The anatomopathological data were reviewed by a pathologist. Paraffinized tumor DNA was extracted with the ReliaPrep™ FFPE gDNA Miniprep System (Promega, USA). Genotyping of target genomic regions (KRAS, NRAS, BRAF, EGFR and PIK3CA) was performed using the customized Ampliseq panel and sequencing performed on the iSeq™ 100 platform (Illumina®, USA). Bioinformatics analyzes were performed on the cloud-based Varstation™ platform. *In silico* analysis using Mupro e I-Mutant 2.0 were performed. **Results:** 54/100 (54%) presented satisfactory results and 46/100 (46%) were inconclusive. 83% were classic papillary thyroid cancer (CPTC), mean age was 34 years, 83% were female and mean tumor size was 2.14 cm. 31 of 54 (57%) had mutations in the analyzed genes. Mutations in the BRAF gene were the most frequent (≥58% of the mutations), mostly found in CPTC. 10/54 (18%) samples had the BRAF V600E mutation, and surprisingly, we found 7 BRAF NO-V600E mutations not yet described in FCDTC (G464E, G464R, G466E, S467L, G469E, G596D and the T599Ifs*10 deletion) and the previously reported BRAF A598V mutation. BRAF G464E and BRAF G596D were detected in two cribform morular CT cases; BRAF G466E, BRAF G469E, BRAF G464R and BRAF A598V were present in CPTC, the BRAF T599Ifs*10 observed in a solid variant of CPT and the BRAF S467L in an infiltrative follicular variant. EGFR gene mutations were found in 16/54 (29%) and KRAS and NRAS alterations were found in 8/54 (14%). No mutation was found in the PIK3CA gene. Interestingly, 12 samples had multiple mutations: 3 (BRAF V600 /EGFR), 3 (BRAF NO-V600 /EGFR), 2 (BRAF V600 /BRAF NO-V600), 3 (BRAF/RAS), with 1 CPTC sample with 4 cm and extra-thyroid extension had three simultaneous mutations in the KRAS D119N, NRAS Q61* and EGFR H850Rfs*26 genes. **Conclusion:** Seven novel BRAF NO-V600E variants were found (five in exon 11 and two in exon 15). These findings bring the relevance of carrying out a multigene panel by NGS with the purpose of expanding knowledge about FCDTC genetic alterations.

CLINICAL/THYROID CANCER CLINICAL

117101 FOLLOW-UP STUDY OF PAPILLARY THYROID CANCER IN PATIENTS WITH BRAF MOLECULAR STUDY

Javier Saldaña[1], Cesar Calderon[1], Barbara Zuñiga[1], Francisco Gutierrez[1], Alejandra Lanas[1], Pedro Pineda[1]

[1] Hospital Clínico de la Universidad de Chile, Santiago, Chile

Introduction: The presence of BRAF V600E gene mutation in patients with papillary thyroid cancer (PTC) is associated with greater histological aggressiveness and apparently worse short-term prognosis; however, there are few and conflicting data regarding its long-term prognostic relevance. In 2011-2012 we conducted a BRAF V600E mutation study in tissue samples from patients with PTC. **Objective:** To determine if the presence of BRAF V600E gene mutation is associated with a higher risk of unfavorable events at 5 and 10 years of follow-up, in patients with PTC studied in 2011-2012. **Patients and methods:** Retrospective cohort study of thyroidectomized patients with PTC recruited in 2011-2012. We obtained values of TSH, Thyroglobulin (TG), antithyroglobulin (ATG) antibodies, imaging studies (ultrasound or others) and biopsy results. Patients were classified according to the risk of recurrence (RR). Concerning the V600E mutation, they were classified as wild type (WT) or mutated (MUT). 10-year follow-up data about recurrence, need for new therapies, and mortality were obtained. In those cases without sufficient data in the clinical records, telephone contact was made to complete the information. Patients without follow-up data and those we were unable to be contacted by telephone were excluded. Adverse prognosis (AP) was considered as a composite outcome, which included structural and/or biochemical recurrence, and/or need for new surgery or treatment with radioiodine, and/or death. In the statistical analysis, frequencies, means with SD and t-test for continuous variables are described. **Results:** From the 62 patients included in the initial study, follow-up was obtained in 56. 84% were women and average age was 40 years (SD 11.6). The initial RR was low in 73% (n = 41), intermediate in 19% (n = 11) and high in 7% (n = 4). Regarding the mutation studied, 67.9% were MUT and 32.1% WT. Patients with MUT were older than WT, 43.5 *vs.* 33 years ($p < 0.01$). All men (n = 9) were MUT compared to 61% of women (n = 47). In patients with intermediate and high risk, a higher frequency of MUT was found, 82.3%, with OR 2.9 (but 95% CI was wide: 0.64-18). All patients with high RR were MUT. Median follow-up was 93 months (range 8-137). 85.7% (n = 48) did not present recurrence and 14.2% had AP (n = 8). Of these, 1.8% (n = 1) had persistent disease, 8.9% (n = 5) biochemical and/or structural recurrence treated with surgery or radioiodine, 1.8% (n = 1) died from PTC and 1.8% (n = 1) died from another cause. All patients with AP were MUT. None of the WT patients presented AP. The patient who died from PTC was MUT. **Conclusions:** In our cohort of patients with PTC, BRAF V600E mutation was associated with short-term poor prognostic factors, such as older age and males. In long term follow-up, patients with this mutation had higher risk of recurrence and adverse prognosis at 10-year follow-up. These results support the inclusion of BRAF V600E mutation in short and long term prognostic classifications.

CLINICAL/THYROID CANCER CLINICAL

117169 FOURIER TRANSFORM INFRARED (FTIR) SPECTROSCOPY APPLIED TO CYTOLOGY FROM FINE NEEDLE ASPIRATION IS ACCURATE IN THE DIAGNOSIS OF DIFFERENTIATED THYROID CARCINOMA

Fabyan Esberard de Lima Beltrão[1], Yuri Gustavo Cavalcanti Brasileiro[1], Ingrid Gabriela Bezerra de Lima Cruz[2], Sherlan Guimarães Lemos[2], Wallace Duarte Fragoso[2], Daniele Carvalhal de Almeida Beltrao[3], Giulia Carvalhal[4], Fabricia Elizabeth de Lima Beltrão[5], Danielle Albino Rafael Matos[5], Helton Estrela Ramos[6]

[1] Federal University of Paraíba (UFPB), Lauro Wanderley University Hospital, Department of Endocrinology, João Pessoa, PB, Brazil. [2] Chemistry Department, Center of Exact and Nature Sciences (CCEN), UFPB, João Pessoa, PB, Brazil. [3] University Centre of João Pessoa (UNIPE), João Pessoa, PB, Brazil. [4] Center for Biological and Health Sciences, Federal University of Campina Grande, Campina Grande, PB, Brazil. [5] Lauro Wanderley University Hospital, UFPB, João Pessoa, PB, Brazil. [6] Post-Graduate Program in Medicine and Health, Medical School of Medicine, Federal University of Bahia, Salvador, BA, Brazil

Introduction: Fourier Transform Infrared (FTIR) spectroscopy has been applied to detect carcinoma of several types of organs, with the advantage of being rapid and preserving the tissue analyzed. **Objectives:** To analyze the ability of FTIR spectroscopy to differentiate pathological tissues (malignancy) from benign thyroid tissue. **Methods:** Patients were selected at the Endocrinology Service of the University Hospital Lauro Wanderley, Federal University of Paraíba – UFPB, João Pessoa-PB, Brazil, from 2020 to 2021. The study employed fine needle aspiration (FNA) samples from 9 patients (n = 61), with 34 samples diagnosed as benign (Bethesda II) and 27 samples diagnosed as thyroid cancer (Bethesda VI). Healthy and pathological thyroid tissues were characterized by FTIR spectroscopy, chemometric classification techniques, and soft independent modeling by class analogy (SIMCA). The experiments used a Shimadzu Spectrophotometer, model IR Prestige-21 (Kyoto, Japan). **Results:** Analyzing each piece by the UV-Vis-NIR spectrum by diffuse reflectance, we found an absorbance equal to or greater than 0.3 Absorbance Units (AU) between wave numbers from 3,200 to 3,600 cm –1 (pattern of slides with material carcinogenic). The spectrometry had a sensitivity of 66.7% and a specificity of 100%, with an accuracy of 85.24%. **Conclusion:** FTIR spectroscopy is a promising tool in diagnosing thyroid cancer and can detect changes at a multi-molecular level. More extensive studies are needed to verify these preliminary results.

CLINICAL/THYROID CANCER CLINICAL

117123 GENETIC TESTING OF FINE-NEEDLE ASPIRATION BIOPSY FOR DIAGNOSIS OF THYROID CANCER

Sofía Savy[1], Victoria Peyret[1], Romina Celeste Geysels[1], Francisco Andrés Montes[1], Eduardo Rafael Cuvertino[2], Juan Pablo Nicola[1]

[1] Departamento de Bioquímica Clínica (CIBICI-CONICET), Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina. [2] Cuvertino Estudios Ecográficos, Córdoba, Argentina

Introduction: The frequency of palpable thyroid nodules is ~5% in the population, but only a small fraction of them are malignant (thyroid cancer). Fine-needle aspiration biopsy (FNAB) is the most reliable tool for malignant thyroid nodule screening. However, indeterminate thyroid nodules are diagnosed in up to 30% of fine-needle aspirations and the risk of malignancy in these cases are highly variable. The understanding of the molecular events that promote thyroid cancer has allowed a substantial theranostic improvement of thyroid nodules. Particularly, genetic testing for proto-oncogene mutations has improved the diagnostic accuracy of indeterminate thyroid nodules. **Objective:** To develop a PCR-based proto-oncogene genetic testing including the analysis of point mutations and gene fusions to improve the theranostic of thyroid cancer. **Methods:** Point mutations in the proto-oncogenes BRAF codons 600 and 601 and H/N/KRAS codons 12, 13 and 61 were assessed using Sanger sequencing. Gene fusion involving the proto-oncogenes RET, NTRK, ALK, BRAF and PPARγ were investigated using multiplex PCR. **Results:** Genetic testing was conducted in a pilot retrospective study including 26 FNAB samples with cytological analysis classified according to Bethesda system as benign (n = 8) or suggestive of malignancy (n = 18). Genomic DNA and total RNA from residual material from FNAB samples was isolated. The point mutations p.V600E BRAF (n = 12) and p.G12V HRAS (n = 1), and the gene fusions RET/PTC1 (n = 2) and ETV6-NTRK3 (n = 1) were detected in FNAB samples suggested of malignancy. The presence of mutation was a strong indicator of cancer as anatomopathological analysis after surgery indicated thyroid cancer in all oncogene-positive nodules. **Conclusion:** Clinically-applicable genetic testing showed significant advance in the diagnostic accuracy of malignancy in the nodules, improving presurgical malignancy risk assessment in order to avoid unnecessary diagnostic surgeries. Moreover, genetic testing allow to design personalized management of patients with thyroid cancer.

CLINICAL/THYROID CANCER CLINICAL

117022 HIGH-GRADE DIFFERENTIATED THYROID CARCINOMA, IMPLICATIONS OF WHO 2022 CLASSIFICATION: CASE REPORT

Patricia Agüero[1], Belén Gordienko[1], Gabriela Mintegui[1], Andrea Cristiani[1], Beatriz Mendoza[1]

[1] Hospital de Clínicas

Case report A 52 years-old female, smoker. Referred due to a 1-year evolution thyroid tumor in euthyroidism. Ultrasound showed a solid, hypoechoic, well-defined nodule on the right lobule, measuring 15 x 18 x 23 mm, and a level III adenopathic mass. Fine needle aspiration reported a papillary carcinoma with metastatic adenopathy. Computed tomography (CT) showed lymph node and lung metastases. Pathology reported a poorly differentiated thyroid carcinoma (5%) and 95% multifocal high-grade invasive follicular variant papillary carcinoma (WHO 2022), largest focus of 65 x 15 mm, lymphovascular emboli and extension to periglandular adipose tissue without muscle invasion. 17 of 48 lymph nodes were involved, largest of 25 mm (Image 1), with extracapsular extension. Molecular genetic testing is not available at our Institution. **Discussion:** Differentiated thyroid carcinoma is the most frequent endocrinological cancer, papillary carcinoma (PTC) represents 85%. 50% of the patients develop lymph node metastases and its rate raises with size and extrathyroidal extension. Poorly differentiated thyroid carcinoma (PDTC) has an intermediate behavior between well-differentiated and anaplastic carcinomas. Its incidence is 2% to 15%. Several studies have shown that the presence of poorly differentiated carcinoma determines poor outcome, regardless of its percentage. The patient had 5% PDTC, which determines a poor prognosis, even more in the presence of pulmonary metastases. The 2022 WHO classification includes PDTC in the category "Follicular-derived carcinomas, high-grade" together with Differentiated high-grade thyroid carcinoma (DHGTC). The last one retains the characteristics of differentiated thyroid carcinomas but adds mitosis and/or necrosis. Regarding treatment, it's recommended total thyroidectomy with lymph node dissection as first line and radiotherapy if lymphadenectomy is contraindicated, although international guidelines including these new entities are not yet been established. Treatment with iodine 131 is individualized according to the tumor's avidity. Iodine treatment was done due to the presence of an unfavorable histology (High grade PTC and PDTC) and distant metastasis. Therefore, 200 mCi were administrated, according to the ATA guidelines. There are several groups investigating other therapies such as immunotherapy, tyrosine kinase inhibitors, and chemotherapy for patients with poor or no response. **Final comments:** WHO classification 2022 recently established the criteria for diagnosing PDTC and DHGTC, with higher radioiodine resistance rate. The lack of scientific knowledge and consensus makes the treatment of these tumors challenging. A B C A. Interphase between HGPTC and PDTC (x40) B. Interphase (x400) showing cells with characteristic PTC nuclei and follicular pattern (right) and cells with oval fine chromatin nuclei and insular pattern (left). C. The PTC areas showed 5 mitosis/2 mm^2.

CLINICAL/THYROID CANCER CLINICAL

117172 HIRSCHSPRUNG DISEASE IN AN MEN2A PATIENT DUE TO A RET 609 PATHOGENIC VARIANT: A RARE ASSOCIATION

Marina Malta Letro Kizys[1], Lucieli Ceolin[1], Flávia de Oliveira Facuri Valente[1], Ilda Sizue Kunii[1], Cléber Pinto Camacho[1], Magnus Regios Dias-da-Silva[1], Rui Monteiro de Barros Maciel[1], Susan Chow Lindsey[1], João Roberto Maciel Martins[1]

[1] Universidade Federal de São Paulo, São Paulo, SP, Brasil

Case presentation: A 43-year old female underwent total thyroidectomy due to a 1.5 cm thyroid nodule with a fine-needle aspiration biopsy suggesting follicular neoplasia and the histopathology showed medullary thyroid carcinoma (MTC). The patient did not have hypertension or nephrolithiasis. She has no family history of thyroid neoplasms, severe hypertension, or nephrolithiasis. Screening of RET gene revealed the variant p.Cys609Ser in exon 10. In the postoperative follow-up, the patient presented with biochemical evidence of disease, but with stable levels of tumor markers (calcitonin and CEA doubling times > 24 months), and she has not presented any evidence of primary hyperparathyroidism (PHPT) or pheochromocytoma (PHEO) during 18 years of follow-up. The patient's parents were deceased. RET sequencing of two brothers and one daughter was negative. One son (25 years old) carries the same RET variant as the mother and his initial evaluation showed a serum calcitonin < 2 pg/mL and serum calcium, PTH and 24-hour urine metanephrines in the normal range. A prophylactic thyroidectomy revealed lymphocytic thyroiditis without MTC or C-cell hyperplasia. After 11 years of follow-up, he continues with undetectable calcitonin levels and no evidence of PHTP or PHEO. The granddaughter of the index case has a history of congenital megacolon (Hirschsprung's disease) and surgery for intestinal obstruction at one month of age. At the age of six, RET testing was positive for the p.Cys609Ser variant. Her baseline calcitonin, plasma catecholamines and urinary metanephrines were in the normal range. She underwent prophylactic thyroidectomy at age 6 and the pathology showed only lymphocytic thyroiditis. She has 11 years of follow-up with undetectable calcitonin levels and no evidence of PHTP or PHEO. **Discussion:** Multiple Endocrine Neoplasia 2A is an autosomal dominant genetic syndrome caused by germline RET mutations and is characterized by MTC, pheochromocytoma, and parathyroid hyperplasia. Herein we report a variant in RET codon 609 in a patient with MTC and two relatives (son and granddaughter), one with Hirschsprung's disease presenting within the first month of life. No other germline variants were detected in classical risk exons 8, 10, 11, 13, 14, 15, and 16. A previously functional study has shown that this RET mutant is constitutively phosphorylated without a ligand. Furthermore, variants in RET exon 10 are considered predisposing to Hirschsprung's disease. It was previously described in a family with PHEO and reduced penetrance of MTC with p.Cys609Ser. This case is the only record in a total of 1081 screened familial MTC (FMTC) patients in our group with p.Cys609Ser and Hirschsprung presentation. **Final comments:** This case report is the first to describe an association of the p.Cys609Ser RET variant with MTC and Hirschsprung's in a family here in Brazil, reinforcing the importance of RET screening in MTC cases and the investigation of other symptoms.

CLINICAL/THYROID CANCER CLINICAL

117139 HÜRTHLE CELL CARCINOMA IN A BRAZILIAN POPULATION: DOES TNM PREDICTS OUTCOMES?

Hugo Fontan Köhler[1], José Guilherme Vartanian[1], Maria Paula Curado[1], Luiz Paulo Kowalski[1]

[1] A.C.Camargo Cancer Center, São Paulo, SP, Brasil

Hürthle cell carcinoma (HCC) is an uncommon thyroid malignancy with conflicting evidence on the literature about its treatment, mainly the use of radioiodine therapy, and survival outcomes. We reviewed a population database from the state of São Paulo and selected patients with differentiated thyroid cancer. Baseline demographic and clinical characteristics of patients with HCC and other morphologies were compared. The Kaplan-Meier and Cox regression analysis were used to evaluate survival outcomes. A total of 17,066 patients were included with 231 cases of HCC. HCC patients were younger (45.3 years *vs.* 50.1 years, $p < 0.001$) and had a higher proportion of neck metastasis than other histologies ($p < 0.001$). Disease-specific and overall survival were similar to papillary thyroid carcinoma (PTC) and significantly better than follicular cell carcinoma (FCC) in this series. The 95 % confidence interval for both survival outcomes for patients with HCC overlaps those of PTC patients. The proportion of patients receiving radioiodine therapy was not statistically different between the groups ($p = 0.875$) and its addition to treatment had no significant impact on survival outcomes in our series for HCC patients staged as pT2-4NxMx or pT1N1Mx ($p = 0.277$). The TNM staging was highly predictive of outcome for patients with PTC and FCC in our series, but not for HCC. The TNM staging system is less informative in these patients than in other histological types.

CLINICAL/THYROID CANCER CLINICAL

116498 IMPACT OF THE CORONAVIRUS DISEASE PANDEMIC ON THYROID CANCER DIAGNOSIS IN OLDER ADULTS. A RETROSPECTIVE ANALYSIS

Yanina Jimena Morosán Allo[1], Zulma Mamani Vela[1], Ayelén Ridolfo[1], Lucía Selvaggio[1], Carina Parisi[1], Maximiliano Lo Tartaro[1], Cristina Faingold[1], Gabriela Brenta[1]

[1] Unidad Asistencial Dr. César Milstein, CABA, Argentina

Introduction: During the COVID-19 pandemic, a more conservative approach to nodular thyroid pathology was adopted worldwide. However, this strategy in older adults, in whom thyroid cancer may be more aggressive, has not yet been evaluated. **Objective:** To analyze the impact of the pandemic on thyroid cancer diagnosis in older adults. **Methods:** Retrospective study of all patients ≥ 60 referred to thyroid surgery (TS) from January2019 to December2022 in a tertiary care center for older adults. The study was subdivided into four periods (P): P1: January2019-February2020 (PRE-COVID-19); P2: March2020-May2021 (1stCOVID-19), P3: June2021-December2021 (2ndCOVID-19 or pandemic decrease) and P4: January2022-December2022 (POST-COVID-19). The number of TS was established in relation to the number of general surgeries (GS) performed. In addition, a delay in days between thyroid nodule biopsy and TS was calculated. Demographic, pre-(ultrasound (US) risk stratification ACR TI-RADS and cytology), and postoperative (extension of surgery and histotype) data were recorded. For thyroid cancer, size ≥ 4 cm, gross extrathyroidal extension, or distant metastasis were considered an advanced form of presentation. In addition, the AJCC/TNM 8th edition (TNM) survival risk and the American Thyroid Association (ATA) structural disease risk of recurrence were also reported for differentiated thyroid cancer. CHI2 and ANOVA were used to compare data among the four periods. **Results:** Out of 4,036 GS throughout the study period, 79 (1.9%) patients were referred to TS (age 69.7 ± 6, 83.5% women). Of these, 33(41%) underwent surgery in P1, 7 (8%) in P2, 15 (18%) in P3, and 24 (30%) in P4. The proportion of TS to GS was lower at P2: 0.8% (n:7/820) compared to P1: 2.4% (n: 33/1352), P3: 2.5% (n: 15/592) and P4: 1.8% (n: 24/1272). The proportion ratio of P2/P1 was 0.33 (95%CI 0.16-0.79), and it returned to similar values to P1 in P3 and 4 (p = ns) The delay in days to TS was 133 (IQR;82-284) and similar among periods. 79% were total thyroidectomies, and 40% were malignant tumors, of which 33% were advanced at presentation, while 10% were 1-2 cm and 56.7% were < 1 cm. There were 28 differentiated thyroid cancers; 60.7% were stage I, 10.7% stage II, 7.1% stage III, and 21.4% stage IVTNM. Low ATA risk was found in 67.9%, while the rest (32.1%) were all high-risk tumors. Thyroid cancer was more frequently found in P4 *vs.* P1 (15/23:65% *vs.* 12/33:36%), p = 0.031, and coincidentally the US risk suspicion of nodules referred to biopsy was also higher: ACR TI-RADS5 in P4 (11/24:45% *vs.* 4/28:14%), p = 0.016. Advanced thyroid cancer in P4 *vs.* P1 (6/15:40% *vs.* 3/11:27%), although more frequent, did not attain a significant difference. **Conclusion:** During the COVID-19 pandemic, TS was reduced in relation to GS, with a 77% decrease in the 1stCOVID-19 period compared to pre-pandemics. The consequences of this reduction in TS could be reflected in the higher proportion of thyroid cancer detected after the quarantine was over.

CLINICAL/THYROID CANCER CLINICAL

117159 IS NCOR1 GENETIC VARIANT SPECIFICALLY ASSOCIATED WITH A SUBTYPE OF THYROID CARCINOMAS?

Débora Mota Dias Thomaz[1], Julia Cavallari Albuquerque[1], Luiza Sisdelli[1], Isabela Nogueira Nunes[1], Larissa Valdemarin Bim[1], Ana Carolina Panizza[1], João Roberto Maciel Martins[2], Janete Maria Cerutti[1]

[1] Genetic Bases of Thyroid Tumors Laboratory, Division of Genetics, Department of Morphology and Genetics, Federal University of São Paulo (Unifesp), São Paulo, SP, Brazil. [2] Laboratory of Molecular and Translational Endocrinology, Division of Endocrinology, Department of Medicine, Unifesp, São Paulo, SP, Brazil

Introduction: Differential diagnosis between oncocytic thyroid carcinomas (OTC) and oncocytic thyroid adenomas (OTA) by fine-needle aspiration (FNA) is challenging due to their similar cytology, so a definitive diagnosis is made only after complete resection of the tumor to search for vascular and/or capsule invasion. Although molecular markers have already been identified for papillary thyroid carcinoma (PTC), the molecular basis of OTC is complex and remains to be elucidated. Through RNA-seq analysis of 14 thyroid carcinomas that were negative for the main driver mutations described in thyroid cancer, we identified a NCOR1 missense variant exclusively in 2 OTC. It's known that NCOR1 (17p12-p11.2) has unique roles in the regulation of thyroid hormone signaling and was found mutated or lost in several human cancers. Therefore, we hypothesized that NCOR1 may play a role in the genesis of OTC. **Objective:** We here sought to investigate whether the identified NCOR1 p.H2252Y variant is specifically associated with OTC pathogenesis. **Material and methods:** To assess the prevalence of NCOR1 p.H2252Y, DNA isolated from 188 thyroid neoplasms was submitted to sanger sequencing. The sample set comprised 37 OTA, 23 OTC, 30 FTA, 30 FTC, 30 PTC, 30 follicular variants of PTC, and 8 NIFTP. To explore the effect of p.H2252Y on the NCOR1 protein expression profile, immunohistochemistry was performed on mutated and non-mutated OTC along with OTA samples. To investigate if the missent variant NCOR1 is associated with CNV, we performed fluorescent in situ hybridization (FISH) using a chromosome 17 alpha-satellite probe on mutated samples. We also investigated the presence of this mutation on over 8000 samples from the Pan-TCGA exome data set. **Results and discussion:** By Sanger sequencing, we identified the NCOR1 p.H2252Y variant in 6/23 (26%) of OTC while it was not identified in any other thyroid neoplasm. Surprisingly, 2 of the 6 samples were first diagnosed as OTA. As they were positive for the NCOR1 variant, H&E-stained slides from deeper sections of the tumor were subjected to re-evaluation by a pathologist. The outcome was assessed and vascular and/or capsular invasion were observed, which altered the initial diagnosis to OTC. All patients are under clinical follow-up. Additionally, NCOR1 protein was not detected on mutated tumors and adjacent thyroid tissues, while it was detected on OTA, suggesting that this protein may act as a tumor suppressor in oncocytic thyroid tumors. We also observed recurrent loss of one or both chromosome 17 on OTC NCOR1-mutated samples. Notably, this variant was not found on any Pan-TCGA samples. **Conclusion:** These data suggest that NCOR1 p.H2252Y has potential use as an OTC molecular marker, which might positively impact the preoperative differential diagnosis of thyroid nodules commonly classified as indeterminate on FNA analysis. Also, for the first time, we are postulating that NCOR1 may be relevant to OCT pathogenesis.

CLINICAL/THYROID CANCER CLINICAL

117023 LOBECTOMY FOR LOW AND LOW-INTERMEDIATE-RISK OF RECURRENCE DIFFERENTIATED THYROID CANCER: MULTICENTRIC STUDY FROM ARGENTINA

Fernando Jerkovich[1], Andrea Cavallo[1], Juliana Fassi[1], Jorgelina Guerra[1], Santiago Zund[1], María del Carmen Negueruela[1], Eduardo Faure[1], Laila Bielski[1], Adriana Reyes[1], Gabriela Brenta[1], Fabián Pitoia[1]

[1] Departamento de Tiroides, Sociedad Argentina de Endocrinología y Metabolismo, CABA, Argentina

Introduction: Thyroid lobectomy is considered an appropriate surgical approach for T1-T2 low and low-intermediate-risk differentiated thyroid carcinomas (DTC). However, historically this procedure has been scarcely accepted in Argentina. **Objective:** To describe the oncological outcomes and postoperative thyroid function of a group of patients with low and low-intermediate risk of recurrence DTC treated with lobectomy. **Methods:** This is a multicentric and retrospective study including 153 patients with DTC who received thyroid lobectomy as initial treatment (March 2001 to November 2021) with at least 12 months follow-up postoperatively. The clinical response was assessed at 1 year and at final follow-up considering serial neck ultrasounds (US) and assessment of thyroglobulin (Tg) and thyroglobulin antibodies (TgAb) levels. Thyroid function was evaluated preoperatively and at final follow-up. **Results:** The mean age of the cohort was 46 ± 12.9 y.o. and 73% were women. Most patients (65%) had classic papillary thyroid carcinoma (PTC), 17% had follicular subtype of PTC, 8% presented follicular thyroid carcinoma and 10% other histologic variants. Most patients had low-risk of recurrence (91.5%) and the tumor size was < 2 cm in 86% and < 1 cm in 45%. Only 5 patients presented postoperative complications (n = 3, transient RLN palsy; n = 1, hematoma; and n = 1, wound infection). During a median follow-up of 42 months (IQR: 27-67), 4 patients (2.6%) had a structural incomplete response (SIR) at 14, 17, 38 and 67 months of follow-up. Three of these patients had recurrences in the contralateral lobe (all papillary microcarcinomas) and the remainder developed metastatic lymph nodes. After completion of total thyroidectomy, three of them achieved and excellent response and one patient had an indeterminate response due to suspicious lymph nodes on serial neck US. Tg levels remained stable in these 4 patients. The 5-year recurrence-free survival rate of the total cohort was 95%. Out of 114 patients with preoperative normal thyroid function, 67 (58.8%) presented subclinical hypothyroidism and 6 (5.3 %) clinical hypothyroidism after the lobectomy and 56 (49%) were treated with levothyroxine. A preoperative TSH value > 2 mIU/L had an OR of 5.1 (95% CI: 1.4-18.4, p = 0.0007) with a PPV 87% and a NPV 42% for the development of thyroid dysfunction. The presence of TPOAb or TgAg was not associated with the risk of postoperative thyroid dysfunction in euthyroid patients. **Conclusion:** Thyroid lobectomy is a reasonable approach for T1-T2 low and low-intermediate-risk patients with low rates of SIR, similar to that observed in patients treated with total thyroidectomy. Nearly half of euthyroid patients will need levothyroxine after surgery. Preoperative TSH levels are significantly associated with postoperative thyroid function regardless the TPOAb or TgAg status. These outcomes would encourage physicians in Argentina to adopt a less aggressive approach for this group of patients.

CLINICAL/THYROID CANCER CLINICAL

117091 MULTIDISCIPLINARY APPROACH AND MOLECULAR TARGETED THERAPY IN POORLY DIFFERENTIATED THYROID CARCINOMA: A CASE REPORT

Kellen Karenine Pinho de Medeiros[1], Thamyris Vilar Correia[1], Hiloma Rayssa Fernandes Siqueira[1], Alana Ferreira de Oliveira[1], Fabiane Kellem Oliveira dos Santos Cesário[2], Gustavo do Vale Gomes[3], Cristiane Jeyce Gomes Lima[4]

[1] Instituto Hospital de Base do Distrito Federal, Brasília, DF, Brasil. [2] Hospital DF Star, Brasília, DF, Brasil. [3] Núcleos Radiologia e Medicina Nuclear, Brasília, DF, Brasil. [4] Cettro Centro de Oncologia/Instituto Hospital de Base do Distrito Federal, Brasília, DF, Brasil

Case presentation: A 62-year-old male patient presented with hoarseness and a thyroid nodule. A fine needle aspiration (FNA) of the nodule and of a right cervical lymph node was performed and cytology was compatible with papillary thyroid carcinoma (PTC) (Bethesda VI). At diagnosis, multiple pulmonary nodules were also present. The patient underwent total thyroidectomy with radical right neck dissection in July 2021, with incomplete tumor resection. Histopathology showed multifocal PTC with well-differentiated (60%) and poorly differentiated (PD) (40%) components. A genetic panel detected a BRAF V600E mutation at the PD area of the tumor. Immunohistochemistry (IHC) for programmed death ligand 1 (PD-L1) was positive at the PD area of the tumor (combined positive score [CPS] = 100) and negative at the well-differentiated area (CPS = 0.3). IHC for pan-TRK was negative in both areas. In September 2021, a PET-CT scan showed uptake on cervical lymph nodes, right paratracheal region, lung nodules, hepatic nodule, and a lumbar vertebra (L2). Given the high burden of disease, the patient was started on lenvatinib and pembrolizumab in October 2021. In November 2021, a lytic lesion at L2 was resected, with pain relief. Lenvatinib was discontinued in May 2022 due to toxicity. He was on pembrolizumab until October 2022, when it was discontinued due to disease progression at neck and mediastinal lymph nodes, and at some lung nodules. Radiotherapy was then performed in the cervical and thoracic regions. In November 2022, the patient was started on dabrafenib and trametinib, with stable disease and good tolerance. **Discussion:** Poorly differentiated thyroid carcinoma (PDTC) is a rare tumor, with an intermediate prognosis and a mortality rate of 38%-57%. These tumors are highly proliferative, with increased tumor mutational burden (TMB) and high expression of PD-L1. The management of distant metastases in PDTC is challenging, as they often do not respond to traditional therapies. In this case, the clinical picture is clearly driven by the behavior of the poorly differentiated component of the tumor. The presence of BRAF mutation and high PD-L1 expression allowed the use of targeted therapy for this patient. Studies of targeted therapy in thyroid cancer have focused primarily on tyrosine kinase inhibitors (TKI), such as sorafenib and lenvatinib. More recently, the combination of a BRAF inhibitor (dabrafenib) with a MEK inhibitor (trametinib) has shown impressive results in anaplastic thyroid cancer. Moreover, access to surgical resection of metastases and modern radiotherapy techniques have contributed to improvement of quality of life and for a longer overall survival. **Final remarks:** PDTC is an aggressive type of thyroid cancer that requires the coordinated work of a multidisciplinary team. The use of targeted therapy, modern surgical and radiotherapy techniques are paramount for a better response to treatment, with reduced morbidity and mortality.

CLINICAL/THYROID CANCER CLINICAL

117148 MULTIPLE RAS/RAF/MAPK PATHWAY GENES WERE IDENTIFIED IN PEDIATRIC PAPILLARY THYROID CARCINOMAS

Yasmin Paz Christiano[1], Luiza Sisdelli[1], Maria Isabel V. Cordioli[1], Gabriel A. Colozza-Gama[1], Débora Mota Dias Thomaz[1], Paulo Alonso Garcia Alves Junior[2], Mario Lucio Araújo Jr.[2], Osmar Monte[3], Carlos Longui[3], Adriano Namo Cury[4], Fernanda Vaisman[2], Janete Maria Cerutti[1]

[1] Federal University of São Paulo, São Paulo, SP, Brazil. [2] National Cancer Institute (Inca), Rio de Janeiro, RJ, Brazil. [3] Department of Pediatrics, Santa Casa de Misericórdia de São Paulo, São Paulo, SP, Brazil. [4] Department of Medicine Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, Brazil

Introduction: Papillary thyroid carcinoma (PTC) is the most prevalent thyroid cancer with a high prevalence of genetic alterations that lead to the activation of the Mitogen-Activated Protein Kinase (MAPK) pathway such as BRAF and RAS mutations and RET/PTC fusions. Although most studies proposed that these driver mutations have a mutually exclusive pattern, we have acknowledged the presence of multiple mutations emerging concurrently in patients with PTC, mainly in the pediatric population. **Objectives:** The objective of this study was to evaluate the genetic heterogeneity of pediatric PTCs that have more than one fusion that result in increased MAPK signaling using the Fluorescence in Situ Hybridization (FISH) break apart analysis. **Methods:** About 79 cases of pediatric PTC (≤18 years old) from Hospital São Paulo, Unifesp, Santa Casa de São Paulo and INCA-RJ were investigated for the presence of RET/PTC, AGK-BRAF and STRN-ALK fusions by RT-PCR. Paraffin-embedded sections (3µm) were obtained from cases with concomitant fusions (n = 3) and submitted to a dual-color interphase break-apart FISH assay for RET, BRAF and ALK genes. To assess the gene rearrangement status, we scored the number of positive nuclei (split signals) per total on nuclei analyzed (minimum of 50 nucleus) in each of the four representative quadrants of respectively tumor tissue. **Results:** In nearly 70% (55/79) of the cases we identified at least one genetic alteration (55/79-70%), being the great majority (62%) genetic fusions. Among the fusions RET/PTC1 was the most prevalent fusion (28%) followed by AGK-BRAF (19%) ETV6-NTRK3 (18%), RET/PTC3 (15%), and STRN-ALK (10%). To confirm the concomitate mutations found in same tumor sample by RT-PCR, of co-occurrence, we selected samples with RET/PTC1 and AGK-BRAF (case 1) RET/PTC1 and AGK-BRAF (case 2) and RET/PTC1, AGK-BRAF and STRN-ALK (case 3). The analysis of case 1 showed that all four quadrants analyzed had nuclei positive for both RET and BRAF probes. The analysis of case 2 showed that only 2 quadrants show rearranged nuclei. In case 3, all quadrants' nuclei positive for BRAF and ALK. **Conclusion:** In our series we observed a high level of genetic heterogeneity involving MAPK pathway genes in pediatric PTC tumors. However, it is still not clear whether different fusions are present in same cell or distinct cells and if MAPK output differs from cells with only one fusion *vs.* cells with concomitant alterations. Additionally, these results highlight the fact that the use of a specific target therapy may not be enough for full therapeutic efficacy.

CLINICAL/THYROID CANCER CLINICAL

117103 SKIN METASTASIS ON THE NECK OF PAPILLARY THYROID CARCINOMA: AN UNUSUAL PRESENTATION

Ana Mayra Andrade de Oliveira[1], Ana Luisa Andrade de Oliveira[2], Mariana Barros Dantas[1], Ramon Reis Silva[1], Vitoria Marques da Fonseca Morais[1], Fernanda Prohmann Villas Boas[1], Atila Andrade de Oliveira[3], Mariana Andrade dos Santos[4], Bruno Cunha Pires[5], Bruno Ribeiro Pinto[6], Antonio Cesar de Oliveira[1]

[1] Universidade Estadual de Feira de Santana (UEFS), Feira de Santana, BA, Brasil.[2] Universidade Estadual de Campinas (Unicamp), Campinas, SP, Brasil.[3] Medicina Diagnóstica (Diagmed), Campinas, SP, Brasil.[4] Centro Universitário de Brasília (CEUB), Brasília, DF, Brasil.[5] Centro Diagnóstico Pires (Cedapi), Feira de Santana, BA, Brasil.[6] Santa Casa de Misericórdia de Feira de Santana, Feira de Santana, BA, Brasil

Case presentation: A 60-year old woman was diagnosed with papillary thyroid carcinoma (PTC) in 2004 and had a total thyroidectomy followed by radioiodine therapy because of its multifocal character. After these treatments, she received hormonal suppression with levothyroxine and there was no distant or local metastasis in that time. Cervical ultrasonography and measurements of thyroglobulin (Tg) and antithyroglobulin antibody were performed regularly and at all times the results were suppressed and negative respectively, so the patient lived without evidence of disease for 18 years. In 2021 she observed a small nodule on the neck with no adhesion to surrounding tissues. It was done a biopsy compatible with epithelioid cell neoplasm with trabecular and papillary patterns compromising subcutaneous cellular tissue and deep dermis and overlying skin without particularities. Immunohistochemistry performed on skin metastasis was positive for Cytokeratin 7 (CK7), Thyroid transcription factor-1 (TTF1) and Thyroglobulin and negative for Cytokeratin 20 (CK20) and GATA3. It was also performed cervical ultrasound, iodine 131 whole body scanning and a single serum thyroid-stimulating hormone (TSH)-stimulated thyroglobulin (STg) measurement and the results were negative. The 2 years follow-up didn't show any recurrence of the disease. **Discussion:** PTC tends to metastasize to regional lymph nodules and distant metastasis are rare, while typically involving lungs, bones and less frequently the brain. In this case report, the distant metastasis to the skin occurred in the neck. In the literature, the incidence of cutaneous metastasis is 5.3% for all visceral malignancies and in PCT the reported prevalence is between 0.06%-0.82%. Approximately 2/3 of metastatic skin lesions involve the scalp, and the remaining cases mostly involve the head and neck regions. There is no gender predominance in skin metastasis of PCT. Cutaneous metastasis usually occurs in the setting of diffuse metastatic disease and in this case, there was no evidence of systemic involvement. The median onset of skin metastasis from initial treatment for primary PCT is 8.25 years while in this patient, the skin metastasis presented itself 18 years after total thyroidectomy and radioactive iodine (RAI). **Final comments:** It was described as an unusual case of PTC with skin metastasis without systemic disease but with distinguishing microscopic images. Although PTC presents a favorable prognosis, less than 10% of patients develop distant metastasis, in this way, skin metastasis of papillary carcinoma should be kept in mind when atypical skin lesions are found.

CLINICAL/THYROID CANCER CLINICAL

117079 USE OF MULTIKINASE AND RET-SELECTIVE INHIBITORS IN PATIENTS WITH MEDULLARY THYROID CARCINOMA: EXPERIENCE FROM TWO UNIVERSITY HOSPITALS IN ARGENTINA

Erika Abelleira[1], Natalia León[1], Inés Califano[2], David Pereira[2], Raúl Giglio[2], Fernando Jerkovich[1], Fabián Pitoia[1]

[1] Hospital de Clínicas "José de San Martín", Universidad de Buenos Aires, Buenos Aires, Argentina.[2] Instituto de Oncología "Angel H. Roffo", Universidad de Buenos Aires, Buenos Aires, Argentina

Introduction: Medullary thyroid carcinoma (MTC) is a rare thyroid malignancy that may present in the hereditary form in approximately 25% of cases. While the hereditary conditions have germline RET mutations, nearly half of the sporadic tumors may present somatic mutations, more frequent M918T, associated with worse outcomes. Up to 20% of MTC patients have a distant metastatic disease with less than a 40% 10-year survival rate. The use of multikinase inhibitors (MKIs) and selective RET inhibitors (RSI) showed improvement in progression-free survival (PFS) in advanced and progressive MTC. In Argentina, vandetanib was the only MKI available, while pralsetinib and selpercatinib could be only used under expanded access programs until 2022. **Objectives:** To describe tumor objective response, PFS, overall survival (OS) and adverse events (AEs) profile in patients with advanced and progressive MTC who received MKIs and RSI in a real-life setting. **Methods:** Retrospective study of patients > 18 years with locally advanced and/or metastatic progressive MTC treated with MKIs and RSI (2013 to 2023). **Results:** Twenty-one patients from two university hospitals in Buenos Aires were included. The median age was 42 years, and 57% were women. The median follow-up was 17 months (range: 1.4 to 99). Four patients (19%) harbored germline mutations. Six of 15 patients with sporadic MTC were studied, and 5 had somatic RET mutations: one carried C634Y and four M918T. Eighteen patients received MKIs: vandetanib (n = 17), sorafenib (n = 4), and pazopanib (n = 1). Four patients (19%) received RSI: selpercatinib was prescribed to 3 patients as first-line and pralsetinib in one patient as second-line treatment. The mean duration of treatment was 21 months (1.4-46). Best overall responses were complete response (CR) in 1 patient (4.7%), partial response (PR) in 5 (23%), and stable disease (SD) in 12 (51%). The median duration of response was 15 months (range 3 to 80). The median PFS was 45 months (95% CI 18-71), and the median OS of 84 months (95% CI 26.4-141.6). The overall mortality rate was 38% (n = 8), related to progressive disease. These patients required dose reductions and interruptions because of AEs or delays in MKIs provision by health insurance (n = 2). All patients experienced at least one AEs. The most frequent were diarrhea (85%) and hand-foot syndrome (62%). Grade ≥ 3 AEs were observed in 8 patients (38%): prolonged QT interval, hypocalcemia, renal injury, hand-foot syndrome, asthenia, pancytopenia, and heart disease. They solved with transient interruption of the drugs. **Conclusion:** We present a real-life experience of MKIs and RSI in patients with advanced MTC. Systemic therapy resulted in a partial response in 23% and disease stabilization in 51% of the total cohort at a mean follow-up of 17 months. Although all patients experienced AEs, most of them were manageable and definitive withdrawal of the drug was unnecessary.

CLINICAL/THYROID GENETICS

117127 A NOVEL CASE OF THYROID HORMONE RESISTANCE WITHOUT ABNORMAL THYROID HORMONE RECEPTORS

Carlos Eduardo Bernal Barquero[1], Gerardo Hernán Carro[1], Patricia Papendieck[2], Ana Elena Chiesa[2], Juan Pablo Nicola[1]

[1] Departamento de Bioquímica Clínica (CIBICI-CONICET), Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina. [2] División de Endocrinología, Hospital de Niños Dr. Ricardo Gutiérrez, Buenos Aires, Argentina

Case presentation: We report a case of a 3-years old female patient suspected of thyroid hormone resistance. The patient presented a developmental delay, cardiac murmur, Silver-Russel syndrome, and abnormal body proportions. Laboratory tests revealed TSH 7.19 mIU/L (0.5-4.7 mUI/L), T3 264 ng/dL (105-245 ng/dL) and T4 10.9 ug/dL (4.5-12.5 ug/dL). Comprehensive genetic testing using whole-exome sequencing revealed the absence of mutations in the coding region of candidate genes involved in thyroid hormone resistance. Nonetheless, further analysis revealed the pathogenic variant p.S1431Y in the X-linked gene BCL6 corepressor (BCOR) as potential cause of the disease. **Discussion:** Approximately 15% of patients suspected of thyroid hormone resistance lack of mutations in the genes encoding the thyroid hormone receptor. Therefore, pathogenic variants in thyroid hormone receptor-associated cofactors may cause abnormal thyroid hormone response. The corepressor BCOR is suggested to be one of the essential coregulator of early embryogenesis, as, in females, pathogenic variants in the X-linked gene BCOR were associated with oculofaciocardiodental. BCOR can form ternary complexes with the corepressors NCOR1 and NCOR2 (also known as SMRT) and recruit histone deacetylase HDAC3 to potently repress the expression of BCL6 target genes. Recently, BCOR was identified as glucocorticoid-induced member of the glucocorticoid receptor protein interaction network. Given that the corepressors NCOR and SMRT interact with the thyroid hormone receptors, we speculate that pathogenic variants in BCOR may also influence thyroid hormone response. Further experimental evidence supporting BCOR-regulated thyroid hormone receptor transcriptional activity is eagerly awaited. **Final comments:** The identification of novel mechanisms involved in thyroid hormone resistance will provide further insights into thyroid hormone receptor-regulated gene expression.

CLINICAL/THYROID GENETICS

117037 DIO2 POLYMORPHISMS AND THYROID HORMONE LEVELS DURING NEONATAL EVALUATION IN CHILDREN WITH THYROID DYSGENESIS: A PRECISION MEDICINE APPROACH

Jessica Fernanda Cassemiro[1], Lorena Rejane Maia de Jesus[1], Fabiane Tavares Carrijo[1], Taíse Lima de Oliveira Cerqueira[1], Tatiana Amorim[2], Fabio Hecht[3], Célia Regina Nogueira[4], Natassia Elena Bufalo[5], Laura Sterian Ward[5], Helton Estrela Ramos[1]

[1] Department of Bioregulation, Health & Science Institute, Federal University of Bahia, Salvador, BA, Brazil. [2] Association of Parents and Friends of Exceptional Friends (Apae), Salvador, BA, Brazil. [3] Instituto de Biofísica Carlos Chagas Filho, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil. [4] Departamento de Clínica Médica, Disciplina de Endocrinologia, Faculdade de Medicina, Universidade Estadual Paulista (Unesp), Botucatu, SP, Brazil. [5] Laboratory of Cancer Molecular Genetics, School of Medical Sciences, University of Campinas, Campinas, SP, Brazil

Introduction: Thyroid dysgenesis (TD) accounts for 85% of congenital hypothyroidism (CH) cases. The polymorphisms in the DIO2 gene have been associated with reduced D2-mediated thyroxine to T3 conversion and tissue insufficiency. No study has evaluated common D2 polymorphisms (SNP) in patients with TD and their impact on disease presentation. **Objective:** To investigate the frequency of common DIO2 SNPs among patients with TD from two institutions (Apae-Salvador and Unesp) and whether these SNPs predict the severity of CH phenotype at neonatal initial evaluation. **Material and methods:** We investigate 34 TD subjects. All children had neonatal TSH measurement and performed thyroid function tests during the first 60 days of life, including thyroid ultrasound and scintigraphy. D2-ORFa-Gly3Asp (rs12885300) and Thr92Ala (rs225014) polymorphisms were evaluated by TaqMan® SNP Genotyping. ANOVA, Kruskal-Wallis, Mann-Whitney, and Test t were used. **Results:** Hypoplasia represented 34% of all cases of TD, followed by ectopy (32%), hemiagenesis (17%) and agenesis (17%). The highest levels of TSH in the neonatal screening were observed in the agenesis group, although the small number of patients impaired the statistical comparison ($p = 0.094$). D2-ORFa-Gly3Asp SNP analysis revealed heterozigozity in 9/34 (26%) subjects. Comparing Wild-type (WT) to Heterozygous (HT) individuals, we found no difference in serum thyroid hormone levels: (i) fT4 (1.09 ± 0.7 *vs.* 0.77 ± 0,4 ng/dL; $p = 0.36$); (ii) TSH (56.6 ± 63.6 *vs.* 76.5 ± 48.5 mIU/L; $p = 0.24$) and tT4 (9.0 ± 5.8 *vs.* 6.9 ± 4.4 ng/dL; $p = 0.47$). Thr92Ala SNP analysis revealed: HT in 18/32 (56%) and homozigozity (HZ) in 9/32 (28%) subjects. Again, the serum thyroid hormone levels were not significantly different among WT, HT and HZ individuals: fT4 (0.73 ± 0.4 *vs.* 0.95 ± 0.7 *vs.* 1.88 ± 0.8 ng/dL; $p = 0.15$); TSH (68.4 ± 50.4 *vs.* 71.4 ± 68.3 *vs.* 42.8 ± 38.5 mIU/L; $p = 0.85$) and tT4 (6.72 ± 4.6 *vs.* 7.8 ± 5.7 *vs.* 13.7 ± 4.4 ng/dL; $p = 0.23$). **Conclusions:** This is the first study to investigate the prevalence and impact of DIO2 SNPs on TD initial clinical presentation. Our preliminary data, although with no statistical significance, show a trend to: (i) Combined higher TSH/lower fT4 in HZ D2-ORFa-Asp3 individuals (ii) Combined lower TSH/higher fT4 in HZ Thr92Ala individuals. These preliminary data suggest that D2 SNPs may become useful in the treatment of patients with TD, helping to determine the eventual need for higher doses of L-T4 to normalize serum TSH levels in certain children.

CLINICAL/THYROID GENETICS

116887 ORFA-GLY3ASP POLYMORPHISM IN THE TYPE 2 DEIODINASE GENE IS NOT ASSOCIATED WITH COVID-19 SEVERITY IN HOSPITALIZED PATIENTS

Fabyan Esberard de Lima Beltrão[1], Daniele Carvalhal de Almeida Beltrão[2], Giulia Carvalhal de Almeida Cordeiro[3], Fabricia Elizabeth de Lima Beltrão[2], Gabriel Jeferson Rodríguez Machado[4], Hatilla dos Santos Silva[5], Helena Mariana Pitangueira Teixeira[5], Juliana Lopes Rodrigues[5], Joice dos Santos de Jesus[5], Jocyel de Brito Oliveira[5], Jair de Souza Braga Filho[5], Fabio Hecht[6], Camila Alexandrina Viana de Figueiredo[5], Ryan dos Santos Costa[5], Maria da Conceição Rodrigues Gonçalves[7], Helton Estrela Ramos[5]

[1] Federal University of Paraíba (UFPB), Lauro Wanderley University Hospital, Department of Endocrinology, João Pessoa, PB, Brazil. [2] Faculty of Medical Sciences of Paraíba, Department of Medicine, Cabedelo, PB, Brazil. [3] Center for Biological and Health Sciences, Federal University of Campina Grande (UFCG), Campina Grande, PB, Brazil. [4] Postgraduate Program in Interactive Processes of Organs and Systems, Institute of Health Sciences, Federal University of Bahia (UFBA), Salvador, BA, Brazil. [5] Department of Bioregulation, UFBA, Salvador, BA, Brazil. [6] Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil. [7] Post-Graduation Program in Nutritional Sciences, Department of Nutrition, Center for Health Sciences, UFPB, João Pessoa, PB, Brazil

Introduction: The rs12885300 SNP (D2-ORFa-Gly3Asp) located on the 5' flanking region of the type II Deiodinase gene (DIO2) was associated with severe sepsis-related acute lung injury, bipolar disorder, and changes in circulating levels of thyroid hormone. The heterozygous DIO2 polymorphic variant (Thr92Ala; rs225014) has been considered protective for COVID-19 disease prognosis. However, it is unknown if the D2-ORFa-Gly3Asp polymorphism has this protective mechanism. **Methods:** We performed a prospective cohort study to investigate an association between the D2-ORFa-Gly3Asp polymorphism and COVID-19 intra-hospital mortality in adult patients admitted between June and August 2020. We analyzed blood biochemistry, thyroid function tests, length of stay, comorbidities, complications, and severity scores. **Results:** 224 patients [median age: 62 (49-75) years] were split into three subgroups: Gly/Gly (n = 123), Gly/Asp (n = 82), and Asp/Asp (n = 19). We find a 14.6% mean mortality and a lower lethality in Gly/Asp patients (14.6%) compared to Gly/Gly patients (17.8%) or Asp/Asp patients (21%). However, the alleles mortality difference was not significant (Chi-square = 0.300, p = 0.86) and neither the disease severity (Chi-square = 0.615, p = 0.73). Serum TSH levels were higher in the homozygous Gly/Gly allele [2.06 (1.0-3.36) µIU/mL] than other alleles [Gly/Asp: 1.59 (0.87-2.92) µIU/mL and Asp/Asp 1.00 (0.77-1.93) µIU/mL, p = 0.021]. The other parameters were not different between the alleles, including the other thyroid hormones (free T3, free T4 and reverse T3). **Conclusion:** D2-ORFa-Gly3Asp polymorphism was not associated with a worse clinical COVID-19 outcome. Future research should investigate a correlation between thyroid hormone metabolism, polymorphisms, and COVID-19 severity.

CLINICAL/THYROID GENETICS

117036 PHENOTYPIC SPECTRUM OF AUDIOLOGICAL ALTERATIONS OF TRB P.M442T INDIVIDUALS WITH RESISTANCE TO THYROID HORMONE EMPHASIZES THE NEED FOR A COMPREHENSIVE EVALUATION DURING LIFE

Alexandre Machado Silva de Oliveira[1], Luciene da Cruz Fernandes[2], Caio Leônidas Andrade[3], Helton Estrela Ramos[1]

[1] Department of Bioregulation, Health & Science Institute, Federal University of Bahia (UFBA), Salvador, BA, Brazil. [2] Multidisciplinary Institute of Rehabilitation and Health, UFBA, Salvador, BA, Brazil. [3] Speech Therapy Course at the State University of Bahia (UNEB), Salvador, BA, Brazil

Introduction: Because of its ontogenic distribution in the cochlea, the TRβ may have a pivotal role in the auditory function and hearing loss might be present. **Objectives:** To assess hearing impairment in a family with RTH. **Material and methods:** Genotyping: Exons 3-10 of the TRβ gene were assessed by PCR sequencing. Clinical evaluation: (i) anamnesis/physical examination, (ii) thyroid function tests, (iii) thyroid ultrasound, (iv) computed tomography of the temporal bone. Audiological evaluation: (i) Middle ear function by acoustic immittance measurements, (ii) Cochlear function by transient-evoked otoacoustic emissions (TEOAEs) and distortion product otoacoustic emissions (DPOAEs), (iii) brain response to an auditory stimulus by Auditory evoked potentials (AEPs). **Results:** Genotyping: A mutation (c.T1325>C) in exon 10 of the TRβ gene resulting in a methionine to threonine substitution at codon 442 was identified in 3 subjects: (i) P1-father,65 years old; (ii) P2-daughter, 25 years-old, (iii) P3-son, 22 years-old. The propositus (P1) and his sibling had typical clinical signs of reduced responsiveness of tissues to thyroid hormones. Clinical phenotype: P1 (hearing loss, recurrent airway infection, osteoporosis, enlarged multinodular thyroid gland); P2 (palpitations, anxiety, excessive sweating, and irregular menstrual cycles); P3 (alopecia, palpitation, insomnia, anxiety, hyperactivity, and difficulty concentrating). Thus, elevated free T3 (fT3) and T4 (fT4) plasma concentrations in coexistence with a no suppressed TSH. Thyroid function (respective results for P1, P2 and P3) were: TSH (2,3; 2,9; 2,4 mUI/L) (normal, 0,45-4,5 mUI/L), fT4(3,4; 3,1; 3,7 ng/dL) (normal: 0,9-1,7 ng/dL) and fT3 (0,58; 0,54; 0,66 ng/dL) (normal: 0,24-0,37ng/dL). Hearing loss was found in P1 and P3. Audiological evaluation showed: (i) In the psychoacoustic evaluation, the presence of sensorineural hearing loss was verified, in descending, progressive, bilateral configuration 2 of 3 subjects; (ii) Cochlear function: all records of transient otoacoustic emissions and distortion products showed better response amplitudes and signal/noise ratio in the low and medium frequency bands and a considerable decline of these parameters in the high frequencies for young individuals, being absent in the older individual. Impairments in high frequencies, as well as the degree of hearing loss, increased when we studied P1 and P3; (iii) In the evaluation of brainstem evoked auditory potentials, all subjects showed no signs suggestive of central auditory alterations at the level of the VIII cranial nerve and brainstem; (iv) Middle ear function: normal. No morphological cochlear abnormalities were detected on computed tomography of the temporal bone. **Conclusion:** Varying degrees of hearing loss have been described in RTH and a comprehensive audiological assessment might be necessary during all life. Hearing loss was a significant problem in our RTH kindred with TRβ p.M442T mutation.

CLINICAL/THYROID NODULE

117044 ASSOCIATION BETWEEN URINARY IODINE, THYROID VOLUME, NODULAR GOITER AND THYROID CANCER IN WOMEN ACCOMPANIED IN A HOSPITAL FROM AN IODINE SUFFICIENT REGION

Ivia Fonseca[1], Tales Aprígio Camargos Ferreira[1], Natalia Treistman[1], Ana Maria Garcia Darze[1], Bianca Freitas dos Santos[1], Mario Vaisman[1], Nathalie Silva de Moraes[1], Patrícia de Fátima dos Santos Teixeira[1]

[1] Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil

Introduction: Some environmental factors have been associated with the risk of developing nodular goiter, such as iodine nutritional status. Both iodine deficiency and excess have been investigated as risk factors for nodular thyroid goiter. Some studies have also sought to demonstrate a relationship between iodine status and papillary thyroid carcinoma (PTC). **Objectives:** To evaluate, in women followed at the outpatient setting of a hospital in an iodine-sufficient region, the association between urinary iodine status, thyroid volume, the presence of thyroid nodules and the risk of papillary thyroid carcinoma. **Methods:** This was a non-populational cross-sectional study, with woman referred to thyroid ultrasound at an university hospital, located in a iodine sufficient region. Patients were evaluated based on a clinical interview and physical examination with anthropometric measurements, analysis of urinary iodine concentration (UIC) in a single sample using the ICP-MS method and blood collection for analysis of thyroid function. **Results:** A group of 107 women being 43 without nodular goiter (NG-) and 64 with nodular goiter (NG+), among whom 17 were diagnosed with papillary thyroid carcinoma (PTC) were evaluated. Age and BMI were similar between NG+ and NG- (53.0 *vs.* 53.5 years and 28.0 *vs.* 28.3 kg/m²). Thyroid volume (TV) was positively correlated with urinary iodine (rs = 0,200; p = 0.043). The median TV tended to be greater (p = 0.10) in women with more than adequate and excessive iodine status (11,98 cm³ and 11,72 cm³), than the group with adequate and insufficient (9,90 cm³ and 8,4 cm³). The median and mean UIC tended to be higher among NG+ (207.05 mcg/L and 234,56 mcg/L) than NG - (164.50 mcg/L and 188,98 mcg/L; p = 0.07). The frequency of excessive and more than adequate iodine status also tended to be higher in NG+ (68.0%) than in TN- patients (32.0%). UIC did not differed statistically in patients with PTC, despite being 243.0 mcg/L *vs.* 173.0 mcg/L in those without PTC. **Conclusion:** These preliminary results show that Iodine excess and/or more than adequate iodine status is correlated to a greater thyroid volume and tended to be correlated with NG. It is necessary to increase the sample size to more accurately assess the relationship between urinary iodine and nodular goiter and PTC, as evidenced in some studies. Our study reinforces the need to be careful with inadvertent iodine supplements that can lead to iodine excess in the population, and the need for further studies to investigate the repercussions of excess iodine and its association with nodules and thyroid cancer.

CLINICAL/THYROID NODULE

117062 BETHESDA I (NONDIAGNOSTIC) FNA SMEAR SLIDES: PRELIMINARY EXPERIENCES OF THIS UNTAPPED RESOURCE FOR A MICRORNA AND DNA-BASED MOLECULAR TESTING

Marcos Tadeu dos Santos[1], Bruno Mari Fredi[1], Isabela Fernanda Morales Martins[1], Andrei Félix de Oliveira[1], Miriane de Oliveira[1], Bruna Frizzo Rabelo[1], Nathalia de Campos Rodrigues[1], Diego Nogueira Vilela[1], Bruna Moretto Rodrigues[1], Léa Maria Zanini Maciel[2]

[1] Onkos Molecular Diagnostics, Ribeirão Preto, SP, Brazil. [2] Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, SP, Brazil

Introduction: Thyroid nodules are common and when evaluated by fine-needle aspiration (FNA) cytology, around 60% are classified as benign (Bethesda II) and less than 10% as highly suspect/malignant (Bethesda V/VI). The remaining ~30% of cases are clinical challenges: up to 20% are classified as "indeterminate" (Bethesda III/IV) and around 10% as "unsatisfactory/nondiagnostic" (Bethesda I). Molecular tests are available and validated to resolve the "indeterminate" cases, but their feasibility and utility in Bethesda I cases has yet to be explored. **Objective:** To evaluate the feasibility of the use of Bethesda I FNA smears slides to perform the microRNA and DNA-based molecular test (mir-THYpe). **Methods:** FNA smear slides of 18 thyroid nodules classified as Bethesda I provided by the *Hospital das Clínicas de Ribeirão Preto* and revised by an independent pathologist, were submitted to the mir-THYpe molecular test, including microRNA expression profile and DNA analysis (BRAF V600E and pTERT C228/250T) by qPCR. **Results:** From the initial cohort composed of 18 FNA samples, four samples were excluded due to be classified as acellular (no material to be used in the test). From the remaining 14 samples, 12 were identified as paucicellular (low number of cells), three of them identified as having low quality material. Of the two samples that were not paucicellular, one had poor quality cell smear preparation. Despite these characteristics, all 14 samples were processed. As result, nine samples (9/14) were able to be analyzed (valid) for both microRNAs and DNA (64.3%), two samples (2/14) had microRNAs valid, but DNA invalid (14.3%) and in three samples (3/14) both microRNAs and DNA were invalid (21.4%). **Conclusion:** Samples from thyroid FNA classified as Bethesda I have known severe limitations, such as the low number of cells and/or quality of material, that prevent a diagnosis by the current technique of cytological analysis. The results of this preliminary study indicate that it is feasible to obtain enough material to perform the molecular testing in the majority of the samples (>60%), with the exception of acellular cases. Some technical difficulties for carrying out the validation were overcome, however, new challenges are now present, such as the improvement in low quality material and for the classification performance, with experiments already being carried out with a larger number of samples from different sites and sources to achieve these objectives.

CLINICAL/THYROID NODULE

117093 BETHESDA III CATEGORY THYROID NODULES: OUR EXPERIENCE IN ITS SUBCATEGORIES AND RISK OF MALIGNANCY

Veronica Ilera[1], Analia Filippini[2], Silvina Deira[2], Rosa Laudi[2], Antonio Colobraro[3], Sebastián Pérez Espinoza[4], Juan Manuel Oyhamburu[4], Gustavo Olstein[5], Alejandro Olmedo[6], Anabela Zunino[1], Laura Delfino[1], Valeria García Roel[1], Alicia Gauna[1], Adriana Reyes[1]

[1] División de Endocrinología, Hospital Ramos Mejía, CABA, Argentina. [2] Unidad de Citología, Hospital Ramos Mejía, CABA, Argentina. [3] División de Anatomía Patológica, Hospital Ramos Mejía, CABA, Argentina. [4] División de Diagnóstico por Imágenes, Hospital Ramos Mejía, CABA, Argentina. [5] Unidad de Quirófano, Hospital Ramos Mejía, CABA, Argentina. [6] División de Cirugía, Hospital Ramos Mejía, CABA, Argentina

Introduction: The category III (BIII) of the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) constitutes the most controversial group due to its heterogeneity. The modifications introduced in 2017 established five subcategories according to the type of atypia, with various risks of malignancy (ROM). However, as great diversity remains in international communications, it is essential for each institution to establish its ROM for an appropriate management. **Objectives:** 1) to assess the prevalence of BIII nodules; 2) to determine the distribution of the subcategories; 3) to describe the diagnostic cytological criteria employed in the subclassification and their possible association with ROM. **Methods:** Retrospective study of fine-needle aspirates (FNAs) performed between 2011-2022 diagnosed as BIII. Aspirates were subclassified according to TBSRTC in: 1) nuclear atypia (AUS-N), 2) architectural atypia (AUS-A), 3) nuclear and architectural atypia (AUS-N+A), 4) predominance of Hürthle cells (AUS-H), 5) non-papillary atypia (AUS-NP). Cytological characteristics evaluated included: cellularity (scarce, moderate or abundant), nuclear changes (chromatin clearing, grooves, inclusions), and enlargement and/or irregularity of nuclear membrane. Outcome was defined as malignant if histological confirmation, or benign if confirmed by histopathology, a new FNA considered benign, or clinical/sonographic stability during follow-up. Statistics: median and range for continuous variables, frequencies for categorical variables, Fisher's exact test for comparisons. **Results:** Of 1,940 sufficient FNAs, 70 were diagnosed as BIII (3.6%) and subclassified as follows: 48 (68.6%) AUS-A, 14 (20%) AUS-N, 3 (4.3%) AUS-N+A, 3 (4.3%) AUS-H, and 2 (2.8%) AUS-NP. Median follow-up was 27 months. No AUS-A nodule had a final diagnosis of malignancy. Both AUS-NP nodules had a final diagnosis of lymphoma. Of lesions classified as AUS-H/AUS-N+A, 2 were benign in the evolution and 4 were lost to follow-up. 42.9% of the AUS-N population had a final diagnosis of malignancy (papillary carcinoma in all cases). AUS-NP nodules were characterized by abundant material with lymphoid infiltrate. In AUS-N aspirates predominated the scarcity of material (78.6%), the presence of nuclear chromatin clearing (85.7%) and nuclear grooves (71.4%). The association of scarce cellularity with two or more nuclear alterations presented a tendency to be more frequently observed in aspirates with malignant final diagnosis ($p = 0.06$). **Conclusions:** 1) In our population, the prevalence of BIII category is very low, fulfilling extensively with TBSRTC recommendations (<7.5%). 2) The AUS-A subcategory predominated in almost 2/3 of BIII nodules, while the subcategory AUS-NP identified two cases with final diagnosis of lymphoma. 3) We consider that the presence of scarce cellularity associated with one or more nuclear abnormalities were decisive for classifying an aspirate as AUS-N.

CLINICAL/THYROID NODULE

117124 CORRELATION BETWEEN EU-TIRADS, BETHESDA AND PATHOLOGY OF 134 THYROID NODULES

Gabriela Mintegui[1], Sofía Saccone[2], Zara Martínez[2]

[1] Hospital de Clínicas Dr. Manuel Quintela, Facultad de Medicina, Udelar, Montevideo, Uruguay. [2] Hospital de Clínicas Dr. Manuel Quintela, Montevideo, Uruguay

Introduction: Assessment of the risk of malignancy is crucial in patients with thyroid nodules in order to select candidates for fine needle aspiration biopsy (FNA) and surgery. **Objectives:** To describe demographic findings and determine sensitivity and specificity of ultrasound, cytology, and pathology in the malignancy assessment of thyroid nodules in 10 years who underwent total thyroidectomy or hemithyroidectomy. **Methods:** Observational, retrospective, analytical study. A data collection form was used and the nodule that determines the surgical indication is analyzed. The descriptive analysis of qualitative variables was performed by frequencies (absolute and relative). Quantitative variables were analyzed using measures of central tendency (mean) and dispersion (range and standard deviation). Confidence intervals for diagnostic test parameters were determined using the "exact" binomial calculus. The sensitivity and specificity between the tests were evaluated using the McNemar test. The tests were carried out with two tails and p values greater than 0.05 were considered significant. The research protocol was accepted by the Ethics Committee of the study center. **Results:** 134 nodules were analyzed. There is a clear female predominance (86%) with a 6:1 female/male ratio, with a mean age of 47.3±15. Most of the nodules measured between 1-4 cm, showing no differences by gender or age. The EU-TIRADS score was used for the ultrasound evaluation, obtaining EU-TIRADS 2: 2%, 3: 38%, 4: 26% and 5: 35%. The Bethesda categories according to ATA 2015 were grouped into: benign (II), indeterminate (III, IV and V) and malignant (VI). It is obtained: benign result 34%, indeterminate 40% and malignant 24%. The results of the pathology reflect malignancy in 37% and benignity in 63%. The ultrasonographic results of the nodules with EU-TIRADS 2 (benign) and 5 (malignant) were compared with the cytological results with Bethesda II and VI nodules. When grouping EU-TIRADS with pathology, ultrasound shows a sensitivity of 96.7% (confidence interval (CI) 82.8-99.9%) and a specificity of 11.1% (CI 1.4-34.7%), with a positive like lihood ratio (LR+) 1.09 (CI 0.91-1.30). By grouping Bethesda with pathology, the FNA shows sensitivity of 87.9% (CI 71.8-96.6%) and specificity of 95.3% (CI 84.2-99.4%) with LR+ 18.9 (CI 4.9-73.6). In the EU TIRADS group with Bethesda, the calculation of sensitivity by the McNemar test is p=1, greater than 0.05 and for the calculation of specificity, p=0.015, less than 0.05. **Conclusions:** Thyroid ultrasound to assess the risk of malignancy in a thyroid nodule has high sensitivity but low specificity. It is good for screening. FNA has high sensitivity and specificity for the diagnosis of malignancy in the thyroid nodule. Bethesda is more specific than EU-TIRADS to assess risk of malignancy in thyroid nodule.

CLINICAL/THYROID NODULE

117118 ROLE OF CONTRAST-ENHANCED ULTRASOUND AND ELASTOGRAPHY ON THE DIAGNOSIS OF THYROID NODULES WITH INDETERMINATE CYTOLOGY

Julia Miguel Leitão[1], Aliny Weber Kuhn[1], Marcus Adriano Trippia[2], Nicolas Galat Ahumada[1], Hans Graf[1], Teresa Cristina Santos Cavalcanti[3], Caio Pereira Mueller[1], Emanuella Roberta Ina Cirino[1], Cleo Otaviano Mesa Júnior [1], Gisah Amaral de Carvalho[1]

[1] Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, PR, Brasil. [2] Instituto de Roentgen Diagnóstico, Curitiba, PR, Brasil. [3] Neopath – Patologia Diagnóstica, Curitiba, PR, Brasil

The main purpose of thyroid nodules evaluation is to identify suspicious lesions for thyroid cancer. Ultrasound (US) is the first-line imaging exam. It has high sensitivity to detect and characterize nodules and helps guiding the decision whether to proceed or not to fine-needle aspiration biopsy (FNAB). But even when a nodule is submitted to FNAB, up to 1/3 of cytology results are indeterminate. Contrast-enhanced ultrasound (CEUS) uses an inert contrast agent that allows a real-time dynamic assessment of the perfusion of the thyroid lesion. It can improve the differentiation between benign and malignant nodules, as vascularization is an important component of neoplastic growth. Thyroid healthy parenchyma demonstrates rapid and uniform enhancement. Thyroid nodules have neovascularization and the patterns of these microperfusion are being studied for its potential to predict malignancy. Other promising method is the assessment of tissue elasticity through shear wave elastography (SWE), in which shear waves are generated by the US machine. The velocity of wave propagation is used to quantify tissue stiffness and probability of malignancy. The objective of this study was to evaluate the efficacy of CEUS and SWE on detecting or excluding thyroid cancer. We included 40 patients which had thyroid nodules with indeterminate cytology results and had surgical indication. Patients were submitted to perfusion assessment (CEUS) and to SWE. Evaluations were realized in the same nodule that had been submitted to FNAB. The radiologist was blind to the FNAB result. According to 6 patterns of contrast perfusion and shear wave velocity, nodules were categorized in: suggestive of benignity or suspicious for malignancy. Results were compared to the anatomopathological (AP) reports of surgical specimen. Twenty percent of the total sample were men. Average age was 53 years. Average of the nodule's largest diameter was 1,97cm. Sixteen patients had FNAB result Bethesda III, 11 patients Bethesda IV and 13 patients Bethesda V. Four patients were excluded from final analysis and other 5 are still waiting for the AP report. Among the remaining 31 patients, malignancy rate of the nodules was 22%. In 28 patients the CEUS and SWE assessment demonstrated results consistent (benign or malign) with the AP report. One patient had a benign nodule that was incorrectly categorized by the non-invasive methods as malign. Two patients had thyroid cancer that were not identified by CEUS nor SWE – both being follicular carcinoma. The 5 cases of papillary carcinoma of the sample were correctly identified. Sensitivity and specificity were 71,4% and 95,8% respectively. Positive predictive value was 83,3% and negative predictive value was 92,0%. In conclusion, CEUS and SWE are valuable methods in the complementary evaluation of thyroid nodules with indeterminate cytology. They were comparable in the detection of benign and malign nodules and can help in the decision of surgical approach.

CLINICAL/THYROID NODULE

117031 SERUM CALCITONIN MEASUREMENT IN BETHESDA III AND IV CYTOLOGY – IS IT COST-EFFECTIVE IN THE DIAGNOSIS OF MEDULLARY THYROID CARCINOMA?

Léa Maria Zanini Maciel[1], Letícia do Espírito Santos Dias[1], Andrea Nishiyama[1], Patrícia Künzle Ribeiro Magalhães[1]

[1] Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, SP, Brazil

Introduction: In a university center, the 30-year survey of patients with Medullary Thyroid Carcinoma (MTC) showed that the cytology was compatible with the diagnosis in 50% of the cases; in the others, the cytological diagnosis was follicular neoplasia (33.3%), papillary carcinoma (8.3%) and colloid goiter (8.3%). **Objectives:** To evaluate the cost-effectiveness of serum calcitonin measurement in patients with thyroid nodules whose cytological diagnosis was Bethesda III and IV. **Methods:** Cytological diagnoses of fine needle thyroid nodule aspiration (FNA) performed between 2010 and 2022 were reviewed and serum calcitonin (Ct) measurements were performed in patients with Bethesda III and IV cytological diagnoses. Ct were measured by chemiluminescence (Immulite – Siemens). Normal Ct results in women were up to 5pg/mL and in men up to 8.4 pg/mL. **Results:** In this period 5,778 FNA were performed and 732 (12.7%) had the diagnosis of Bethesda III and IV. Of the 406 patients with Bethesda III and IV cytology, 344 patients (84.7%) had Ct undetectable (≤2 pg/mL), 59 (14.5%) Ct >2-<20 pg/mL and 3 patients (0.73%) Ct ≥ 20 pg/mL (of these, 2 patients with Ct = 20.8 and 33.8 pg/mL were diagnosed with autoimmune thyroid disease and 1 with Ct > 100 pg/mL (>6,000) was diagnosed with metastatic MTC). In the last 12 years, 31 new patients with MTC have been followed up at our Institution, 25 of them were referred with cytological suspicion or already operated. Of the remaining 6 patients, only 1 patient had a cytological diagnosis of CMT, 3 had the cytological diagnosis of papillary thyroid carcinoma, 2 patients with cytological diagnosis of Bethesda III (one of them underwent surgery without Ct measurement result and the other the diagnosis was based on Ct measurement). **Conclusion:** Nodular thyroid disease is frequent and MTC accounts for only 1%-2% of thyroid carcinomas. Cytological diagnosis of MTC is difficult due to the multiple presentations, with various cellular morphologies and no typical cell shapes. In this study, which gathered a significant amount of samples, only 1 case of MTC was diagnosed in Bethesda III and IV cytology with Ct measurement. We conclude that serum Ct measurement was not cost-effective in the diagnosis of MTC in Bethesda III and IV nodules.

CLINICAL/THYROID NODULE

117064 VALIDATION OF AN OPTIMIZED MICRORNA AND DNA-BASED THYROID MOLECULAR CLASSIFIER IN AN ARGENTINE POPULATION COHORT

Marcos Tadeu dos Santos[1], Andrei Félix de Oliveira[1], Diego Nogueira Vilela[1], Bruna Moretto Rodrigues[1], Bruno Mari Fredi[1], Isabela Fernanda Morales Martins[1], Miriane de Oliveira[1], Bruna Frizzo Rabelo[1], Nathalia de Campos Rodrigues[1], Gabriela Brenta[2]

[1] Onkos Molecular Diagnostics, Ribeirão Preto, SP, Brazil. [2] Dr. Cesar Milstein Hospital, Buenos Aires, Argentina

Introduction: The presence of thyroid nodules in the adult population is a common event. The evaluation by fine-needle aspiration (FNA) cytology (gold-standard technique) can identify the majority of these nodules, with 60%-65% being diagnosed as benign and less than 10% as cancer. However, the clinical challenge is the remaining 25%-30% of the cases, classified as "indeterminates" (Bethesda III/IV), a scenario in which molecular tests can help to early diagnosis and to avoid "potential unnecessary" surgeries. Previously, we have performed a multicentre study to optimize the algorithm and the performance of the mir-THYpe full test, a microRNA and DNA-based thyroid molecular classifier for early diagnosis of indeterminate thyroid nodules, using samples of patients from three Latin American countries: Brazil, Argentina and Peru. **Objective:** To evaluate the diagnostic performance of the mir-THYpe full molecular test specifically in the Argentine cohort of samples which were utilized in the development and validation study of the optimized algorithm of the molecular test. **Methods:** The Argentine cohort was composed of 13 samples represented by FNA slides (13 patients) from Dr. Cesar Milstein Hospital (Buenos Aires – Argentina) that were utilized in the previous study. All samples were analyzed for microRNA expression profiling and DNA mutation analysis (BRAF V600E and pTERT C228/250T) by qPCR. The classification of the algorithm (positive or negative for malignancy) was confronted with the post-surgery anatomopathological (AP) data (gold-standard) to evaluate the test performance. **Results:** All 13 samples (12 Bethesda III and one Bethesda IV) were correctly classified by the mir-THYpe full molecular test (100% accuracy), being 11 samples classified as negative (six thyroid follicular nodular disease, three follicular adenoma and two oncocytic adenoma of the thyroid) and two as positive for malignancy (papillary thyroid microcarcinoma and oncocytic carcinoma of the thyroid, the last one with TERT C228T mutation detected). **Conclusion:** The optimized algorithm demonstrated a high diagnostic performance in the Argentine population cohort, which may potentially obviate diagnostic surgery of patients with indeterminate nodules. However, due to the small number of samples, more studies are needed to evaluate the real-world performance of the test in this population.

CLINICAL/THYROID REGULATION

117073 COMBINATION THERAPY WITH LEVOTHYROXINE/LIOTHYRONINE TO THYROID-STIMULATING HORMONE SUPPRESSION IN DIFFERENTIATED THYROID CANCER

Anna Catarina Gatzk de Arruda[1], Alexandre José Faria Carrilho[1]

[1] Universidade Estadual de Londrina, Londrina, PR, Brasil

Case presentation: A 22-year-old women, previously healthy, complaining of palpitation, anxiety and irritability was diagnosed with hyperthyroidism due to Graves disease – low thyroid stimulating hormone (TSH) 0.03 mUI/L (0.4-4.3 mUI/L), elevated free thyroxine (T4) 1.46 ng/dL (0.70-1.80 ng/dL) and free triiodothyronine (T3) 4.18 ng/dL (2.5-3.9 ng/dL), and positive thyroid receptor antibody (TRAb) 9.62 U/L (<1.75 U/L). The patient was initially treated with antithyroid drug (methimazole), and clinical laboratory parameters were showing consistent improvement. Ultrasound of the thyroid revealed two nodules with approximately 1.5 cm in greatest diameter in the right lobe; scintigraphy suggesting one cold nodule. After 1 year of methimazole, and with a Bethesda IV category on fine-needle aspiration, the patient was submitted to total thyroidectomy. The anatomopathological study confirmed classic papillary thyroid carcinoma (PTC) with lymph nodes metastasis. Radioiodine therapy (100 mCi) was administered, and levothyroxine (LT4) initiated. Regarding thyrotropin suppression therapy, TSH suppression wasn't achieved easily during follow up, even with high doses of LT4 (3.5 mcg/kg/day) and elevated free T4 levels, with appropriate use. After combination treatment of LT4 (2 mcg/kg/day) with liothyronine (25 mcg/day), TSH suppression was finally achieved, with normal free T4 and T3 levels, and complete resolution of hypothyroid symptoms. After 7 months of initial surgery, she presented with locoregional metastasis and was submitted to lymphadenectomy. The patient is currently on excellent response to therapy of PTC, with undetectable thyroglobulin and anti-thyroglobulin until this moment. **Discussion:** Thyroid cancer is the most common endocrine malignancy, largely represented by differentiated thyroid carcinoma (DTC), mostly papillary. In the management of DTC, surgery followed or not by radioiodine therapy and TSH suppression is the standard of care in most patients, depending on the tumor related risk factors. Serum TSH suppression is specifically recommended in those patients with advanced or more aggressive cancer. LT4 is recommended for long-term TSH suppression, as it has a longer half-life, which tends to yield more stable levels of T3 conversion from T4 in the periphery. In fact, the peripheral activity of deiodinases is a tightly and tissue specific regulated process. The T3 and T4 combination therapy for TSH suppression in the management of thyroid cancer is uncommon and there is very little evidence supporting it in the published literature, most evidence for combination treatment comes mainly from studies on hypothyroidism focusing on symptoms and quality of life. **Final comments:** The role for a combination treatment does not have a strong evidence base but there may be individual circumstances that prompt its consideration, as shown in this report.

CLINICAL/THYROID SURGERY

117114 PREVALENCE AND CLINICAL FACTORS ASSOCIATED WITH HYPOPARATHYROIDISM IN PATIENTS UNDERGOING TOTAL THYROIDECTOMY IN A TERTIARY HOSPITAL

Stephanie Theisen Konzen[1], Ramona Paula Fernandes Reckziegel[1], Lenara Golbert[1], Erika Laurini de Souza Meyer[1]

[1] Irmandade Santa Casa de Misericórdia de Porto Alegre, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, RS, Brasil

Introduction: Hypoparathyroidism is the most common complication observed after total thyroidectomy and its incidence varies in the literature, with scarce epidemiological data in Brazil. There are several risk factors already described, but recent studies have shown new predictors of evolution to transient and/or definitive hypoparathyroidism after total thyroidectomy. **Objectives:** We aimed to determine the frequency and to evaluate the clinicopathological factors that predict postoperative hypocalcemia and definitive hypoparathyroidism in patients undergoing total thyroidectomy in a tertiary hospital, as well as to evaluate the role of parathyroid hormone (PTH) as an early marker of definitive hypoparathyroidism. **Methods:** This is a retrospective study based on the review of medical records. All patients who underwent total thyroidectomy with or without associated lymph node resection from 2014 to 2021 were included. Exclusion criteria were under 18 years of age, preoperative hypoparathyroidism and parathyroidectomy. Hypoparathyroidism was defined when PTH less than or equal to 12 pg/mL and/or hypocalcemia (calcium levels below laboratory reference values) within the first 72 hours after the procedure. Transient hypoparathyroidism was defined in patients who recovered parathyroid function within 12 months and permanent was defined in those who remained with hypoparathyroidism after 12 months and required treatment with calcium and calcitriol supplementation. **Results:** The study included 433 patients, the mean age was 53 years ± 13.4 years, and 380 (87.8%) were female. Hypoparathyroidism was diagnosed in 220 patients (50.8% of the sample), being 12.5% definitive and 35.6% transient. Of them, 85% were asymptomatic. There was a statistically significant correlation between definitive hypoparathyroidism and performing neck dissection and longer surgical time. Malignancy and low preoperative calcium levels were associated with a higher risk of transient hypocalcemia. Using the ROC curve, a postoperative PTH < 6.85 pg/mL had a sensitivity of 94.2% and specificity of 56.6% for predicting definitive hypoparathyroidism (AUC 0.72; 95% CI 0.65-0.78; p = 0.000). **Conclusion:** In our sample, the prevalence of definitive hypoparathyroidism was 12.5%. Predictive factors associated with permanent postoperative hypoparathyroidism include neck dissection, longer surgical time and lower postoperative PTH levels.

CLINICAL/THYROID SURGERY

117153 RADIOFREQUENCY ABLATION OF BENIGN THYROID NODULES – LATAM EXPERIENCE

Leonardo Rangel[1], Pedro Henrique Esteves Gonçalves[2], Patrícia de Fátima dos Santos Teixeira[2], Mario Vaisman[2], Jose Higino Steck[3], Erivelto Martinho Volpi[4]

[1] Universidade do Estado do Rio de Janeiro (UERJ), Rio de Janeiro, RJ, Brasil. [2] Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brasil. [3] Universidade Estadual de Campinas (Unicamp), Campinas, SP, Brasil. [4] Hospital Alemão Oswaldo Cruz, São Paulo, SP, Brasil

Introduction: The thyroid nodule is a very prevalent disease, but about 85%-95% are benign. However, many of these nodules may indicate specific treatment, especially in cases where the nodules are large and may cause compressive symptoms or even aesthetic symptoms. In addition, approximately 16% of small and benign nodules present rapid growth and can be considered for specific treatment6. Surgical treatment is feasible in these cases, but it is an invasive procedure, which may present a risk of complications. For this reason, minimally invasive therapies for treating thyroid nodules have been studied since the 1990s. The present study intends to analyze the results of radiofrequency ablation (RFA) as an alternative to conventional treatment (surgery) for treating thyroid nodules. **Materials and methods:** A retrospective study analyzes medical records of cases performed by the same head and neck surgeon in a private clinic and at the Pedro Ernesto University Hospital. Patients with a diagnosis of nodular or multinodular goiter who underwent radiofrequency ablation between the years 2017 to 2022 were included, with a total of 161 nodules. Patients who lost to follow-up or underwent ablation for papillary microcarcinoma were excluded, resulting in 101 ablations in 81 patients. **Results:** A total of 101 ablations of thyroid nodules were performed in 81 patients, 69 women, and 12 men, with a mean age of 48 years. Each patient underwent an ablation of 1 to 3 nodes per session. Nodules ranged from 149 cm^3 to 0.1 cm^3. Regarding the indications, benign nodule with recorded growth was the most frequent in 37 patients (46%), followed by aesthetic symptoms in 30 cases (37%), compressive symptoms in 9 patients (12%), a hyperfunctioning nodule in 3 cases (3%) and a substernal goiter in 3 cases (2%). The overall rate of nodular volume reduction was 68.2% during the first six months of follow-up. In 4 cases, the nodules disappeared after this period, and all had an initial volume of less than 0.35 cm^3. The nodule regrowth rate was 13% (13 nodules). The most frequent complication was temporary vocal cord paralysis. **Discussion:** The RFA technique uses thermal energy, causing coagulative necrosis with progressive reduction of the nodule. This brought a new perspective to Thyroid nodule treatment. A meta-analysis published by Trimboli *et al.* (2019) analyzed 24 studies with 963 patients, showing an average nodule reduction rate of 68% at six months and 75% in 1 year. The patients in the study showed a significant reduction in aesthetic and compressive symptoms. In our study, we obtained results similar to those in the literature, with a significant reduction of nodules in the first year of follow-up (68.2%) and satisfactory control of aesthetic and cosmetic symptoms. **Conclusion:** RFA is a safe technique capable of obtaining satisfactory results for reducing the volume of thyroid nodules and reasonable symptom control.

CLINICAL/THYROID SURGERY

117113 TRANSORAL THYROID AND PARATHYROID SURGERY IN BRAZIL: WHERE ARE WE?

Lucas Ribeiro Tenório[1], Antonio Augusto Bertelli[1], Marianne Yumi Nakai[1], Marcelo Benedito Menezes[1], Jonathon Owen Russell[2], Antonio José Gonçalves[1]

[1] Santa Casa de São Paulo School of Medicine, São Paulo, SP, Brasil. [2] Johns Hopkins University, Baltimore, Maryland, USA

Introduction: Thyroid surgery through the transoral vestibular approach is a reality in many countries. While several competing remote access techniques have been developed in the last 20 years, many were not reproducible. Transoral Endoscopic Neck Surgery (TNS) has been shown to be reproducible in different centers around the world, and approximately five years after its description it has been adopted relatively quickly for various reasons. To date, there are at least 7 Brazilian studies published, including a series of more than 400 cases. The aim of this work is to study the progression of Transoral Neck Surgery in Brazil and describe the profile of surgeons involved in this new approach. **Methods:** This is a retrospective study with descriptive statistics. A REDCap based survey about transoral endoscopic thyroidectomy and parathyroidectomy vestibular approach (TOETVA/TOEPVA) was done with 66 Brazilian surgeons regarding surgeon profile, numbers of cases performed by geographic region, what kind of training was necessary prior to the first case and behavior of the surgeon proposing these new approaches. **Results:** Response rate of this survey was 53%, although some teams have chosen to gather data from different surgeons in one questionnaire what could lead to a higher response rate. To date, 1,275 TOETVA/TOEPVA cases had been performed in Brazil, 1,229 thyroidectomies (96.4%), 42 parathyroidectomies (3.3%) and 4 combined procedures (0.3%). Most of the cases were done in the southeast region (821, 64.4%), 538 (42.2%) cases in the State of São Paulo and 283 (22.2%) cases in the State of Rio de Janeiro. Surgeons from 14 Brazilian states, including Brasilia (Federal District), and 26 different cities are already performing TOETVA/TOEPVA. Surgeons' ages varied from 30 to 63 years old with a median age of 41 years old. Altogether 75.8% of surgeons had previous videosurgery training before starting TNS. Most of them (50%,) had this training during medical residency only, 25% (n = 17) did short term courses only and 25% (n = 16) had both. When asked if they were used to perform videosurgery in their daily practice 57.6% (n = 38) said yes. Among all surgeons, 27.3% (n = 18) were already trained in robotic surgery. The majority of surgeons (80.3%) involved in this sample have had specific TOETVA training, some in cadaver lab and others in animal lab. Those who didn't have specific training were already trained in robotic surgery and some travelled abroad for training and observerships before starting. Most surgeons (85%) have watched cases from an experienced colleague before performing their first case. The number of observed cases before beginning the technique varied from 1 to 30 (median: 5). The majority of surgeons (63.6%) have had a proctor in their first cases. **Conclusions:** TOETVA is becoming popular in Brazil. Younger surgeons, especially those between 30 and 50 years old were more likely to adopt this approach.

XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Poster Presentation – Basic

BASIC/THYROID CANCER BASIC

117102 ECTOPIC EXPRESSION OF MIR-200C CONTROLS ANAPLASTIC THYROID CANCER (ATC) DIFFERENTIATION AND AGGRESSIVENESS

Hugo Werner Huth[1], Cesar Seigi Fuziwara[1], Edna Teruko Kimura[1]

[1] Institute of Biomedical Science, University of São Paulo, São Paulo, SP, Brasil

Introduction: MicroRNAs (miRNAs) are a class of small non-coding RNAs of 21 to 23 nucleotides that post-transcriptionally regulates protein expression. Deregulation of miRNAs has been implicated in tumorigenesis and tumor progression, including in Thyroid Cancer (TC). Some miRNAs control cell proliferation, migration and the balance between epithelial and mesenchymal cell states through Epithelial-Mesenchymal Transition (EMT), a critical process for tumor metastasis and recurrence. Specifically, the miR-200c-3p, miRNA of miR-200 family, is downregulated in anaplastic thyroid cancer (ATC), an undifferentiated TC, in contrast to the high expression observed in differentiated TC. However, the biological effect of miR-200c deregulation on thyroid malignancy remains unclear. **Objective:** This study aims to evaluate the influence of miR-200c on human ATC cell aggressive behavior. **Methods:** The ectopic expression of miR-200c was performed in two different human ATC cell lines, KTC2 (KTC2-200c) and SW1736 (SW-200c) cells using plasmid (pmscv-miR200-c) in order to analyze the role of miR-200c in cell counting, colony formation, migration, cell differentiation, EMT markers and EMT transcription factors (EMT-TFs) gene and protein expression, such as ZEB, SNAI and TWIST families. **Results:** Cell counting and clonogenic assay performed with KTC2-200c and SW-200c cells showed a reduced cell proliferation and colony formation. Additionally, a reduced cell migration was visualized by wound healing assay and transwell assay in transfected cells. Light microscope images showed that KTC-200c and SW-200c cells presented an epithelial morphology in contrast to the control group which displayed mesenchymal morphology. Analysis by RT-qPCR showed that restoring miR-200c expression enhanced the mRNA expression of the epithelial marker E-cadherin, while diminished the mRNAs levels of the mesenchymal marker Vimentin in KTC-200c and SW-200c cells. The similar pattern was observed in protein expression of E-cadherin and Vimentin by western blot. Concerning EMT-TFs, a downregulation of ZEB1, ZEB2 and SNAI1 mRNA levels were observed by RT-qPCR, but not for TWIST1, and a diminished ZEB1 protein expression was visualized by western blot in miR-200c-3p transfected cells. **Conclusion:** This study evidences the tumor suppressor effect of miR-200c-3p and its role in ATC aggressiveness. The ectopic expression of miR-200c-3p could be useful as a molecular tool to reverse the undifferentiated profile of thyroid cancer. Funding and Grants from Fapesp (2021/12284-0, 2019/17282-5, 2019/25116-8) and CNPq (311210/2021-0, 409443/2021-2).

BASIC/THYROID CANCER BASIC

117069 MOLECULAR ANALYSIS OF MIR146B PROMOTER ACTIVATION IN THYROID CANCER

Cesar Seigi Fuziwara[1], Marcella Maringolo Cristóvão[1], Edna Teruko Kimura[1]

[1] Institute of Biomedical Sciences, University of São Paulo, São Paulo, SP, Brazil

Introduction: microRNAs (miRNAs) are a class of small noncoding RNAs that regulate gene expression post-transcriptionally by modulating mRNA translation and stability. miR-146b is a hallmark of thyroid cancer, and its overexpression correlates with BRAF mutation, TERT mutation and poor prognosis. Moreover, the detection of miR-146b-5p serum levels has been shown as a potential marker for thyroid cancer prognosis in patients. Functionally, miR-146b controls several target mRNAs involved in cell migration, invasion and genes involved in thyroid cell biology. Although the overexpression of miR-146 isoforms has been reported in other cancers, the activation of MIR146B in thyroid cancer is singular and frequently is among the top overactivated miRNAs. Nevertheless, the molecular basis for MIR146B transcriptional activation is still poorly understood. **Objective:** To study the putative promoter region of MIR146B to identify the transcription factors involved in miR-146b induction in thyroid cancer. **Methods:** First, we used the FANTOM5 to investigate the primary miRNA start site and delimitate the MIR146B putative promoter region. Next, different fragments of the putative promoter (P1, P2, P3-P3A and P3B) were PCR-cloned into the luciferase plasmid pGL4-20 minP, using primers with XhoI/BglII overhang. For luciferase assay, thyroid cancer cell lines were transfected with Luc plasmid + pRl (Renilla) as control, and luciferase activity was measured after 24h. Transcription factor (TF) binding site prediction was performed in the Lasagna tool, and gene expression by RT-qPCR. **Results:** We defined a region of ~1Kb as putative promoter for MIR146B that was divided into three fragments, P1 (293 bp), P2 (312 bp) and P3(392 bp). We observed that the fragments P1, P2 and P3 exhibited higher luciferase activation compared to control empty plasmid, with 2, 5 and 100-fold activation, respectively. As P3 showed the stronger activation, it was divided into P3A (204 bp) and P3B (154 bp). We found that P3B, a 154 nt fragment, is the minimal promoter for MIR146B. Next, we searched for potential TF binding site in P3B fragment using Lasagna algorithm, and found several TFs such as YY1, STAT5A/B, E2F1/4, SOX2, SP1 and AP4. Gene expression analysis showed high levels of YY1, STAT5A/B and E2F1 in ATC cell lines. Deletion of YY1 binding site reduced the luminescence in 18%, 22% and 42% compared to wild-type P3B plasmid in KTC2, SW1736 and 8305C cells, respectively. On the other hand, deletion of STAT5 and SP1 binding sites did not change P3B luminescence. However, the blockage of MAPK signaling with U0126 reduced more than 50% the luminescence of P3B in KTC2, SW1736 and 8305C cell lines. **Conclusion:** Our finding shows that the minimal promoter region of MIR146B is a 154 nt fragment located just upstream to the MIR146B gene transcription starting site. This fragment contains binding sites for TFs that include YY1, STAT5 and SP1, which are responsive to MAPK signaling modulation.

BASIC/THYROID CANCER BASIC

117080 THE ROLE OF MICRORNAS IN THE REGULATION OF TERT EXPRESSION IN THYROID CANCER

Antônio Tarelo Freitas de Oliveira[1], Edna Teruko Kimura[1], Cesar Seigi Fuziwara[1]

[1] Institute of Biomedical Sciences, University of São Paulo, São Paulo, SP, Brazil

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 treatment. Mutations in the promoter of the TERT (Telomerase Reverse-transcriptase) gene, frequent in ATC, result in its overexpression and correlate with clinicopathological characteristics such as invasion, recurrence and death. MicroRNAs, small endogenous RNAs that interact with the 3'-untranslated region (UTR) of target mRNAs and block protein translation, are frequently deregulated in cancer, resulting in unbalanced oncogene and tumor suppressor expression. Thus, identifying miRNAs which potentially target TERT mRNA may improve the understanding of TERT regulation/function in thyroid cancer. **Objective:** Investigate the role of microRNAs in the regulation of TERT in thyroid cancer. **Methods:** We used TargetScan software to identify miRNAs that may bind to the 3-UTR of human TERT mRNA. We designed primers to amplify the precursor sequence of miR-143, miR-145, miR-15b and miR-16 for cloning in XhoI/EcoRI sites of MSCVpuro plasmid with puromycin resistance. After PCR amplification of the pre-miRNA sequences from human genomic DNA, the double digested XhoI/EcoRI fragments were ligated into XhoI/EcoRI sites of pMSCVpuro. ATC cell line KTC2 was transfected with the obtained plasmids. miRNA and mRNA expression has been measured through qPCR, TERT protein expression has been evaluated through western-blotting. Proliferation and MTT cell viability assays have been performed to evaluate functional effects of the miRNAs on the transfected cell lines. **Results:** TERT 3'-UTR is a ~3kb sequence that shows several potential binding sites for down-regulated miRNAs in thyroid cancer. We identified five binding sites for miR-143-3p, two for miR-145-5p and three for miR-15b-5p/miR16-5p in the 3'-UTR of human TERT mRNA. We designed primers to clone the precursor sequence of the four miRNAs and an additional ~100 bp region in the 5' and 3' of the precursor sequences. The resulting plasmids were transfected into cells of the KTC2 line. We confirmed a >200 fold increase of miR-143 expression and a moderate reduction of TERT protein expression in the KTC2-MSCV-mir143 line. Functional assays performed with this line did not show a significant antitumor effect of miR-143 overexpression in KTC2 cells. We also generated KTC2-MSCV-mir145 cell line with a >600 fold increase of miR-145. **Conclusion:** *In silico* analysis shows that TERT mRNA 3'-UTR is predicted to be controlled by several miRNAs, many of which are downregulated in thyroid cancer, indicating another mechanism for TERT overexpression. Among those, miR-143 seems to be a potential regulator of TERT expression. Further studies are necessary to elucidate if miR-143 directly inhibits TERT mRNA translation and if miRNA restoration is sufficient to reduce TERT expression in TERT promoter mutated cell lines. **Funding:** Fapesp and CNPq.

BASIC/THYROID GENETICS

117128 FUNCTIONAL ANALYSIS OF CONGENITAL HYPOTHYROIDISM-ASSOCIATED SLC5A5 GENE VARIANTS

Gerardo Hernán Carro[1], Mariano Martín[1], María Celeste Abregú[1], Juan Pablo Nicola[1]

[1] Departamento de Bioquímica Clínica (CIBICI-CONICET), Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina

Introduction: Iodide transport defect is an uncommon cause of dyshormonogenic congenital hypothyroidism due to homozygous or compound heterozygous pathogenic variants in the sodium iodide symporter (NIS)-coding gene SLC5A5 causing deficient iodide accumulation in thyroid follicular cells, thus impairing thyroid hormonogenesis. The increasing application of next-generation sequencing technology has revealed an enormous amount of novel variants in congenital hypothyroidism-associated genes; however, the clinical impact of most variants remains unsolved. **Objectives:** To investigate the pathogenicity of uncharacterized congenital hypothyroidism-associated SLC5A5 gene variants. **Materials and methods:** Bibliographic compilation and bioinformatic analysis of pathogenicity of SLC5A5 gene variants identified in patients with congenital hypothyroidism. Functional analysis conducted in HEK-293T cells, which do not express NIS endogenously, transiently transfected with expression vectors encoding wild-type NIS or its variants. **Results:** Bibliographic search revealed missense (p.G18R, p.D191G, p.G250V, p.Q265R, p.A320T, p.G341R, p.R376W, p.I386S & p.P560L) and nonsense (p.L336*, K388*, p.R516* & Q639*) SLC5A5 gene variants. Bioinformatics analysis using a NIS-specific variant classifier predicted p.A320T, p.R376W, and p.P560L as benign, p.I386S as likely pathogenic, and p.G18R, p.D191G, p.G250V, p.Q265R, p.G341R and p.Y348D as pathogenic. Nonsense variants were classified as pathogenic as they eliminate essential elements for NIS transport to the plasma membrane. *In vitro* functional assays showed that the benign p.A320T and p.R376W NIS variants retained over 50% of wild-type NIS activity. Conversely, the pathogenic p.D191G and p.G250V NIS variants did not show iodide transport activity. Significantly, immunofluorescence assays revealed that all four NIS variants were expressed at the plasma membrane. **Conclusions:** The increasing application of next-generation sequencing has expanded the mutational landscape of genes involved in thyroid hormonogenesis, allowing a deeper understanding of the molecular mechanisms underlying congenital hypothyroidism. However, the clinical significance of variants of uncertain significance remains currently unresolved. Our data reinforce the importance of conducting functional *in vitro* assays to underscore the pathogenicity of variants of uncertain significance, thus allowing the development of protein-specific classifiers to be incorporated in pipelines to assess the pathogenicity of novel genetic variants.

BASIC/THYROID HORMONE ACTION

117087 SPHINGOSINE KINASE 1 IS INVOLVED IN TRIIODOTHYRONINE EFFECTS IN MURINE DENDRITIC CELLS AND THE DRIVEN ADAPTIVE IMMUNITY

Dana María Negretti-Borga[1], Antonella Blanco[1], Mariana Pires Teixeira[1], Vanina Alejandra Alamino[1], Elida Nahir Puentes[1], María Florencia Soler[1], Ana Carolina Donadio[1], Christopher James Clarke[2], María del Mar Montesinos[1], Yusuf Awni Hannun[2], Claudia Gabriela Pellizas[1]

[1] Centro de Investigaciones en Bioquímica Clínica e Inmunología (CIBICI-CONICET), Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina. [2] Stony Brook Cancer Center, Department of Medicine, Stony Brook University, New York, USA

Triiodothyronine (T3) is the biologically active thyroid hormone (TH), essential for homeostatic control. Dendritic cells (DCs) are highly phagocytic, specialized antigen presenting cells. They orchestrate the adaptive immune response through T-cell activation, leading to the production of pro-inflammatory cytokines. DCs additionally control immunity through the generation of regulatory T cells. Our research group reported that mice DCs express TH receptor β1 (TRβ1) and that physiological levels of T3 promotes DCs' maturation, survival, and ability to direct pro-inflammatory responses with Th1, Th17 and cytotoxic profiles, restraining tolerogenic signals. These findings were successfully exploited in T3-activated DC-based antitumor vaccines against melanoma and colon carcinoma in mice. T3 effects in DCs are mainly triggered by non-genomic mechanisms involving TRβ1, Akt and NF-kB. In turn, Sphingolipids and their synthetic enzymes have been involved in inflammation, aging and cancer. Sphingosine-1-phosphate (S1P) is produced by Sphingosine Kinase 1 (SK1) and 2. Although this pathway is involved in many pro-inflammatory conditions, little is known about its role in innate immune cells. Moreover, the putative role of this pathway in the reported pro-inflammatory effects induced by T3 in DCs, is of high interest. The aim of this study was to evaluate the role of SK1 in T3-stimulated DCs, and the driven adaptive immunity. DCs differentiated from bone marrow precursors from Wild-Type (WT) and SK1 Knockout (KO) C57BL/6 mice were stimulated with T3 (10 nM, T3-DC) for 18h. Immature DCs (iDC) from WT mice were incubated with PF-543 (SK1 inhibitor, 100 nM), and 30 min later with the T3 stimuli (PF-T3-DC). After 30 min, p-Akt and total Akt were analyzed by Western Blot. Allogenic splenocytes isolated from BALB/c mice were co-cultured with T3-DC or PF-T3-DC (exposed to T3 for 18h), for 3 days. Viability and proliferation were evaluated by FACS. Cytokines were measured by FACS and ELISA. Statistical significance of differences between means was determined by Two-way ANOVA/Tukey test, and paired t test ($p < 0.05$, statistically significant). Results showed that intracellular IL-12 production was increased in T3-DC from SK1-KO *vs.* WT mice($p < 0.0001$). Accordingly, IL-12 secretion was higher in PF-T3-DC *vs.* T3-DC ($p < 0.005$). Of note, DC viability was not modified by PF-543. In turn, SK1 inhibition reduced p-Akt in T3-DC ($p < 0.005$). Splenocytes proliferation, as well as IFN-γ and IL-17 production and secretion, markers of pro-inflammatory adaptive responses, were modified in the co-culture with PF-T3-DC (*vs.* T3-DC, $p < 0.05$). Our results revealed for the first time that the Sphingolipid intracellular pathway is involved in T3-DC activation. The immunomodulation exerted by SK1 on T3-DC and the driven adaptive response provide the first insights into a novel role of Sphingolipids in the immune-endocrine crosstalk, which will be intimately unveiled by further research.

XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Poster Presentation – Clinical

CLINICAL/THYROID AND METABOLISM

117122 ASSOCIATION BETWEEN PROTEINURIA AND THYROID FUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGES 3 AND 4

Karina Schiavoni Scandelai Cardoso dos Reis[1], Pietra Desiree B. F. A. Vianna[1], João Pedro B. Sanches[1], Rachel Bregman[1], Ana Beatriz Winter Tavares[1]

[1] Universidade do Estado do Rio de Janeiro (UERJ), Rio de Janeiro, RJ, Brasil

Introduction: The relationship between proteinuria and thyroid function remains controversial in patients with chronic kidney disease (CKD). It is known that thyroid hormones in serum are bound to thyroxine-binding globulin (TBG) and albumin. Thus, proteinuria in the nephrotic range (>3 g/day) is associated with loss of TBG, levothyroxine or both, which may lead to (subclinical) hypothyroidism. Thyroid function is also influenced by kidney function; patients with CKD might demonstrate lower levels of T3 and higher levels of TSH. So far, there is scarce literature about thyroid function in patients with proteinuria and CKD, with discordant results. **Objectives:** To correlate TSH and free T4 levels with proteinuria in patients with CKD stages 3 and 4. **Methods:** Observational, cross-sectional study, including 77 patients with CKD stages 3 and 4, followed at the Nephrology outpatient clinic of an universitary hospital. 33 patients had stage 3 CKD (GFR 30-59 mL/min/1.73 m²), and 44 patients had stage 4 CKD (GFR 15-29 mL/min/1.73 m²) – GFR calculated by the CKD-EPI formula. Patients with known hypothyroidism were excluded. Laboratory analysis of TSH and free T4 was performed using chemiluminescence (reference ranges: TSH: 0.3-4.0 µUI/mL; free T4: 0.7-1.8 ng/dL) and proteinuria was performed in an isolated sample of urine, with results expressed as proteinuria/creatininuria (mg/g). Proteinuria was defined as values > 150 mg/g. **Results:** The studied population had a median age of 68 (41-92) years, median TGF 27 mL/min/ 1.73 m² (15-57), median TSH 2.44 µUI/L (0.24- 13.04), median free T4 1.26 ng/dL (0.78-1.86), and median proteinuria 400 mg/g (2.0-5.700). 54 (70.1%) patients had established proteinuria at exam. There was no statistically significant correlation between TSH and proteinuria, or free T4 and proteinuria in the total sample. Median TSH and proteinuria in patients with CKD 3 were, respectively, 2.36 µUI/L (0.77-13.04) and 329.9 mg/g (8.0-3.870); and in patients with CKD 4, 2.36 µUI/L (0.77-13.04) and 452.6 mg/g (2.0-5.700). There was no statistical difference between TSH levels or between proteinuria levels in CKD stages 3 and 4. **Conclusion:** Our findings demonstrated that there is no correlation between proteinuria and TSH or free T4 in patients with CKD stages 3 and 4, neither in the subgroup of patients with established proteinuria. An increase in the sample may evidence different results from our initial results, which will be increased.

CLINICAL/THYROID CANCER CLINICAL

117133 CLINICAL AND MOLECULAR ANALYSIS OF A MEN2A KINDRED HABORING THE RARE RET VARIANT P.SER904PHE

Jessica Oliboni Scapineli[1], Giulia Limana Guerra[1], Marli Terezinha Viapiana Camelier[2], Carla Vaz Ferreira[2], Iracema Cunha Ribeiro Gonçalves[1], Ana Luiza Maia[2]

[1] Hospital Nossa Senhora da Conceição, Porto Alegre, RS, Brasil. [2] Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brasil

Introduction: Medullary thyroid carcinoma (MTC) is a rare malignant tumor originating from parafollicular C cells of the thyroid. MTC may occur sporadically (75%) or as part of the inherited cancer syndrome known as multiple endocrine neoplasia (MEN) type 2A or 2B (MEN 2A or MEN 2B). Hereditary MTC is associated with germ-line mutations in the RET (REarranged during Transfection) proto-oncogene, an autosomal dominant disease with almost 100% penetrance and variable phenotype. The pathogenic variants at codon 634 are the most prevalent (30%-50%), followed by p.Val804Met, p.Leu790Phe, p.Ser891Ala in Europe, and p.Gly533Cys and p.Cys620 in Brazil. The other pathogenic variants are found in less than 10% of MEN2A patients. The variant p.Met918Thr corresponds to 4.6%-13.5% of affected patients with MEN2B phenotype. The RET variant p.Ser904Phe has been reported in only fifteen patients worldwide: 10 in Italy, 1 in Germany, and 4 in England, and it is currently classified as likely pathogenic. Here, we describe a large kindred harboring the p.Ser904Phe. **Objectives:** The present study aimed to characterize clinical and molecular MEN 2A family with a variant at codon 904, investigate the penetrance of this variant in this family and its evolutionary risk and compare with data from the literature. **Methods:** The ascending, collateral, and descending relatives of the patients who had the p.Ser904Phe variant identified were invited to participate in the study. Genetic screening (molecular analysis of RET exon 15) was performed on all subjects who agreed to participate in the study using Sanger sequencing. **Results:** Forty-eight family members were included in this study. In 31 (64,5%) individuals, we observed the presence of the p.Ser904Phe variant; 17 (54%) patients were women, and the median age was 34,4 ± 15,7 years. A thyroid ultrasound was performed on 24 patients, and a nodule was detected in 12 of them (50%; size = 0.8 cm ± 0.46). All patients with thyroid nodules have calcitonin above the reference value. Patients with the genetic variant and clinical disease (thyroid nodule and elevated calcitonin) were referred for total thyroidectomy. Patients with the genetic variant but without evidence of clinical illness will be followed. Twelve relatives await sample collection for molecular screening and clinical evaluation. **Conclusions:** Our study is the first to describe cases of hereditary MTC with the rare RET variant p.Ser904Phe in Latin America, the largest kindred reported. The follow-up of these patients in the coming months and years will be necessary for a better understanding of the behavior of the disease in carriers of this rare variant.

CLINICAL/THYROID CANCER CLINICAL

117156 EXOMIC ANALYSIS OF YOUNG PATIENTS WITH AGGRESSIVE SPORADIC MEDULLARY THYROID CARCINOMA

Luciana Audi de Castro Neves[1], Flavia Regina Rotea Mangone[1], Antonio Lerario[2], Luciana Rodrigues Carvalho Barros[1], Ana Maria da Cunha Mercante[1], Maria Aparecida Nagai[1], Alexander Jorge[3], Ana Amelia Fialho de Oliveira Hoff[1]

[1] Instituto do Câncer do Estado de São Paulo (ICESP), São Paulo, SP, Brasil.[2] University of Michigan, Michigan, USA.[3] Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), São Paulo, SP, Brasil

Introduction: Medullary thyroid carcinoma (MTC) is a neuroendocrine tumor arising from the parafollicular cells. This tumor is familial in 25% of the cases. When hereditary, is associated with the multiple endocrine neoplasia type 2 syndrome (MEN2), an autosomal dominant disorder caused by germline variants of the RET proto-oncogene, classified in: MEN2A and MEN2B. The mean age of presentation of hereditary MTC varies according to the RET variant, but generally occurs before the third decade of life; in MEN2B (p.Met918Thr) MTC develops usually within the first year of life. Sporadic MTC, not associated with germline RET variants, is usually diagnosed between the fourth and sixth decades of life. Genetic analysis of sporadic tumors identified somatic variants in RET, HRAS and KRAS and less frequently in other genes. However, approximately 30% of sporadic MTC patients are still orphans of a genetic driver. In the literature, tumor exome sequencing studies were done in a few number of patients without clinical data correlation. **Objective:** Genetic analysis of patients with aggressive MTC and early disease onset without germline RET mutation. **Methods:** Perform germline and somatic DNA exome sequencing in 19 patients with aggressive MTC, diagnosed prior to 30 years of age and negative germline RET. The staging and outcome of the chosen cohort was compared to MEN2A, MEN2B and sporadic MTC cohorts. All patients had structural incomplete response, 68% with distant metastasis and 47 % required tyrosine kinase inhibitors, findings similar to our MEN2B cohort. Somatic DNA was obtained from formalin-fixed paraffin-embedded tissues of the primary tumor or lymph node metastasis. **Results:** From a total of 19 patients; tumor and germline sequencing was successful in 15 and germline in 4 patients. Somatic RET variants were detected in 80% of the patients; p.Met918Thr was the most frequent (60%) and associated with more aggressive disease (78% distant metastasis and 67% required tyrosine kinase inhibitors). The other RET pathogenic variants included 2 novel (p.Arg873Trp and p.Glu632_Ser645dup). From the group of patients without somatic RET, pathogenic variants were detected in HRAS (p.Ala11_Gly12dup) and NF1 (p.Leu1064fs). Interestingly, NF1 somatic pathogenic variant was observed in a patient initially referred with suspicion of MEN2B, presented with marfanoid habitus but no other features of MEN2B and at initial inspection 3 small café-au-lait spots were observed. Exome sequencing of this patient also revealed a germline NF1 pathogenic variant (c.1527+1G>T). **Conclusion:** This study confirms the importance of RET as a genetic driver in sporadic MTC, specifically in this cohort of patients with aggressive and early onset disease in which the frequency of RET variants was higher than the reported in most studies. In addition, pathogenic variants were found in 2 other patients, in HRAS and in NF1, a tumor suppressor gene and a potential new driver for MTC.

CLINICAL/THYROID CANCER CLINICAL

117055 IDENTIFYING NUCLEAR GROOVES IN WHOLE-SLIDE IMAGES OF PAPILLARY THYROID CARCINOMA CYTOLOGY IN DIFF-QUIK STAINING USING ARTIFICIAL INTELLIGENCE

Pedro Resende Ferreira Rende[1], Kátia Nakadaira[2], Joel Pires[3], Sara Gomes de Campos Lopes[4], Gabriel Rodriguez[1], Ana Marques[5], Jorge Pinheiro[5], João Vale[5], Fabyan Esberard de Lima Beltrão[6], Fabio Hecht[7], Edna Teruko Kimura[8], Catarina Eloy[5], Helton Estrela Ramos[1]

[1] Department of Bioregulation, Federal University of Bahia (UFBA), Salvador, BA, Brazil.[2] Institute of Biomedical Science, University of São Paulo (USP), São Paulo, SP, Brazil.[3] Center for Exact and Technological Sciences, Federal University of Recôncavo da Bahia, Cruz das Almas, BA, Brazil.[4] Hospital de Braga, Endocrinology Department, Braga, Portugal.[5] Institute of Molecular Pathology and Immunology, University of Porto, Porto, Portugal.[6] Federal University of Paraíba, Lauro Wanderley University Hospital, Department of Endocrinology, João Pessoa, PB, Brazil.[7] Instituto de Ciências, Tecnologia e Inovação, UFBA, Camaçari, BA, Brazil.[8] Department of Cellular and Developmental Biology, USP, São Paulo, SP, Brazil

Introduction: Fine needle aspiration of the thyroid (FNA) associated with ultrasound is an important test in the investigation of thyroid nodules malignancy. However, the Bethesda Thyroid Cytopathological Assessment System has some limitations: it is laborious, time-consuming and has great interobserver variability. In cytology, nuclear alterations are important milestones for malignancy diagnosis and have gained more preeminence. Among them, nuclear grooves stand out and constitute a sensitive marker in the cytological diagnosis of papillary thyroid carcinoma (PTC). The application of Artificial Intelligence (AI) models has been exploited in the field of cytology, with promising results, and is now gradually being expanded to thyroid samples. **Objectives:** To evaluate the ability to detect nuclear grooves in whole-slide images (WSI) of PTC cytology in Diff-Quik staining using a Convolutional Neural Network (CNN) model. **Methods:** 22 whole-slides images from cytology with Diff-Quik staining from 21 cases with cytological diagnosis of PTC confirmed by histology were retrieved from the archive of the IPATIMUP Pathology Laboratory. The pathologist observed the WSIs of the 21 cases after three scanning protocols: P1000_20x (scanning with P1000 using the 20x protocol validated for clinical usage in our laboratory), P1000_40x (scanning with P1000 using a 40x protocol), and DP200_20x (scanning with VENTANA DP 200 using a 20x protocol). Nuclear grooves were defined as a longitudinal invagination of the nuclear envelope. WSIs were scanned with 3DHISTECH scanner, followed by the manual clipping of the regions of interest. Each crop resulted in an image in jpg format that has been resized. All these images were annotated by a pathologist, subjected to data augmentation techniques and divided into an adjustment and test group in a 7:3 ratio. The transfer of learning technique was used, with the use of weights from the YOLOv5 object detection model, to adjust the model for nuclear groove detection. **Results:** 7.255 clippings were made from 22 digital images, in which 7,242 nuclear grooves were annotated. The best model was fitted 14 times (epochs), with 67% true positives for groove detection. Specifically, it scored 0.45664 for Mean Average Precision (mAP), 0.49837 for recall, and 0.43099 for precision. **Conclusion:** In the present study, an average result was obtained. Some factors greatly influenced the result: (1) the type of staining, that does not show enough details of the cells, (2) the number of slides diagnosed, that was low, and (3) the number of groove annotations, that may not have been the most representative. It is noted that we can improve a lot with these points. The results demonstrated that the detection of grooves through computer vision, using Deep Learning, is feasible and that the quality of the database for model adjustment has a lot of weight. Still, we have many possibilities with architectures based on CNNs and Attention.

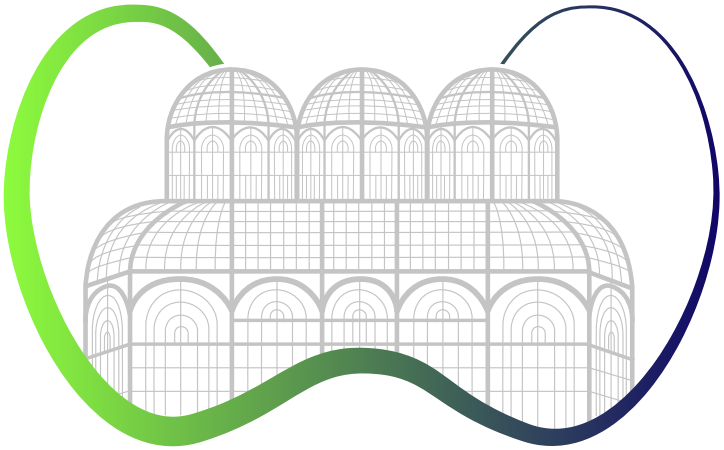
CLINICAL/THYROID CANCER CLINICAL

117092 WHOLE-BODY SCAN (WBS) EVALUATION BEFORE 131 IODINE TREATMENT MIGHT HAVE LIMITED USE FOR DETECTION OF DISTANT METASTASIS IN PEDIATRIC DIFFERENTIATED THYROID CARCINOMA

Paulo Alonso Garcia Alves Junior[1], Paulo Alonso Garcia Alves Junior[1], Marise Codeço de Andrade Barreto[1], Fernanda Aciolly Andrade[1], Daniel Buzico[1], Rossana Corbo[1], Fernanda Vaisman[1]

[1] National Cancer Institute (Inca), Rio de Janeiro, RJ, Brazil

Introduction: Thyroglobulin and whole-body scan (WBS) based on radioiodine uptake are tumor markers related to the presence of residual disease or distant metastasis after surgery and frequently use to tailor the indication of radioiodine therapy (RAI) and the activity in pediatric differentiated thyroid carcinoma (DTC). Although rare, DTC in the pediatric population is more aggressive and has a greater chance of distant metastasis. Objective Evaluate stimulated thyroglobulin, diagnostic WBS (Dx WBS) and post-treatment WBS (PTx WBS) as predictors of distant metastasis. of the presence of RAI avid distant metastasis. **Materials and methods:** We retrospectively evaluated patients with pediatric DTC from 1980 to 2022 at a national reference cancer center. Stimulated thyroglobulin was measured prior to the first RAI treatment (Rand correlated with the possibility of finding distant metastasis. Radioactive iodine WBS was performed before RAI and compared with post-RAI WBS or other imaging tests in detecting residual disease/distant metastasis. **Results:** 142 patients (71.8% female) with a median age of 14.6 (4-18) years were followed for 9.5 ± 7.2 years and classified according to TCA risk as Low (28%), Moderate (16%) and High (56%). Factors such as gender, follow-up time, type of surgery, histological parameters, mean dose of radioactive iodine were not significantly different between groups. The percentage of patients who achieved an excellent response to treatment between within the first year after RAI was 40% in the Low group, 32% in the Moderate group, and 17.5% in the High group (p 0.024), with 65%, 59%, and 36 % respectively at the end of follow-up (p 0.006). Stimulated thyroglobulin values of 21.7 ng/dL showed specificity of 60% with a negative predictive value of 93% predicting distant metastases but a positive predictive value of 39%. On the other hand, DxWAS showed specificity of 100% and sensitivity of 30% with negative predictive value 74% with a positive predictive value of 100%. Thirty tree percent had Dx WBS with uptake only in the neck and had distant metastases in the post therapy scan. **Conclusions:** Dx WBS showed a lower negative predictive value when compared to stimulated post-operative thyroglobulin. Hence, we suggest that DxWBS in pediatric DTC can lead to underestimation of distant metastases, consequently to undertreatment in these group when stimulated thyroglobulin is already suggestive of distant metastases. Once DxWBS is positive, 100% had uptake on the post therapy WBS but they also had high thyroglobulin values that could predict the same outcome.



XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL

Remissive index

A

B

C

I

J

K

L

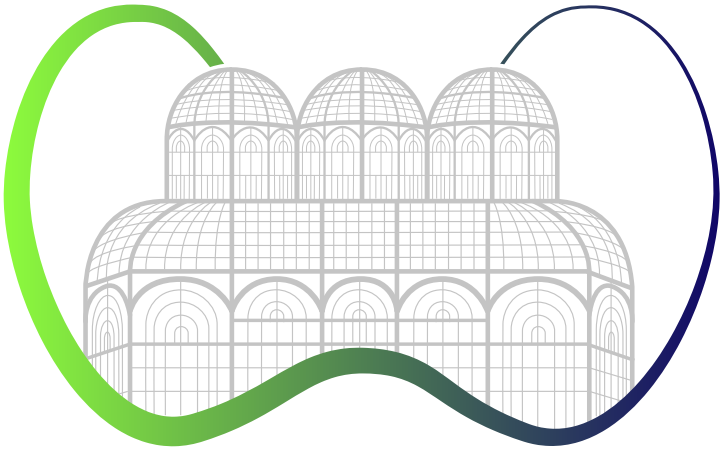
M

N

O

P

R



XIX LATIN AMERICAN THYROID CONGRESS

20TH | 23RD APRIL 2023

CURITIBA | PR | BRAZIL