*El material que se presenta a continuación proviene de los datos recolectados por nuestra Revista.*

# Resúmenes de las publicaciones WOS 2024 realizadas por nuestros académicos

## SERVICIO ANATOMÍA PATOLÓGICA

**CURR ONCOL. 2024 JAN 3;31(1):274-295. DOI: 10.3390/CURRONCOL31010018.**

GENETIC POLYMORPHISMS AND TUMORAL MUTATIONAL PROFILES OVER SURVIVAL IN ADVANCED COLORECTAL CANCER PATIENTS: AN EXPLORATORY STUDY

Juan Pablo Cayún, Leslie Carol Cerpa, Alicia Colombo, Dante Daniel Cáceres, José Luis Leal, Felipe Reyes, Carolina Gutiérrez-Cáceres, Susan Calfunao, Nelson Miguel Varela, Luis Abel Quiñones

Colorectal cancer is a common disease, both in Chile and worldwide. The most widely used chemotherapy schemes are based on 5-fluorouracil (5FU) as the foundational drug (FOLFOX, CapeOX). Genetic polymorphisms have emerged as potential predictive biomarkers of response to chemotherapy, but conclusive evidence is lacking. This study aimed to investigate the role of genetic variants associated with 5FU-based chemotherapy on therapeutic response, considering their interaction with oncogene mutations (KRAS, NRAS, PI3KCA, AKT1, BRAF). In a retrospective cohort of 63 patients diagnosed with metastatic colorectal cancer, a multivariate analysis revealed that liver metastases, DPYD, ABCB1, and MTHFR polymorphisms are independent indicators of poor prognosis, irrespective of oncogene mutations. BRAF wild-type status and high-risk drug-metabolism polymorphisms correlated with a poor prognosis in this Chilean cohort. Additionally, findings from the genomics of drug sensitivity (GDSC) project demonstrated that cell lines with wild-type BRAF have higher IC50 values for 5-FU compared to BRAF-mutated cell lines. In conclusion, the genetic polymorphisms DPYDrs1801265, ABCB1rs1045642, and MTHFRrs180113 may serve as useful biomarkers for predicting a poor prognosis in patients undergoing 5-fluorouracil chemotherapy, regardless of oncogene mutations.

**REV MED CHIL. 2024 FEB;152(2):197-210. DOI: 10.4067/S0034-98872024000200197.**

DESARROLLO DE LA APLICACIÓN EULAT ECOLLECT PARA EL REGISTRO ELECTRÓNICO DE DATOS DEL CONSORCIO EUROPEO-LATINOAMERICANO CONTRA EL CÁNCER DE VESÍCULA BILIAR-EULAT ERADICATE GBC.

Justo Lorenzo Bermejo, Carol Barahona Ponce, Alicia Colombo, Gerardo Donoso, Jaime González Díaz, Sergio Guinez-Molinos

El Consorcio Europeo-Latinoamericano contra el Cáncer de Vesícula Biliar (CVB) EULAT Eradicate GBC está recopilando datos y muestras de alta calidad en cuatro países latinoamericanos con una alta incidencia de esta enfermedad: Argentina, Bolivia, Chile y Perú (www.SaludVesiculaBiliar.org). Los objetivos del consorcio incluyen la creación de un biorepositorio único integrado en una plataforma informática a medida, la identificación, validación y caracterización funcional de nuevos biomarcadores de riesgo del CVB, y el desarrollo de modelos predictivos que integren factores de riesgo tanto epidemiológicos como genético-moleculares. Para facilitar la recolección y la calidad de los datos sociodemográficos, clínicos, sobre las muestras, de estilo de vida y nutricionales de los 15.000 participantes latinoamericanos que están siendo reclutados, decidimos desarrollar la aplicación EULAT eCollect para reducir el tiempo invertido por los participantes en el estudio, limitar el uso de papel y tinta, minimizar los costes y errores asociados a la cumplimentación de formularios escritos y su posterior digitalización, automatizando además el monitoreo de las tasas de reclutamiento y de la calidad de los datos en cada centro participante. Este artículo describe el diseño e implementación de la aplicación EULAT eCollect, desde la especificación de los requisitos funcionales y no funcionales, hasta la implementación y validación de los cuatro módulos de la aplicación: I Entrevista sociodemográfica, II Información sobre las muestras, III Formulario de informe de casos y IV Cuestionario de hábitos alimenticios. Además de nuestra experiencia con el software Open Data Kit, presentamos resultados tanto generales como técnicos que pueden ser de interés para futuros proyectos de investigación, especialmente los estudios de prevención personalizada del cáncer llevados a cabo en regiones con niveles de ingreso bajos y medios.

**INT J MOL SCI. 2024 APR 25;25(9):4695. DOI: 10.3390/IJMS25094695.**

DISTINCT DRIVER PATHWAY ENRICHMENTS AND A HIGH PREVALENCE OF TSC2 MUTATIONS IN RIGHT COLON CANCER IN CHILE: A PRELIMINARY COMPARATIVE ANALYSIS

Camilo Tapia-Valladares, Guillermo Valenzuela, Evelin González, Ignacio Maureira, Jessica Toro, Matías Freire, Gonzalo Sepúlveda-Hermosilla, Diego Ampuero, Alejandro Blanco, Iván Gallegos, Fernanda Morales, José I Erices, Olga Barajas, Mónica Ahumada, Héctor R Contreras, Jaime González, Ricardo Armisén, Katherine Marcelain

Colorectal cancer (CRC) is the second leading cause of cancer deaths globally. While ethnic differences in driver gene mutations have been documented, the South American population remains understudied at the genomic level, despite facing a rising burden of CRC. We analyzed tumors of 40 Chilean CRC patients (Chp) using next-generation sequencing and compared them to data from mainly Caucasian cohorts (TCGA and MSK-IMPACT). We identified 388 mutations in 96 out of 135 genes, with TP53 (45%), KRAS (30%), PIK3CA (22.5%), ATM (20%), and POLE (20%) being the most frequently mutated. TSC2 mutations were associated with right colon cancer (44.44% in RCRC vs. 6.45% in LCRC, p-value = 0.016), and overall frequency was higher compared to TCGA (p-value = 1.847 × 10-5) and MSK-IMPACT cohorts (p-value = 3.062 × 10-2). Limited sample size restricts definitive conclusions, but our data suggest potential differences in driver mutations for Chilean patients, being that the RTK-RAS oncogenic pathway is less affected and the PI3K pathway is more altered in Chp compared to TCGA (45% vs. 25.56%, respectively). The prevalence of actionable pathways and driver mutations can guide therapeutic choices, but can also impact treatment effectiveness. Thus, these findings warrant further investigation in larger Chilean cohorts to confirm these initial observations. Understanding population-specific driver mutations can guide the development of precision medicine programs for CRC patients.

**GENES (BASEL). 2024 OCT 22;15(11):1352. DOI: 10.3390/GENES15111352.**

THE CHILEAN COVID-19 GENOMICS NETWORK BIOREPOSITORY: A RESOURCE FOR MULTI-OMICS STUDIES OF COVID-19 AND LONG COVID IN A LATIN AMERICAN POPULATION

Iskra A Signore, Gerardo Donoso, Pamela Bocchieri, Eduardo A Tobar-Calfucoy, Cristian E Yáñez, Laura Carvajal-Silva, Andrea X Silva, Carola Otth, Claudio Cappelli, Héctor Valenzuela Jorquera, Daniela Zapata-Contreras, Yolanda Espinosa-Parrilla, Paula Zúñiga-Pacheco, Macarena Fuentes-Guajardo, Virginia A Monardes-Ramírez, Pia Kochifas Velasquez, Christian A Muñoz, Cristina Dorador, Jonathan García-Araya, Claudia P Campillay-Véliz, Cesar Echeverria, Rodolfo Alejandro Santander, Leslie C Cerpa, Matías F Martínez, Luis Abel Quiñones, Eduardo Roberto Lamoza Galleguillos, Juan Saez Hidalgo, Estefanía Nova-Lamperti, Sergio Sanhueza, Annesi Giacaman, Gerardo Acosta-Jamett, Cristóbal Verdugo, Anita Plaza, Claudio Verdugo, Carolina Selman, Ricardo Alejandro Verdugo, Alicia Colombo

Although a lack of diversity in genetic studies is an acknowledged obstacle for personalized medicine and precision public health, Latin American populations remain particularly understudied despite their heterogeneity and mixed ancestry. This gap extends to COVID-19 despite its variability in susceptibility and clinical course, where ethnic background appears to influence disease severity, with non-Europeans facing higher hospitalization rates. In addition, access to high-quality samples and data is a critical issue for personalized and precision medicine, and it has become clear that the solution lies in biobanks. The creation of the Chilean COVID-19 Biorepository reported here addresses these gaps, representing the first nationwide multicentric Chilean initiative. It operates under rigorous biobanking standards and serves as one of South America's largest COVID cohorts. A centralized harmonization strategy was chosen and included unified standard operating procedures, a sampling coding system, and biobanking staff training. Adults with confirmed SARS-CoV-2 infection provided broad informed consent. Samples were collected to preserve blood, plasma, buffy coat, and DNA. Quality controls included adherence to the standard preanalytical code, incident reporting, and DNA concentration and absorbance ratio 260/280 assessments. Detailed sociodemographic, health, medication, and preexisting condition data were gathered. In five months, 2262 participants were enrolled, pseudonymized, and sorted by disease severity. The average Amerindian ancestry considering all participant was 44.0% [SD 15.5%], and this value increased to 61.2% [SD 19.5%] among those who self-identified as Native South Americans. Notably, 279 participants self-identified with one of 12 ethnic groups. High compliance (>90%) in all assessed quality controls was achieved. Looking ahead, our team founded the COVID-19 Genomics Network (C19-GenoNet) focused on identifying genetic factors influencing SARS-CoV-2 outcomes. In conclusion, this bottom-up collaborative effort aims to promote the integration of Latin American populations into global genetic research and welcomes collaborations supporting this endeavor. Interested parties are invited to explore collaboration opportunities through our catalog, accessible online.

## SERVICIO ANESTESIOLOGÍA Y MEDICINA PERIOPERATORIA

**REV ESP ANEST REANIM (ENGL ED). 2024 JAN;71(1):8-16. DOI: 10.1016/J.REDARE.2023.05.004.**

STUDENT SURVEY AFTER TEN YEARS OF CONTINUOUS BLENDED TEACHING OF ECHOCARDIOGRAPHY

Víctor M Parra, Guillermina Fita, Manel Azqueta, Mauricio González, Fernando Aranda, M Luz Maestre, Jorge Silva, Javier Hortal, Daniel Morales, Emiliano Bórquez, Fabián Adasme, María Isabel Real, Jordi Mercadal, Pamela Zelada, Gonzalo Riobó, Katia Galdames, Raúl J Domenech

Objective: To analyse the impact of 10 years of blended echocardiography teaching. Methods and results: A questionnaire was emailed to all medical doctors who graduated from the blended learning diploma in echocardiography developed by the University of Chile

and taught by a team from Chile and Spain. One hundred and forty of the 210 students who graduated from the program between 2011 and 2020 completed the questionnaire: 53.57% were anaesthesiologists, and 26.42% were intensivists. More than 85% of respondents indicated that the online teaching met their expectations, and 70.2% indicated that the hands-on practice fulfilled the stated objectives. In a retrospective analysis using self-reported data, graduates reported that their use of transthoracic and transoesophageal echocardiography has increased from 24.29% to 40.71% and from 13.57% to 27.86%, repectively, after the programme compared to before the programme. They used echocardiography mainly in the perioperative period (56.7%) and during intensive care (32.3%), while only 11% of respondents used it in emergency care units. Nearly all (92.4%) respondents reported that the skills learned was very useful in their professional practice. Conclusions: Ten years after its launch, the blended learning diploma in echocardiography was well rated by graduate specialists, and is associated with a significant increase in the use of echocardiography in the perioperative period and during intensive care. The main challenges are to establish a longer period of practice and achieve greater implantation in emergency medicine.

**NAT COMMUN. 2024 JUL 10;15(1):5788. DOI: 10.1038/S41467-024-50204-4.**

DEVELOPMENTAL TRAJECTORIES OF EEG APERIODIC AND PERIODIC COMPONENTS IN CHILDREN 2-44 MONTHS OF AGE

Carol L Wilkinson, Lisa D Yankowitz, Jerry Y Chao, Rodrigo Gutiérrez, Jeff L Rhoades, Shlomo Shinnar, Patrick L Purdon, Charles A Nelson

The development of neural circuits has long-lasting effects on brain function, yet our understanding of early circuit development in humans remains limited. Here, periodic EEG power features and aperiodic components were examined from longitudinal EEGs collected from 592 healthy 2-44 month-old infants, revealing age-dependent nonlinear changes suggestive of distinct milestones in early brain maturation. Developmental changes in periodic peaks include (1) the presence and then absence of a 9-10 Hz alpha peak between 2-6 months, (2) nonlinear changes in high beta peaks (20-30 Hz) between 4-18 months, and (3) the emergence of a low beta peak (12-20 Hz) in some infants after six months of age. We hypothesized that the emergence of the low beta peak may reflect maturation of thalamocortical network development. Infant anesthesia studies observe that GABA-modulating anesthetics do not induce thalamocortical mediated frontal alpha coherence until 10-12 months of age. Using a small cohort of infants (n = 23) with EEG before and during GABA-modulating anesthesia, we provide preliminary evidence that infants with a low beta peak have higher anesthesia-induced alpha coherence compared to those without a low beta peak.

**BMC ANESTHESIOL. 2024 SEP 17;24(1):329. DOI: 10.1186/S12871-024-02718-Z.**

ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO WITH AGE AND 180-DAY MORTALITY AFTER EMERGENCY SURGERY

Felipe Maldonado, Manuel Albornoz, Ignacia Enríquez, Catalina Espinoza, Hui Chang, Laura Carrasco, Catalina Díaz-Papapietro, Felipe Medina, Roberto González, Mónica Cáceres

Background: To examine the relationship between neutrophil-to-lymphocyte ratio (NLR), age, and mortality rates after emergency surgery. Methods: In this observational study, a total of 851 patients undergoing emergency surgery between January 2022 and January 2023 were retrospective examined. Using 30 and 180 days mortality data, NLR differences and receiver operating characteristic (ROC) curves were analyzed using a 65-year threshold. A multiple logistic regression model was constructed incorporating age and NLR. Finally, Kaplan-Meier curves were constructed for mortality. Results: Among 851 patients, the 30 and 180 days mortality rates were 5.2% and 10.8%, respectively. Median NLR in 30 days was 5.6 (3.1 to 9.6) in survivors and 8.7 (4.6 to 13.4) in deceased patients ($p < 0.0001$); in 180 days, it was 5.5 (3.1 to 9.8) and 8.8 (4.8 to 14.5), respectively ($p < 0.0001$). In the 30- and 180-days mortality analyses, median NLRs were 5.1 (2.9 to 8.9) and 4.9 (2.9 to 8.8) in survivors and 10.6 (6.9 to 16.6) and 9.3 (5.4 to 14.9) in deceased patients aged < 65 years, respectively. The ROC AUC in patients younger than 65 years was higher for 30 days (AUC 0.75; 95% CI 0.72 to 0.87) and 180 days (AUC 0.73; 95% CI 0.64 to 0.81). Multivariate logistic regression revealed that the NLR (odds ratio, 1.03 [95% CI 1.005 to 1.053; $p = 0.0133$) and age (odds ratio, 1.05 [95% CI 1.034 to 1.064; $p < 0.0001$) significantly contributed to the model. Survival analysis revealed differences in the 180 days mortality ($p = 0.0006$). Conclusion: We observed differences in preoperative NLR between patients who survived and those who died after emergency surgery. Age impacts the use of NLR as a mortality risk factor.

**CUREUS. 2024 NOV 27;16(11):E74606. DOI: 10.7759/CUREUS.74606.**

EFFICACY AND SAFETY IN THE IMPLANTATION OF TOTALLY IMPLANTABLE VENOUS ACCESS DEVICES BY ANESTHESIOLOGISTS: PERSPECTIVES FROM A RETROSPECTIVE ONCOLOGY COHORT

Nicolás Valls, Nicolás Villablanca, Roberto González, María Soledad Ramirez, Carla Almeida, Julio Lopez

Background: Totally implantable venous access devices (TIVADs) are widely used in oncology patients to facilitate central venous access. Although they offer benefits, TIVADs can be associated with complications. Materials and methods: This retrospective cohort study included all oncology patients 18 years or older who underwent TIVAD implantation between September 2015 and October 2019. Data were obtained from clinical records at the National Cancer Institute. Results: A total of 556 TIVAD implantations were performed in cancer patients throughout the study period. The success rate for the first attempts was 91% (506/556). Infectious complications were documented in six patients (1.1%), while non-infectious complications manifested in less than 1% of cases, with hematoma at the insertion site being the most common. Additionally, catheter thrombosis was identified in

three asymptomatic patients (0.5%). Conclusion: The implantation of TIVADs by anesthesiologists in cancer patients at the National Cancer Institute was predominantly successful and safe, exhibiting a low complication rate. The findings reinforce the efficacy and safety of the employed technique, exceeding the outcomes reported in existing medical literature.

**PAEDIATR ANAESTH. 2024 APR;34(4):318-323. DOI: 10.1111/PAN.14817.**

A PRAGMATIC METHODOLOGY TO EXTRACT ANESTHETIC AND PHYSIOLOGICAL DATA FROM THE ELECTRONIC HEALTH RECORD

Arshia Aalami Harandi, Katherine McPherson, Yungtai Lo, Rodrigo Gutiérrez, Jerry Y Chao

Background/aims: Traditional manual methods of extracting anesthetic and physiological data from the electronic health record rely upon visual transcription by a human analyst that can be labor-intensive and prone to error. Technical complexity, relative inexperience in computer coding, and decreased access to data warehouses can deter investigators from obtaining valuable electronic health record data for research studies, especially in under-resourced settings. We therefore aimed to develop, pilot, and demonstrate the effectiveness and utility of a pragmatic data extraction methodology. Methods: Expired sevoflurane concentration data from the electronic health record transcribed by eye was compared to an intermediate preprocessing method in which the entire anesthetic flowsheet narrative report was selected, copy-pasted, and processed using only Microsoft Word and Excel software to generate a comma-delimited (.csv) file. A step-by-step presentation of this method is presented. Concordance rates, Pearson correlation coefficients, and scatterplots with lines of best fit were used to compare the two methods of data extraction. Results: A total of 1132 datapoints across eight subjects were analyzed, accounting for 18.9 h of anesthesia time. There was a high concordance rate of data extracted using the two methods (median concordance rate 100% range [96%, 100%]). The median time required to complete manual data extraction was significantly longer compared to the time required using the intermediate method (240 IQR [199, 482.5] seconds vs 92.5 IQR [69, 99] seconds, $p = .01$) and was linearly associated with the number of datapoints ($r_{manual} = .97$, $p < .0001$), whereas time required to complete data extraction using the intermediate approach was independent of the number of datapoints ($r_{intermediate} = -.02$, $p = .99$). Conclusions: We describe a pragmatic data extraction methodology that does not require additional software or coding skills intended to enhance the ease, speed, and accuracy of data collection that could assist in clinician investigator-initiated research and quality/process improvement projects.

**BR J ANAESTH. 2024 MAY;132(5):1041-1048. DOI: 10.1016/J.BJA.2024.01.033.**

RESEARCH PRIORITIES IN REGIONAL ANAESTHESIA: AN INTERNATIONAL DELPHI STUDY

Jenny Ferry, Owen Lewis, James Lloyd, Kariem El-Boghdadly, Rachel Kearns, Eric Albrecht, Fernando Altermatt, Balakrishnan Ashokka, Amany E Ayad, Ezzat S Aziz, Lutful Aziz, Balavenkatasubramanian Jagannathan 9, Noreddine Bouarroudj, Ki Jinn Chin, Alain Delbos, Alex de Gracia, Vivian H Y Ip, Kwesi Kwofie, Sebastian Layera *et al.*

Background: Regional anaesthesia use is growing worldwide, and there is an increasing emphasis on research in regional anaesthesia to improve patient outcomes. However, priorities for future study remain unclear. We therefore conducted an international research prioritisation exercise, setting the agenda for future investigators and funding bodies. Methods: We invited members of specialist regional anaesthesia societies from six continents to propose research questions that they felt were unanswered. These were consolidated into representative indicative questions, and a literature review was undertaken to determine if any indicative questions were already answered by published work. Unanswered indicative questions entered a three-round modified Delphi process, whereby 29 experts in regional anaesthesia (representing all participating specialist societies) rated each indicative question for inclusion on a final high priority shortlist. If ≥75% of participants rated an indicative question as 'definitely' include in any round, it was accepted. Indicative questions rated as 'definitely' or 'probably' by <50% of participants in any round were excluded. Retained indicative questions were further ranked based on the rating score in the final Delphi round. The final research priorities were ratified by the Delphi expert group. Results: There were 1318 responses from 516 people in the initial survey, from which 71 indicative questions were formed, of which 68 entered the modified Delphi process. Eleven 'highest priority' research questions were short listed, covering themes of pain management; training and assessment; clinical practice and efficacy; technology and equipment. Conclusions: We prioritised unanswered research questions in regional anaesthesia. These will inform a coordinated global research strategy for regional anaesthesia and direct investigators to address high-priority areas.

## DEPARTAMENTO CARDIOVASCULAR

**REV MED CHIL. 2024 JUN;152(6):718-723. DOI: 10.4067/S0034-98872024000600718.**

ENDOCARDITIS INFECCIOSA BIVALVULAR CON COMPROMISO DE LA FIBROSA MITROAÓRTICA POR STAPHYLOCOCCUS LUGDUNENSIS

Francisco José Ayala Ruiquelme, Juan Espinoza Huircalaf, Maximiliano Acevedo de la Barra, Tamara Vergara Cerón, Gonzalo Miranda Gonzalez, Carla Parra Albornoz, Angela Pino Labrador, Katia Galdames Ibañez

Bivalvular infective endocarditis is a clinical presentation that is associated to a greater extent with adverse outcomes. The involvement of the intervalvular mitral-aortic fibrosa is a rare complication associated with high mortality rates, requiring high

complexity surgery. We report a case of a young male presenting to the emergency department with bivalvular endocarditis and mitral-aortic intervalvular fibrosa involvement.

**DIAGNOSTICS (BASEL). 2024 APR 25;14(9):893. DOI: 10.3390/DIAGNOSTICS14090893.**

CLINICAL IMPLICATIONS OF HIGH-SENSITIVITY TROPONIN ELEVATION LEVELS IN NON-ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION PATIENTS: BEYOND DIAGNOSTICS

Constanza Bravo, Geovanna Vizcarra, Antonia Sánchez, Francisca Cárdenas, Juan Pablo Canales, Héctor Ugalde, Alfredo Parra-Lucares

Standard troponin has long been pivotal in diagnosing coronary syndrome, especially Non-ST-Segment Elevation Myocardial Infarction (NSTEMI). The recent introduction of high-sensitivity troponin (hs-cTnI) has elevated it to the gold standard. Yet, its nuanced role in predicting angiographic lesions and clinical outcomes, notably in specific populations like obesity, remains underexplored. Aim: To evaluate the association between hs-cTnI magnitude in NSTEMI patients and angiographic findings, progression to acute heart failure, and its performance in obesity. Methods: Retrospective study of 208 NSTEMI patients at a large university center (2020-2023). Hs-cTnI values were assessed for angiographic severity, acute heart failure, and characteristics in the obese population. Data collected and diagnostic performance were evaluated using manufacturer-specified cutoffs. Results: 97.12% of patients had a single culprit vessel. Hs-cTnI elevation correlated with angiographic stenosis severity. Performance for detecting severe coronary disease was low, with no improvement using a higher cutoff. No association was found between hs-cTnI and the culprit vessel location. Hs-cTnI did not predict acute heart failure progression. In the obese population, hs-cTnI levels were higher, but acute heart failure occurred less frequently than in non-obese counterparts. Conclusions: In NSTEMI, hs-cTnI elevation is associated with significant stenosis, but not with location or acute heart failure. Obesity correlates with higher hs-cTnI levels but a reduced risk of acute heart failure during NSTEMI.

**REV MED CHIL. 2024 FEB;152(2):235-243. DOI: 10.4067/S0034-98872024000200235.**

FORMACIÓN DEL CARDIÓLOGO EN CHILE Y CONTRIBUCIONES DESDE LA SOCIEDAD CHILENA DE CARDIOLOGÍA Y CIRUGÍA CARDIOVASCULAR

Víctor Rossel, Jorge Gajardo, Rodrigo Miranda, Yalile Nauhm, Ricardo Larrea, Douglas Greig, Flor Fernández, Alex Bittner, Rubén Aguayo, Paola Varleta, Gonzalo Sanhueza, Claudio Bugueño, Luis Quiñiñir, Marcelo Llancaqueo *et al.*

La Sociedad Chilena de Cardiología y Cirugía Cardiovascular (SOCHICAR) es una entidad científica cuya misión es mejorar la salud cardiovascular del país y entre sus objetivos principales está el debatir los problemas de la especialidad y realizar diferentes actividades que tiendan a fomentar su progreso. Para cumplir con ellos se realizan diversas actividades de educación dirigidas a profesionales de la salud, entre los cuales se encuentran los médicos en programas de formación de cardiología. La formación de especialistas en Chile es responsabilidad de las Universidades, quienes diseñan la malla curricular y planifican las distintas actividades del programa de acuerdo con el perfil de egreso. La SOCHICAR busca integrar a estas nuevas generaciones de cardiólogos, implementando una serie de actividades dirigidas a ellos que contribuyan en su período de formación. Nos pareció relevante entregar nuestra posición como Sociedad Científica en importantes aspectos relacionados con este proceso: el perfil de egreso del cardiólogo clínico, las competencias necesarias para su desempeño en el país, la identificación de áreas deficitarias en su etapa formativa y las contribuciones desde la Sociedad a este proceso dependiente de las universidades. Se convocó a cardiólogos de SOCHICAR, en distintas etapas de desarrollo profesional, diferentes áreas geográficas y ámbitos de desempeño y funciones, en total, 15 cardiólogos (as), distribuidos en tres grupos de trabajo. Esta declaración de posición de la SOCHICAR puede ser de utilidad y una fuente de información importante a considerar por autoridades, entidades acreditadoras, centros formadores y la Sociedad Chilena de Cardiología.

## DEPARTAMENTO CIRUGÍA

**J SURG CASE REP. 2024 AUG 8;2024(8):RJAE347. DOI: 10.1093/JSCR/RJAE347.**

PURE LAPAROSCOPIC BILATERAL ARCUATE LINE HERNIA REPAIR (WITH VIDEO)

J Rappoport, J Carrasco, B Gamez

An arcuate line hernia is a generally asymptomatic, ascending protrusion of intraperitoneal structures over the linea arcuata. Arcuate line herniae are scarcely reported in the literature. Only a few publications were found. No clear descriptions of the techniques for repair have been published either. We aim to provide diagnostic images and illustrate our method to repair this hernia.

**OBES REV. 2024 JAN;25(1):E13642. DOI: 10.1111/OBR.13642.**

CHANGING THE GLOBAL OBESITY NARRATIVE TO RECOGNIZE AND REDUCE WEIGHT STIGMA: A POSITION STATEMENT FROM THE WORLD OBESITY FEDERATION

Sarah Nutter, Laura A Eggerichs, Taniya S Nagpal, Ximena Ramos Salas, Christine Chin Chea, Shubo Saiful, Johanna Ralston, Olivia Barata-Cavalcanti, Claudia Batz, Louise A Baur, Susie Birney, Sheree Bryant, Kent Buse, Michelle I Cardel, Aastha Chugh, Ada Cuevas, Mychelle Farmer, Allison Ibrahim, Ishu Kataria, Catherine Kotz, Ted Kyle, Sara le Brocq, Vicki Mooney, Clare Mullen, Joe Nadglowski, Margot Neveux, Karin Papapietro y otros

Weight stigma, defined as pervasive misconceptions and stereotypes associated with higher body weight, is both a social determinant of health and a human rights issue. It is imperative to consider how weight stigma may be impeding health promotion efforts on a global scale. The World Obesity Federation (WOF) convened a global working group of practitioners, researchers, policymakers, youth advocates, and individuals with lived experience of obesity to consider the ways that global obesity narratives may contribute to weight stigma. Specifically, the working group focused on how overall obesity narratives, food and physical activity narratives, and scientific and public-facing language may contribute to weight stigma. The impact of weight stigma across the lifespan was also considered. Taking a global perspective, nine recommendations resulted from this work for global health research and health promotion efforts that can help to reduce harmful obesity narratives, both inside and outside health contexts.

**ARQ BRAS CIR DIG. 2024 MAY 20:37:E1801. DOI: 10.1590/0102-672020240008E1801.**

CLINICAL AND SURGICAL DILEMMAS IN OCTOGENARIAN PATIENTS WITH SMALL BOWEL OBSTRUCTION

Tomás González-Arestizábal, Álvaro Morales, Tania Avayú-Zaliasnik, Attila Csendes, Owen Korn, Manuel Figueroa-Giralt

Background: Small bowel obstruction (SBO) is a major problem in emergencies. Comorbidities increase morbimortality, which is reflected in higher costs. There is a lack of Latin American evidence comparing the differences in postoperative results and costs associated with SBO management. Aims: To compare the risk of surgical morbimortality and costs of SBO surgery treatment in patients older and younger than 80 years. Methods: Retrospective analysis of patients diagnosed with SBO at the University of Chile Clinic Hospital from January 2014 to December 2017. Patients with any medical treatment were excluded. Parametric statistics were used (a 5% error was considered statistically significant, with a 95% confidence interval). Results: A total of 218 patients were included, of which 18.8% aged 80 years and older. There were no differences in comorbidities between octogenarians and non-octogenarians. The most frequent etiologies were adhesions, hernias, and tumors. In octogenarian patients, there were significantly more complications (46.3 vs. 24.3%, p=0.007, p<0.050). There were no statistically significant differences in terms of surgical complications: 9.6% in <80 years and 14.6% in octogenarians (p=0.390, p>0.050). In medical complications, a statistically significant difference was evidenced with 22.5% in <80 years vs 39.0% in octogenarians (p=0.040, p<0.050). There were 20 reoperated patients: 30% octogenarians and 70% non-octogenarians without statistically significant differences (p=0.220, p>0.050). Regarding hospital stay, the average was significantly higher in octogenarians (17.4 vs. 11.0 days; p=0.005, p<0.050), and so were the costs, being USD 9,555 vs. USD 4,214 (p=0.013, p<0.050). Conclusions: Patients aged 80 years and older with surgical SBO treatment have a higher risk of medical complications, length of hospital stay, and associated costs compared to those younger.

**ARQ BRAS CIR DIG. 2024 AUG 30:37:E1818. DOI: 10.1590/0102-6720202400025E1818.**

RESULTS OF MECHANIC VERSUS MOTORIZED STAPLER USED IN GASTRIC SURGERY: PROSPECTIVE STUDY

Italo Braghetto, Gustavo Czwiklitzer, Owen Korn, Percy Brante, Ana Burgos

Background: Mechanic sutures represent an enormous benefit for digestive surgery in decreasing postoperative complications. Currently, the advantages of motorized stapler are under evaluation. Aims: To compare the efficacy of mechanic versus motorized stapler in gastric surgery, analyzing rate of leaks, bleeding, time of stapling, and postoperative complications. Methods: Ninety-eight patients were submitted to gastric surgery, divided into three groups: laparoscopic sleeve gastrectomy (LSG) (n=47), Roux-en-Y gastric bypass (LRYGB) (n=30), and laparoscopic distal gastrectomy (LDG) (n=21). Motorized staplers were employed in 61 patients. The number of firings, number of clips, time of total firings, total time to complete the surgery, and postoperative outcome were recorded in a specific protocol. Results: Patients submitted to LSG, LRYGB, and LDG recorded a shorter time to complete the procedure and a smaller number of firings were observed using motorized stapler (p<0.0001). No differences were identified regarding the number of clips used in patients submitted to LSG. In the group that used mechanic stapler to complete gastrojejunostomy, jejuno-jejuno-anastomosis, and jejunal transection, it was observed more prolonged time of firing and total time for finishing the procedure (p=0.0001). No intraoperative complications were found comparing the two devices used. Very similar findings were noted in the group of patients undergoing LDG. Conclusions: The motorized stapler offers safety and efficacy as demonstrated in prior reports and is relevant since less total time of surgical procedure without intraoperative or postoperative complications were confirmed.

**INDIAN J SURG 2024; 86 (SUPPL 3): 571–575. DOI: 0.1007/S12262-021-02897-W**

COMPARISON OF THE INTRAGASTRIC VOLUME AND PRESSURE REQUIRED TO CAUSE A LEAK ALONG THE SUTURE LINE IN A RESECTED STOMACH POST SLEEVE GASTRECTOMY.

Braghetto I, Burgos A, Lasnibat JP

Laparoscopic sleeve gastrectomy can be associated with significant morbidity. Dehiscence of the staple line and gastric leak are some of the severest complications. The aim of this study was to compare three different methods of gastric suture in terms of staple line strength and leak volume/pressure of the sleeved stomach. The resected stomachs of 20 patients subjected to laparoscopic sleeve gastrectomy were evaluated for bursting volume/pressure after extraction from the abdomen. The specimens were categorized into three groups according to the staples that were used. The staple line of each specimen was divided into three groups: group A, standard green cartridge stapler [stapler closure 4.0 mm] and standard blue cartridge [stapler closure 3.5 mm] for antrum and body/fundus, respectively, with interrupted suture over the intersection of stapler suture line for reinforcement [n=10]; group B, standard green and blue loads but without reinforcement [n=4]; and group C, Tri-Stapler® mechanical [stapler closing 3.0–3.5–4.0 mm] devices without reinforcement [n=6]. Leak volume/pressure was determined by injection of methylene blue solution into the lumen of the resected stomach and by recording the pressure at which the leakage occurred. Intragastric pressure and volume of first leak and location of leak were recorded. Twenty sleeved gastrectomy specimens were included. The leak pressure was significantly higher [34.0 SD 20.7 mm Hg] in group C. The volume of the resected stomach was also greater in group C [1083.3 SD 343 cc]. Leaks were observed indistinctly in the antrum body or fundus of the stomach. We found higher burst pressure and volume in stomachs resected with Tri-Stapler®. It could be a safer device for performing sleeve gastrectomy.

**OBES SURG. 2024 SEP;34(9):3266-3274. DOI: 10.1007/S11695-024-07249-7.**

LONG-TERM (11 YEARS) RESULTS OF LAPAROSCOPIC GASTRIC BYPASS: CHANGES IN WEIGHT, BLOOD LEVELS OF SUGAR AND LIPIDS, AND LATE ADVERSE EFFECTS: LAPAROSCOPIC GASTRIC BYPASS RESULTS

L Deycies Gaete, J Attila Csendes, A Tomás González, P Álvaro Morales, Benjamín Panza

Purpose: Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) remains the most effective procedure to treat severe obesity with proven short- and intermediate-term benefits. The main goal is to describe the effects on weight and biochemical laboratory tests after long-term follow-up (11 years). Materials and methods: A prospective cohort of adults with obesity treated with LRYGB between 2004 and 2010 in one center were studied. Patients with prior bariatric or upper digestive tract surgery, hiatal hernia >4 cm, alcoholism, or decompensated conditions were excluded. The study enrolled 123 patients, with a mean follow-up of 133±29 months and a 14% loss of participants. Results: The percentage of Total Weight Loss (%TWL) at one, five, and eleven years was 30.3±8.4%, 29.1±6.9%, and 23.4±7%, respectively. Of the patients, 61.3% (65/106) maintained a %TWL≥20 after eleven years. Recurrent Weight Gain (RWG) at five and eleven years was 2.6±11.4% and 11 ±11.5%, respectively. At the end of the follow-up, 31.1% (33/106) of patients had RWG≥15%. Hypercholesterolemia and hypertriglyceridemia improved in 85.7% (54/63) and 90.2% (7/61) of the cohort, respectively. Remission of diabetes occurred in 80% of this subgroup. Gallstones developed in 28% of patients, and bowel obstruction due to internal hernia occurred in 9.4%. Anemia due to iron deficiency appeared in 25 patients. Conclusion: After surgery, there is a significant and durable loss of weight, with a tendency for late Recurrent Weight Gain. Furthermore, the improvement in biochemical parameters is sustained over time, but surgery's adverse effects may appear later.

**COLORECTAL DIS. 2024 MAY;26(5):940-948. DOI: 10.1111/CODI.16962.**

INTRACORPOREAL ANASTOMOSIS COULD BE ASSOCIATED WITH A HIGHER LYMPH NODE YIELD IN RIGHT COLON CANCER SURGERY: RESULTS OF THE ICA-LATAM STUDY, A RETROSPECTIVE, MULTICENTRE, COMPARATIVE ANALYSIS IN LATIN AMERICA

Juan C Patrón Uriburu, Sergio Araujo, Abedrapo Mario, Jimenez Billy, Ramón Méndez, Gustavo Rossi, Nicolás Rotholtz, Romagnolo Luis, Nicolas Avellaneda, Armando Melani

Aim: The aim of this work was to compare lymph node (LN) yield in patients operated on for right colon cancer (RCC) using a laparoscopic approach between those receiving an intracorporeal (ICA) or extracorporeal anastomosis (ECA). Method: This is a retrospective multicentre study involving patients operated on for RCC in nine tertiary referral centres in Latin America during a 2-year period. The main comparative outcome between groups was the number of LNs harvested between groups. Results: The study included 416 patients, 261 (62.7%) in the ECA group and 155 (37.3%) in the ICA group. Patients in the ECA group were elderly (66 vs. 61 years, $p < 0.001$). Patients receiving an ICA achieved a significantly higher LN yield than those receiving an ECA (24 vs. 18, $p < 0.001$). This group also had a lower percentage of patients achieving a substandard LN yield (<12 LNs) (10% vs. 24.8%, $p = 0.001$) and more patients achieving a high number of harvested LNs (>32 LNs) (15.5% vs. 8.3%, $p = 0.039$). In the multivariate analysis, ICA was independently related to the primary outcome (LN yield) (OR 3.28, $p = 0.027$, 95% CI 1.14-9.38). Conclusion: In this retrospective study, patients operated on for RCC who received an ICA achieved a higher LN yield. Further studies are needed to reconfirm these findings, and also to find an explanation for these results.

## SERVICIO DENTOMAXILOFACIAL

**J CLIN MED. 2024 MAY 30;13(11):3228. DOI: 10.3390/JCM13113228.**

INVISIBLE, UNCONTROLLABLE, UNPREDICTABLE: ILLNESS EXPERIENCES IN WOMEN WITH SJÖGREN SYNDROME

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Background/Objectives: Sjögren's Syndrome (SS) is a chronic degenerative rheumatic disease. Because of its chronic nature, it significantly affects the quality of life of those who suffer from it. Methods: This qualitative study investigated disease experience among women suffering from SS to understand its impact on their overall well-being. In-depth interviews were conducted with 15 women who suffer from SS. Interviews were analyzed using the Grounded Theory methodology, using open, axial, and selective coding. Results: Three central phenomena of disease experience were identified: invisibility; uncontrollability; and unpredictability. Conclusions: SS disease experience has a strong imprint on emotional well-being and sense of self-control among middle-aged women. Understanding SS impacts on women's lives is important to better understand the disease and contribute to recognizing potential areas of management and social support in relevant windows of opportunity within the health-disease continuum.

## SERVICIO DERMATOLOGÍA

**REV MED CHIL. 2024 APR;152(4):514-517. DOI: 10.4067/S0034-98872024000400514.**

EPIDERMODISPLASIA VERRUCIFORME ADQUIRIDA EN UNA PACIENTE TRASPLANTADA RENAL. CASO CLÍNICO Y REVISIÓN DE LA LITERATURA

Vicente Orellana-Westermeyer, Claudia Quiroz Palominos, Laura Carreño Toro

Acquired epidermodysplasia verruciformis is a rare condition, secondary to a state of acquired immunosuppression and is characterized by a susceptibility to infection by human papillomavirus of the beta genus, which carries an increased risk of developing non-melanoma skin cancer. We report the case of a 39-year-old woman receiving a kidney transplant, treated with prednisone and tacrolimus, who after starting immunosuppressive therapy developed papules and warty plaques in the inguinal region. A skin biopsy was performed that was consistent with epidermodysplasia verruciformis, so it was decided to adjust immunosuppressive therapy to everolimus, which achieved a reduction in lesions. There are only 13 other cases of acquired epidermodysplasia verruciformis in kidney transplant recipients; to our knowledge this is the first case reported in Chile.

**J ULTRASOUND MED. 2024 SEP;43(9):1605-1610. DOI: 10.1002/JUM.16481.**

ULTRASOUND PATTERNS OF VITILIGO AT HIGH FREQUENCY AND ULTRA-HIGH FREQUENCY

Ximena Wortsman, Irene Araya, Maximiliano Maass, Pilar Valdes, Viviana Zemelman

Objectives: To detect ultrasonographic anatomical alterations in all the skin layers in patients with vitiligo. Methods: A prospective observational color Doppler ultrasound study was performed in nonsegmental face and/or neck vitiligo patients without a history of previous treatments. Two sites, a lesional area and a contralateral clinically healthy region, were ultrasonographically studied and compared in the same patient. All cases were studied in high-frequency (24 MHz) and ultra-high-frequency (70 MHz) ultrasound devices with the highest axial spatial resolution available in the market. Demographic data of the sample, ultrasound grayscale, and color Doppler features were recorded and analyzed. Results: Ten patients met the study criteria (60% females; mean age 49 years). All cases presented ultrasonographic undulation of the epidermis in the affected zones vs 50% in the healthy control regions, being more prominent in the vitiligo areas. Eighty percent demonstrated intense hypoechoic thin plaques in the upper dermis (subepidermal). All vitiligo areas presented thickening and hypoechogenicity of the regional hair follicles and/or pilosebaceous units. Ninety percent showed prominent sebaceous glands, and 20% demonstrated a hypoechoic cap surrounding the sebaceous glands in the lesional areas. Dermal hypervascularity was detected in 100% of the affected regions and 40% of the clinically healthy areas. Conclusion: Ultrasound can identify subclinical inflammatory cutaneous patterns in the epidermis, dermis, hair follicles, pilosebaceous units, and sebaceous glands in vitiligo. This noninvasive information can support early detection, monitoring, and research, including the clinical trials of drugs used to manage this devastating disease.

## SERVICIO DE EMERGENCIA

**EMERGENCIAS. 2024 JAN;36(1):33-40. DOI: 10.55633/S3ME/02.2023.**

EFECTO DEL FARMACÉUTICO CLÍNICO EN LAS RECONSULTAS A LOS 30 DÍAS POSALTA DEL SERVICIO DE URGENCIAS: ENSAYO CLÍNICO CONTROLADO

Matías F Martínez, Luis Herrada, Carolina Gutiérrez-Cáceres, Sandra Espinoza-Muñoz, Daniel Palma, Marcela Jirón

Objetivos. Determinar el efecto de la inclusión del farmacéutico clínico en el servicio de urgencias (SU) en las reconsultas durante 30 días posalta y la satisfacción de los pacientes. Métodos. Ensayo clínico controlado, aleatorizado, paralelo y pragmático,

realizado en el SU de un hospital universitario. Los pacientes reclutados fueron asignados aleatoriamente al grupo control (GC) que recibió la atención habitual o al grupo intervenido (GI) que recibió además la atención de un farmacéutico clínico, el cual se integró al equipo clínico para optimizar la selección, evaluación y educación farmacoterapéutica en el SU y al alta. El desenlace primario fue reconsultas no programadas 30 días posaltarelacionadas con la atención inicial al SU. Las diferencias entre grupos se analizaron por curvas de supervivencia de Kaplan-Meier y prueba de log-rank. La asociación entre intervención y tiempo al evento fue analizada mediante regresión multivariada de riesgos proporcionales de Cox y se expresó como hazard ratio ajustada (HRa). Resultados. Un total de 1.001 pacientes ingresaron al estudio (GI = 500 y GC = 501). Ambos grupos eran similares, predominaron las mujeres (61,5%), edad 51 años (RIC: 33-65). La intervención redujo significativamente las reconsultas a cualquier centro durante 30 días posalta comparado con GC [25 (6,3%) vs 66 (16,7%); HRa: 0,29 (IC 95%: 0,17-0,50)] y para el mismo centro [15 (3,0%) vs 32 (6,5%); HRa: 0,46 (IC 95%: 0,24-0,87)]. La satisfacción del usuario fue mayor en el GI que GC (87,2% vs 83,2%; p < 0,05). Conclusiones. La inclusión del farmacéutico clínico en un SU reduce sustancialmente las reconsultas durante 30 días posalta y mejora la satisfacción de los usuarios.

## CENTRO IMAGENOLOGÍA

### J CLIN MED. 2024 JUN 30;13(13):3866. DOI: 10.3390/JCM13133866.

IONIZING RADIATION-INDUCED OXIDATIVE STRESS IN COMPUTED TOMOGRAPHY-EFFECT OF VITAMIN C ON PREVENTION OF DNA DAMAGE: PREVIR-C RANDOMIZED CONTROLLED TRIAL STUDY PROTOCOL

Çamilo G Sotomayor, Camila González, Miki Soto, Nicolás Moreno-Bertero, Claudina Opazo, Baltasar Ramos, Gonzalo Espinoza, Álvaro Sanhueza, Gonzalo Cárdenas, Sebastián Yévenes, Jorge Díaz-Jara, José de Grazia, Marcia Manterola, Daniel Castro, Abraham A I J Gajardo, Ramón Rodrigo

Exposure to ionizing radiation (IR) is inevitable in various X-ray imaging examinations, with computed tomography (CT) being a major contributor to increased human radiation exposure. Ionizing radiation may cause structural damage to macromolecules, particularly DNA, mostly through an indirect pathway in diagnostic imaging. The indirect pathway primarily involves the generation of reactive oxygen species (ROS) due to water radiolysis induced by IR, leading to DNA damage, including double-strand breaks (DSB), which are highly cytotoxic. Antioxidants, substances that prevent oxidative damage, are proposed as potential radioprotective agents. This Study Protocol article presents the rationale for selecting vitamin C as a preventive measure against CT-associated IR-induced DNA damage, to be investigated in a randomized placebo-controlled trial, with a full in vivo design, using an oral easy-to-use schedule administration in the outpatient setting, for the single CT examination with the highest total global IR dose burden (contrast-enhanced abdomen and pelvis CT). The study also aims to explore the mediating role of oxidative stress, and it has been written in adherence to the Standard Protocol Items recommendations.

### J CLIN MED. 2024 SEP 4;13(17):5231. DOI: 10.3390/JCM13175231.

HUMAN-IN-THE-LOOP-A DEEP LEARNING STRATEGY IN COMBINATION WITH A PATIENT-SPECIFIC GAUSSIAN MIXTURE MODEL LEADS TO THE FAST CHARACTERIZATION OF VOLUMETRIC GROUND-GLASS OPACITY AND CONSOLIDATION IN THE COMPUTED TOMOGRAPHY SCANS OF COVID-19 PATIENTS

Constanza Vásquez-Venegas, Camilo G Sotomayor, Baltasar Ramos, Víctor Castañeda, Gonzalo Pereira, Guillermo Cabrera-Vives, Steffen Härtel

Background/Objectives: The accurate quantification of ground-glass opacities (GGOs) and consolidation volumes has prognostic value in COVID-19 patients. Nevertheless, the accurate manual quantification of the corresponding volumes remains a time-consuming task. Deep learning (DL) has demonstrated good performance in the segmentation of normal lung parenchyma and COVID-19 pneumonia. We introduce a Human-in-the-Loop (HITL) strategy for the segmentation of normal lung parenchyma and COVID-19 pneumonia that is both time efficient and quality effective. Furthermore, we propose a Gaussian Mixture Model (GMM) to classify GGO and consolidation based on a probabilistic characterization and case-sensitive thresholds. Methods: A total of 65 Computed Tomography (CT) scans from 64 patients, acquired between March 2020 and June 2021, were randomly selected. We pretrained a 3D-UNet with an international dataset and implemented a HITL strategy to refine the local dataset with delineations by teams of medical interns, radiology residents, and radiologists. Following each HITL cycle, 3D-UNet was re-trained until the Dice Similarity Coefficients (DSCs) reached the quality criteria set by radiologists (DSC = 0.95/0.8 for the normal lung parenchyma/COVID-19 pneumonia). For the probabilistic characterization, a Gaussian Mixture Model (GMM) was fitted to the Hounsfield Units (HUs) of voxels from the CT scans of patients with COVID-19 pneumonia on the assumption that two distinct populations were superimposed: one for GGO and one for consolidation. Results: Manual delineation of the normal lung parenchyma and COVID-19 pneumonia was performed by seven teams on 65 CT scans from 64 patients (56 ± 16 years old ($\mu \pm \sigma$), 46 males, 62 with reported symptoms). Automated lung/COVID-19 pneumonia segmentation with a DSC > 0.96/0.81 was achieved after three HITL cycles. The HITL strategy improved the DSC by 0.2 and 0.5 for the normal lung parenchyma and COVID-19 pneumonia segmentation, respectively. The distribution of the patient-specific thresholds derived from the GMM yielded a mean of -528.4 ± 99.5 HU ($\mu \pm \sigma$), which is below most of the reported fixed HU thresholds.

Conclusions: The HITL strategy allowed for fast and effective annotations, thereby enhancing the quality of segmentation for a local CT dataset. Probabilistic characterization of COVID-19 pneumonia by the GMM enabled patient-specific segmentation of GGO and consolidation. The combination of both approaches is essential to gain confidence in DL approaches in our local environment. The patient-specific probabilistic approach, when combined with the automatic quantification of COVID-19 imaging findings, enhances the understanding of GGO and consolidation during the course of the disease, with the potential to improve the accuracy of clinical predictions.

**EUR J NUTR. 2024 SEP;63(6):2357-2366. DOI: 10.1007/S00394-024-03426-7.**

VITAMIN C DEFICIENCY AFTER KIDNEY TRANSPLANTATION: A COHORT AND CROSS-SECTIONAL STUDY OF THE TRANSPLANTLINES BIOBANK

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Purpose: Vitamin C deficiency is associated with excess mortality in kidney transplant recipients (KTR). We aim to evaluate plasma vitamin C status at different post-transplantation moments and assess the main characteristics associated with vitamin C deficiency in KTR. Methods: Plasma vitamin C was assessed in 598 KTR at 3-, 6-, 12-, 24-, and 60-months post-transplantation, 374 late KTR with a functioning graft ≥ 1 year, and 395 potential donors. Vitamin C deficiency was defined as plasma vitamin C ≤ 28 µmol/L. Diet was assessed by a 177-item food frequency questionnaire. Data on vitamin C-containing supplements use were extracted from patient records and verified with the patients. Results: Vitamin C deficiency ranged from 46% (6-months post-transplantation) to 30% (≥ 1 year post-transplantation). At all time points, KTR had lower plasma vitamin C than potential donors (30-41 µmol/L vs 58 µmol/L). In cross-sectional analyses of the 953 KTR at their first visit ≥ 12 months after transplantation (55 ± 14 years, 62% male, eGFR 55 ± 19 mL/min/1.73 m2), the characteristics with the strongest association with vitamin C deficiency were diabetes and smoking (OR 2.67 [95% CI 1.84-3.87] and OR 1.84 [95% CI 1.16-2.91], respectively). Dietary vitamin C intake and vitamin C supplementation were associated with lower odds (OR per 100 mg/day 0.38, 95% CI 0.24-0.61 and OR 0.21, 95% CI 0.09-0.44, respectively). Conclusion: Vitamin C deficiency is frequent among KTR regardless of the time after transplantation, especially among those with diabetes and active smokers. The prevalence of vitamin C deficiency was lower among KTR with higher vitamin C intake, both dietary and supplemented. Further research is warranted to assess whether correcting this modifiable risk factor could improve survival in KTR.

## LABORATORIO CLÍNICO

**INT J MOL SCI. 2024 JUN 17;25(12):6657. DOI: 10.3390/IJMS25126657.**

DISTRIBUTION OF PAPA AND PAPG VARIANTS AMONG ESCHERICHIA COLI GENOTYPES: ASSOCIATION WITH MAJOR EXTRAINTESTINAL PATHOGENIC LINEAGES

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The pyelonephritis-associated fimbria (P fimbria) is one of the most recognized adhesion determinants of extraintestinal pathogenic Escherichia coli strains (ExPECs). Twelve variants have been described for the gene encoding the P fimbria major structural subunit PapA and three variants for the gene encoding the adhesin subunit PapG. However, their distribution among the ExPEC diversity has not been comprehensively addressed. A complete landscape of that distribution might be valuable for delineating basic studies about the pathogenicity mechanisms of ExPECs and following up on the evolution of ExPEC lineages, particularly those most epidemiologically relevant. Therefore, we performed a massive descriptive study to detect the papA and papG variants along different E. coli genotypes represented by genomic sequences contained in the NCBI Assembly Refseq database. The most common papA variants were F11, F10, F48, F16, F12, and F7-2, which were found in significant association with the most relevant ExPEC genotypes, the phylogroups B2 and D, and the sequence types ST95, ST131, ST127, ST69, ST12, and ST73. On the other hand, the papGII variant was by far the most common followed by papGIII, and both were also found to have a significant association with common ExPEC genotypes. We noticed the presence of genomes, mainly belonging to the sequence type ST12, harboring two or three papA variants and two papG variants. Furthermore, the most common papA and papG variants were also detected in records representing strains isolated from humans and animals such as poultry, bovine, and dogs, supporting previous hypotheses of potential cross-transmission. Finally, we characterized a set of 17 genomes from Chilean uropathogenic E. coli strains and found that ST12 and ST73 were the predominant sequence types. Variants F7-1, F7-2, F8, F9, F11, F13, F14, F16, and F48 were detected for papA, and papGII and papGIII variants were detected for papG. Significant associations with the sequence types observed in the analysis of genomes contained in the NCBI Assembly Refseq database were also found in this collection in 16 of 19 cases for papA variants and 7 of 9 cases for the papG variants. This comprehensive characterization might support future basic studies about P fimbria-mediated ExPEC adherence and future typing or epidemiological studies to monitor the evolution of ExPECs producing P fimbria.

**REV CHILENA INFECTOL 2024; 41 (5): 561-582 DOI: 10.4067/S0716-10182024000500156**

GUÍA DE PRÁCTICA CLÍNICA PARA EL TRATAMIENTO DE INFECCIONES POR BACILOS GRAM NEGATIVOS DEL COMITÉ AMPLIADO DE ANTIMICROBIANOS DE LA SOCIEDAD CHILENA DE INFECTOLOGÍA

Daniela Pavez, Catalina Gutiérrez, Loreto Rojas, Mirta Acuña, Dona Benadof, Regina Pérez, Ruth Rosales, Claudio González1, Francisco Silva, Felipe Bravo, José Miguel Arancibia, Jorge Amadory Luis Bavestrello

Bacterial resistance constitutes a growing public health problem worldwide, causing 5 million deaths and projecting to rise to 10 million by 2050, unless a global response is established to contain its advance. It is associated with greater morbidity and mortality and economic burden and occurs more frequently in hospital environments, especially in critical units, where Gram-negative bacilli are the most frequently isolated. The objective of this article is to provide evidence-based recommendations on the clinical management of Gram-negative bacterial infections.

# DEPARTAMENTO DE MEDICINA

## BANCO DE SANGRE

**VACCINES (BASEL). 2024 MAR 27;12(4):357. DOI: 10.3390/VACCINES12040357.**

LONG-TERM SURVIVAL AND IMMUNE RESPONSE DYNAMICS IN MELANOMA PATIENTS UNDERGOING TAPCELLS-BASED VACCINATION THERAPY

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Cancer vaccines present a promising avenue for treating immune checkpoint blockers (ICBs)-refractory patients, fostering immune responses to modulate the tumor microenvironment. We revisit a phase I/II trial using Tumor Antigen-Presenting Cells (TAPCells) (NCT06152367), an autologous antigen-presenting cell vaccine loaded with heat-shocked allogeneic melanoma cell lysates. Initial findings showcased TAPCells inducing lysate-specific delayed-type hypersensitivity (DTH) reactions, correlating with prolonged survival. Here, we extend our analysis over 15 years, categorizing patients into short-term (<36 months) and long-term (≥36 months) survivors, exploring novel associations between clinical outcomes and demographic, genetic, and immunologic parameters. Notably, DTHpos patients exhibit a 53.1% three-year survival compared to 16.1% in DTHneg patients. Extended remissions are observed in long-term survivors, particularly DTHpos/M1cneg patients. Younger age, stage III disease, and moderate immune events also benefit short-term survivors. Immunomarkers like increased C-type lectin domain family 2 member D on CD4+ T cells and elevated interleukin-17A were detected in long-term survivors. In contrast, toll-like receptor-4 D229G polymorphism and reduced CD32 on B cells are associated with reduced survival. TAPCells achieved stable long remissions in 35.2% of patients, especially M1cneg/DTHpos cases. Conclusions: Our study underscores the potential of vaccine-induced immune responses in melanoma, emphasizing the identification of emerging biological markers and clinical parameters for predicting long-term remission.

## ENDOCRINOLOGÍA

**J ENDOCRINOL INVEST. 2024 APR;47(4):903-911. DOI: 10.1007/S40618-023-02207-Z.**

BODY WEIGHT VARIATION IS NOT AN INDEPENDENT FACTOR IN THE DETERMINATION OF FUNCTIONAL HYPOTHALAMIC AMENORRHEA IN ANOREXIA NERVOSA

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Objective: Functional hypothalamic amenorrhea (FHA) is one of the foremost manifestations in anorexia nervosa (AN), but a subset of patients have menses despite marked weight loss and underweight. The aim of our study was to investigate parameters potentially influencing FHA in AN. Design and methods: In this observational retrospective study, we selected 114 female patients with AN who completed a 12 months semi-residential rehabilitation program and a subsequent 12 months outpatient follow-up. We divided our sample into three groups: "Group 0" patients who experienced FHA and recovered their menses, "Group 1" persistent FHA, "Group 2" never experienced FHA, and looked for clinical and hormonal correlations. Results: At the enrollment, the BMI was higher in Group 2 than in Group 1 ($p = 0.0202$), but the last follow-up weight was higher in Group 1 ($p < 0.0001$) despite persistent amenorrhea. At logistic regression, the higher BMI at which patients experienced amenorrhea was the main prediction factor for persistent FHA. Notwithstanding comparable leptin levels at admission, they improved significantly at discharge only in Groups 0 and 2 ($p = 0.0054$ and $p = 0.0104$, respectively). FT3 at admission was significantly higher in Group 2 than in Group 0 ($p = 0.0249$). Conclusions: FHA does not correlate strictly with body weight variations in AN patients, indicating a multifactorial origin, likely including an individual predisposition. Higher FT3 levels identify patients who continue having menses at extremely low BMI. AN patients with persistent FHA constitute a subgroup in whom estroprogestins should be considered after significant weight recovery to prevent prolonged tissue hypoestrogenism.

## GASTROENTEROLOGÍA

### HELICOBACTER. 2024 JAN-FEB;29(1):E13052. DOI: 10.1111/HEL.13052.

ERADICATION RATE AND ADHERENCE WITH HIGH-DOSE AMOXICILLIN AND PROTON PUMP INHIBITOR AS FIRST-LINE TREATMENT FOR HELICOBACTER PYLORI INFECTION: EXPERIENCE FROM UNIVERSITY HOSPITAL IN CHILE

Christian von Muhlenbrock, Andrea Cordova, Paulina Nuñez, Nicole Pacheco, Karin Herrera, Rodrigo Quera

Introduction: In Chile, more than 70% of adults are infected by Helicobacter pylori. Clarithromycin should not be used in any regimen if there is >15% resistance to this antibiotic, being greater than 26% in our population. In this scenario, the effectiveness of triple therapy (proton pump inhibitor [PPI], clarithromycin, amoxicillin) was only 63.8%. Aim: To evaluate the eradication rate and safety of dual therapy (esomeprazole and amoxicillin) in high doses, through a prospective, observational, and descriptive study. Methods: Patients with a positive urease test obtained in an upper digestive endoscopy were included. Any other previous H. pylori eradication regimen were excluded. All patients were treated with esomeprazole 40 mg three times a day and amoxicillin 750 mg four times a day for 14 days. The eradication rate of the dual therapy was evaluated with the H. pylori stool antigen test (the Pylori-Strip® test used) 6 weeks after completing the eradication treatment and with at least 14 days without PPI, being a negative result, confirmation of the effectiveness of this regimen. Results: Of 122 patients, 106 had a negative H. pylori antigen in stool; The intention-to-treat and per protocol analysis, the eradication rates were 91.8% [95% CI: 87%-97%] and 94% [95% CI: 90%-98%], respectively. Four patients discontinued treatment due to adverse effects. Smoking and adherence to treatment were associated with eradication rate. Conclusions: In this cohort of patients with H. pylori infection, high-dose dual therapy has a high eradication rate and good adherence, raising the possibility that it could be used as first-line therapy in our country. Studies with a larger number of patients should confirm these results.

### J HEPATOL. 2024 MAR;80(3):409-418. DOI: 10.1016/J.JHEP.2023.11.006.

ASSOCIATION BETWEEN PUBLIC HEALTH POLICIES ON ALCOHOL AND WORLDWIDE CANCER, LIVER DISEASE AND CARDIOVASCULAR DISEASE OUTCOMES

Luis Antonio Díaz, Eduardo Fuentes-López, Francisco Idalsoaga, Gustavo Ayares, Oscar Corsi, Jorge Arnold, Macarena Cannistra, Danae Vio, Andrea Márquez-Lomas, Carolina Ramirez-Cadiz, María Paz Medel, María Hernandez-Tejero, Catterina Ferreccio, Mariana Lazo, Juan Pablo Roblero y otros.

Background & aims: The long-term impact of alcohol-related public health policies (PHPs) on disease burden is unclear. We aimed to assess the association between alcohol-related PHPs and alcohol-related health consequences. Methods: We conducted an ecological multi-national study including 169 countries. We collected data on alcohol-related PHPs from the WHO Global Information System of Alcohol and Health 2010. Data on alcohol-related health consequences between 2010-2019 were obtained from the Global Burden of Disease database. We classified PHPs into five items, including criteria for low, moderate, and strong PHP establishment. We estimated an alcohol preparedness index (API) using multiple correspondence analysis (0 lowest and 100 highest establishment). We estimated an incidence rate ratio (IRR) for outcomes according to API using adjusted multilevel generalized linear models with a Poisson family distribution. Results: The median API in the 169 countries was 54 [IQR 34.9-76.8]. The API was inversely associated with alcohol use disorder (AUD) prevalence (IRR 0.13; 95% CI 0.03-0.60; p = 0.010), alcohol-associated liver disease (ALD) mortality (IRR 0.14; 95% CI 0.03-0.79; p = 0.025), mortality due to neoplasms (IRR 0.09; 95% CI 0.02-0.40; p = 0.002), alcohol-attributable hepatocellular carcinoma (HCC) (IRR 0.13; 95% CI 0.02-0.65; p = 0.014), and cardiovascular diseases (IRR 0.09; 95% CI 0.02-0.41; p = 0.002). The highest associations were observed in the Americas, Africa, and Europe. These associations became stronger over time, and AUD prevalence was significantly lower after 2 years, while ALD mortality and alcohol-attributable HCC incidence decreased after 4 and 8 years from baseline API assessment, respectively (p <0.05). Conclusions: The API is a valuable instrument to quantify the robustness of alcohol-related PHP establishment. Lower AUD prevalence and lower mortality related to ALD, neoplasms, alcohol-attributable HCC, and cardiovascular diseases were observed in countries with a higher API. Our results encourage the development and strengthening of alcohol-related policies worldwide. Impact and implications: We first developed an alcohol preparedness index, an instrument to assess the existence of alcohol-related public policies for each country. We then evaluated the long-term association of the country's alcohol preparedness index in 2010 with the burden of chronic liver disease, hepatocellular carcinoma, other neoplasms, and cardiovascular disease. The strengthening of alcohol-related public health policies could impact long-term mortality rates from cardiovascular disease, neoplasms, and liver disease. These conditions are the main contributors to the global burden of disease related to alcohol use. Over time, this association has not only persisted but also grown stronger. Our results expand the preliminary evidence regarding the importance of public health policies in controlling alcohol-related health consequences.

### REV MED CHIL. 2024 JUN;152(6):730-735. DOI: 10.4067/S0034-98872024000600730.

¿GRANULOMAS EN BIOPSIAS DE INTESTINO? TUBERCULOSIS INTESTINAL SIMULANDO UNA ENFERMEDAD DE CROHN. A PROPÓSITO DE UN CASO

Francisca Carvajal, Pamela Gil, Edith Pérez de Arce, Luis Carlos Gil

Intestinal tuberculosis is a bacterial infection that represents 10% of extrapulmonary tuberculosis. It is known as the great

mimicker due to its clinical presentation similar to other diseases such as Crohn's Disease or Neoplastic Intestinal Disease. Its diagnosis is complex, given the paucibacillary characteristic of the disease. We present the case of a 57-year-old patient with an initial diagnosis of Crohn's Disease, starting immunosuppressive therapy. After no response to the initial therapy and with a new endoscopic and anatomopathological study, Intestinal Tuberculosis was concluded, which after starting therapy evolved favorably.

**ANN HEPATOL. 2024 JUL-AUG;29(4):101511. DOI: 10.1016/J.AOHEP.2024.101511.**

CORONARY ARTERY DISEASE AS A RISK FACTOR FOR METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AND LIVER FIBROSIS

Luis Vega, Daniela Simian, Abraham I Gajardo, Marcelo Salinas, Andrea Urra, Máximo Cattaneo, Rosario Pino, Juan P Roblero, Álvaro Urzúa, Katherine Rojas, Jaime Poniachik

Introduction and objectives: Patients with metabolic dysfunction-associated steatotic liver disease (MASLD) are at an increased cardiovascular risk. On the contrary, non-alcoholic fatty liver disease (NAFLD) is highly prevalent in patients with coronary heart disease (CHD). However, it is not known whether patients with significant CHD show a higher frequency of liver fibrosis. This study aimed to determine the frequency of MASLD and liver fibrosis in patients with CHD and to assess whether coronary stenosis is significantly associated with MASLD and fibrosis. Patients and methods: This observational and analytical study included adult patients without any known liver disease who underwent coronary angiography for suspected coronary artery disease (Jul 2021-Jul 2022). The presence of significant CHD (> 50% stenosis of at least one coronary artery) was determined. Liver elastography (FibroScan®) was performed up to 6 months after the coronary angiographic study to determine liver fibrosis, a measurement of liver stiffness (> 6.5 Kpa). Fisher's test, Mann-Whitney U test, and logistic regression models were used ($p < 0.05$). Results: The study included 113 patients (76% men, average age: 63 years [standard deviation: 9.9]), of which 72% presented with significant CHD. The prevalence rate of MASLD was 52%. Liver fibrosis was present in 12% of the patients and all patients in the significant CHD group ($p = 0.007$). An increase in the number of vessels with significant CHD increased the probability of liver fibrosis (odds ratio, 1.79; 95% confidence interval, 1.06-3.04; $p = 0.029$). Conclusions: MASLD is highly prevalent in patients with significant CHD but without known liver damage. These data suggest that MASLD and liver fibrosis should be investigated in patients with CHD. The presence of confounding variables, especially the presence of type 2 diabetes mellitus, should be evaluated in further studies.

**GASTROENTEROL HEPATOL. 2024 JUN-JUL;47(6):562-573. DOI: 10.1016/J.GASTROHEP.2023.09.006**

EL CONSUMO ACTIVO DE ALCOHOL SE ASOCIA CON INSUFICIENCIA HEPÁTICA AGUDA A CRÓNICA EN PACIENTES HISPANOS

Francisco Idalsoaga, Luis Antonio Díaz, Eduardo Fuentes-López, Gustavo Ayares, Francisco Valenzuela, Victor Meza, Franco Manzur, Joaquín Sotomayor, Hernán Rodriguez, Franco Chianale, Sofía Villagrán, Maximiliano Schalper, Pablo Villafranca, Maria Jesus Veliz, Paz Uribe, Maximiliano Puebla, Pablo Bustamante, Herman Aguirre, Javiera Busquets, Juan Pablo Roblero, Gabriel Mezzano, Maria Hernandez-Tejero, Marco Arrese, Juan Pablo Arab

Background: Acute-on-chronic liver failure (ACLF) is a severe clinical entity associated with elevated short-term mortality. We aimed to characterize patients with decompensated cirrhosis according to presence of ACLF, their association with active alcohol intake, and long-term survival in Latin America. Methods: Retrospective cohort study of decompensated cirrhotic in three Chilean university centers (2017-2019). ACLF was diagnosed according EASL-CLIF criteria. We assessed survival using competing-risk and time-to-event analyses. We evaluated the time to death using accelerated failure time (AFT) models. Results: We included 320 patients, median age of 65.3±11.7 years old, and 48.4% were women. 92 (28.7%) patients met ACLF criteria (ACLF-1: 29.3%, ACLF-2: 27.1%, and ACLF-3: 43.4%). The most common precipitants were infections (39.1%), and the leading organ failure was kidney (59.8%). Active alcohol consumption was frequent (27.7%), even in patients with a prior diagnosis of non-alcoholic fatty liver disease (NAFLD) (16.2%). Ninety-two (28.7%) patients had ACLF (ACLF-1: 8.4%, ACLF-2: 7.8%, and ACLF-3: 12.5%). ACLF patients had a higher MELD-Na score at admission (27 [22-31] versus 16 [12-21], $p<0.0001$), a higher frequency of alcohol-associated liver disease (36.7% versus 24.9%, $p=0.039$), and a more frequent active alcohol intake (37.2% versus 23.8%, $p=0.019$). In a multivariate model, ACLF was associated with higher mortality (subdistribution hazard ratio 1.735, 95%CI: 1.153-2.609; $p<0.008$). In the AFT models, the presence of ACLF during hospitalization correlated with a shorter time to death: ACLF-1 shortens the time to death by 4.7 times (time ratio [TR] 0.214, 95%CI: 0.075-0.615; $p<0.004$), ACLF-2 by 4.4 times (TR 0.224, 95%CI: 0.070-0.713; $p<0.011$), and ACLF-3 by 37 times (TR 0.027, 95%CI: 0.006-0.129; $p<0.001$). Conclusions: Patients with decompensated cirrhosis and ACLF exhibited a high frequency ofactive alcohol consumption. Patients with ACLF showed higher mortality and shorter time todeath than those without ACLF.

**DIGES DIS SCI. 2024 JAN;69(1):191-199. DOI: 10.1007/S10620-023-08151-5.**

DIFFUSE GASTROINTESTINAL MOTOR COMPROMISE IN PATIENTS WITH SCLERODERMA: UTILITY OF MINIMALLY INVASIVE TECHNIQUES

Christian von Mühlenbrock, Ana María Madrid, Claudia Defilippi, Carlos Defilippi, Lilian Soto

Background: Scleroderma is a systemic inflammatory disorder that can compromise the gastrointestinal tract in up to 90% of patients. Aim: The purpose of this work is to characterize esophageal, gastric, and intestinal compromise in patients with

scleroderma by means of minimally invasive methods and its association with symptoms and severity of their rheumatological condition. Methods: Patients with systemic sclerosis were recruited according to the criteria of the American College of Rheumatology. The study of digestive involvement was carried out on four consecutive days: esophageal manometry was performed on the first day, intestinal manometry on the second day, surface electrogastrography on the third, and hydrogen breath test on the fourth. The Mann-Whitney test was used for quantitative variables and the chi-squared test for categorical variables ($p < 0.05$). Results: A total of 30 patients were included, with an average age of 52.7 years and 93% women. Average disease evolution duration was 6.5 years, 70% with limited variety. Rodnan averaged 12 points, being higher in the diffuse variety. The main symptom was heartburn, followed by abdominal distension, with no differences between subtypes except for diffuse nausea; 80% had intestinal manometric compromise, 76% esophageal manometric compromise, and 30% electrogastrographic compromise. Bacterial overgrowth was evidenced in two-thirds (66%) of the patients, and 23% of the patients had simultaneous esophageal, gastric, and intestinal involvement, which correlated with greater skin involvement but not with gastrointestinal symptoms. Conclusions: Gastrointestinal involvement in patients with scleroderma is frequent and is observed regardless of the symptoms and clinical characteristics of the latter, except for skin involvement.

**REV GASTROENTEROL MEX (ENGL ED). 2024 OCT-DEC;89(4):513-520. DOI: 10.1016/J.RGMXEN.2024.03.004.**

FECAL MICROBIOTA TRANSPLANTATION THROUGH COLONOSCOPY IN THE TREATMENT OF RECURRENT CLOSTRIDIOIDES DIFFICILE: EXPERIENCE AT A UNIVERSITY CENTER

R Quera, P Nuñez, C von Muhlenbrock, R Espinoza

Introduction: The majority of cases of Clostridioides difficile infection (CDI) respond to antibiotic treatment. Fecal microbiota transplantation (FMT) has been accepted as an effective treatment in cases of recurrent CDI. Aim: Our aim was to describe the clinical results of FMT performed for the treatment of recurrent CDI. Material and methods: The study was conducted on patients with recurrent CDI treated with FMT through colonoscopy, within the time frame of January 2021 and December 2023. Demographic and clinical data were collected, including pre-FMT treatment data, the FMT success rate, and clinical progression during follow-up. Telephone surveys were carried out to evaluate satisfaction. Results: Thirteen patients with a mean age of 55 years underwent FMT (including 7 patients above 65 years of age and one pregnant woman). Patients presented with a median of 3 previous episodes of CDI (range 2-4). The median time interval from first episode of CDI to FMT was 4 months (range 3-10). The effectiveness of a single FMT session was 100%. During post-FMT follow-up (median of 11 months, range 3-32), 3 patients have presented with a new CDI episode, and a successful second FMT was performed on 2 of them. No adverse events were registered, and all patients had a positive perception of FMT. Conclusions: In the present study, despite its small size, FMT through colonoscopy was shown to be a safe, effective, and lasting therapy in cases of recurrent CDI, concurring with results from larger studies.

**J GASTROINTESTIN LIVER DIS. 2024 DEC 28;33(4):535-541. DOI: 10.15403/JGLD-5942.**

A HISTORY OF THE DISCOVERY OF HELICOBACTER PYLORI, WITH SPECIAL REFERENCE TO GIULIO BIZZOZERO

Raul Jesus Lazarate Cuba, Eamonn Martin Quigley

Helicobacter pylori is a microorganism that is highly prevalent in mankind and closely linked to several gastroduodenal disorders. Though Helicobacter pylori was introduced to the scientific community in 1983 by Robin Warren and Barry Marshall, a closely related Helicobacter species had been described one hundred years earlier by the Italian pathologist Giulio Bizzozero in the canine stomach. In this review we analyze the different steps involved in the discovery of Helicobacter and provide a biography of the pioneer Giulio Bizzozero.

**SCI REP. 2024 APR 17;14(1):8817. DOI: 10.1038/S41598-024-58920-Z.**

BARRIERS TO THE USE OF TESTS FOR EARLY DETECTION OF COLORECTAL CANCER IN CHILE

Gabriela Alfaro, Zoltan Berger, Susana Mondschein, Felipe Subiabre, Natalia Yankovic

This study aimed to assess the use of colorectal cancer (CRC) tests for prevention and early detection, alongside exploring the associated barriers to these tests. A stratified national survey was conducted in Chile, involving 1893 respondents (with a 2.3% error margin and 95% confidence interval). Logistic and multinomial regression analyses were employed to examine variations in test utilization likelihood and barrier. We found that the key determinants for undergoing CRC tests included age, health status, possession of private health insurance, and attainment of postgraduate education. Notably, 18% and 29% of respondents covered by public and private insurance, respectively, cited personal prevention as the primary motivation for test uptake. The principal obstacle identified was lack of knowledge, mentioned by 65% of respondents, while 29% and 19% of the publicly and privately insured respectively highlighted lack of access as a barrier. The results of this study provide valuable insights into factors influencing CRC screening, aiming to inform public health policies for expanding national coverage beyond diagnosis and treatment to encompass preventive measures.

**HEPATOLOGY. 2024 MAY 1;79(5):1019-1032. DOI: 10.1097/HEP.0000000000000653.**

DETERMINANTS OF CLINICAL RESPONSE TO EMPIRICAL ANTIBIOTIC TREATMENT IN PATIENTS WITH CIRRHOSIS AND BACTERIAL AND FUNGAL INFECTIONS-RESULTS FROM THE ICA "GLOBAL STUDY" (EABCIR-GLOBAL STUDY)

Rakhi Maiwall, Salvatore Piano, Virendra Singh, Paolo Caraceni, Carlo Alessandria, Javier Fernandez, Elza Cotrim Soares, Dong Joon Kim, Sung Eun Kim, Monica Marino, Julio Vorobioff, Rita de Cassia Ribeiro Barea, Manuela Merli, Laure Elkrief, Victor Vargas, Aleksander Krag, Shivaram Prasad Singh, Laurentius Adrianto Lesmana, Claudio Toledo, Sebastian Marciano, Xavier Verhelst, Florence Wong, Nicolas Intagliata, Liane Rabinowich, Luis Colombato, Sang Gyune Kim, Alexander Gerbes, Francois Durand, Juan Pablo Roblero *et al.*

Background: The administration of an appropriate empirical antibiotic treatment is essential in cirrhosis and severe bacterial infections. We aimed to investigate the predictors of clinical response of empirical antibiotic treatment in a prospective cohort of patients with cirrhosis and bacterial and fungal infections included in the International Club of Ascites "Global Study." Methods: Patients hospitalized with cirrhosis and bacterial/fungal infection were prospectively enrolled at 46 centers. Clinical response to antibiotic treatment was defined according to changes in markers of infection/inflammation, vital signs, improvement of organ failure, and results of cultures. Results: From October 2015 to September 2016, 1302 patients were included at 46 centers. A clinical response was achieved in only 61% of cases. Independent predictors of lack of clinical response to empirical treatment were C-reactive protein (OR = 1.16; 95% CI = 1.02-1.31), blood leukocyte count (OR = 1.39;95% CI = 1.09-1.77), serum albumin (OR = 0.70; 95% CI = 0.55-0.88), nosocomial infections (OR = 1.96; 95% CI = 1.20-2.38), pneumonia (OR = 1.75; 95% CI = 1.22-2.53), and ineffective treatment according to antibiotic susceptibility test (OR = 5.32; 95% CI = 3.47-8.57). Patients with a lack of clinical response to first-line antibiotic treatment had a significantly lower resolution rate of infections (55% vs. 96%; $p < 0.001$), a higher incidence of second infections (29% vs. 15%; $p < 0.001$), shock (35% vs. 7%; $p < 0.001$) and new organ failures (52% vs. 19 %; $p < 0.001$) than responders. Clinical response to empirical treatment was an independent predictor of 28-day survival (subdistribution = 0.20; 95% CI = 0.14-0.27). Conclusions: Four out of 10 patients with cirrhosis do not respond to the first-line antibiotic therapy, leading to lower resolution of infections and higher mortality. Broader-spectrum antibiotics and strategies targeting systemic inflammation may improve prognosis in patients with a high degree of inflammation, low serum albumin levels, and severe liver impairment.

**REV CHILENA INFECTOL 2024; 41 (3): 453-456 DOI: 10.4067/S0716-10182024000300132**

PRESENCIA DE ANTICUERPOS ANTI VIRUS HEPATITIS E EN PACIENTES CON INFECCIÓN AGUDA POR VIRUS HEPATITIS A

Natalia Covarrubias, Julio Miranda, Caterina Chesta, Mauricio Venegas y Carmen Hurtado

Los agentes virales de transmisión entérica, como el virus de la hepatitis A (VHA) y el virus de la hepatitis E (VHE), constituyen causas frecuentes de hepatitis viral aguda en los países en desarrollo. Dada la similitud en las vías de transmisión, la coinfección podría ser común. Se analizaron 100 muestras con resultados positivos para IgM anti-VHA de la seroteca del Hospital Clínico de la Universidad de Chile, entre el 2016 y el 2018, determinando la presencia de IgM e IgG anti-VHE por método automatizado ELFA, mini VIDAS® (BioMérieux SA). Se identificaron 7 muestras positivas (7%) para IgM anti-VHE, 6 fueron hombres, con una mediana de edad de 20 años. La IgG anti-VHE fue detectada en 11 pacientes (11%) y en solo 3 casos existió presencia concomitante de IgM e IgG anti-VHE. Se observó una disminución de la prevalencia de la coinfección de VHA y VHE con respecto a datos previos, sin embargo, aún está presente. Estos resultados son relevantes para la vigilancia epidemiológica, destacando la importancia de la búsqueda activa del VHE en los cuadros de hepatitis aguda.

## LABORATORIO INMUNOGASTROENTEROLOGÍA

**INT J MOL SCI. 2024 APR 16;25(8):4387. DOI: 10.3390/IJMS25084387.**

ALTERATION OF GUT MICROBIOTA COMPOSITION IN THE PROGRESSION OF LIVER DAMAGE IN PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is a complex disorder whose prevalence is rapidly growing in South America. The disturbances in the microbiota-gut-liver axis impact the liver damaging processes toward fibrosis. Gut microbiota status is shaped by dietary and lifestyle factors, depending on geographic location. We aimed to identify microbial signatures in a group of Chilean MASLD patients. Forty subjects were recruited, including healthy controls (HCs), overweight/obese subjects (Ow/Ob), patients with MASLD without fibrosis (MASLD/F-), and MASLD with fibrosis (MASLD/F+). Both MASLD and fibrosis were detected through elastography and/or biopsy, and fecal microbiota were analyzed through deep sequencing. Despite no differences in $\alpha$- and $\beta$-diversity among all groups, a higher abundance of Bilophila and a lower presence of Defluviitaleaceae, Lachnospiraceae ND3007, and Coprobacter was found in MASLD/F- and MASLD/F+, compared to HC. Ruminococcaceae UCG-013

and Sellimonas were more abundant in MASLD/F+ than in Ow/Ob; both significantly differed between MASLD/F- and MASLD/F+, compared to HC. Significant positive correlations were observed between liver stiffness and Bifidobacterium, Prevotella, Sarcina, and Acidaminococcus abundance. Our results show that MASLD is associated with changes in bacterial taxa that are known to be involved in bile acid metabolism and SCFA production, with some of them being more specifically linked to fibrosis.

**FRONT MED (LAUSANNE). 2024 MAY 24:11:1376148. DOI: 10.3389/FMED.2024.1376148. ECOLLECTION 2024.**

SMALL INTESTINAL BACTERIAL OVERGROWTH IN OBESE PATIENTS WITH BIOPSY-CONFIRMED METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE: A CROSS-SECTIONAL STUDY

Nicolás Ortiz-López, Ana María Madrid, Larissa Aleman, Alejandra Zazueta, Gladys Smok, Lucía Valenzuela-Pérez, Jaime Poniachik, Caroll J Beltrán

Background/aims: The metabolic dysfunction-associated steatotic liver disease (MASLD) and obesity are frequent comorbidities with a high prevalence worldwide. Their pathogenesis are multifactorial, including intestinal dysbiosis. The role of small intestinal bacterial overgrowth (SIBO) in MASLD progression in obese patients remains unknown. We aimed to determine the association between SIBO and the severity of MASLD in obese patients. Methods: An observational and cross-sectional study was conducted in obese patients, diagnosed with or without MASLD by liver biopsy. Metabolic dysfunction-associated steatotic liver (MASL), metabolic dysfunction-associated steatohepatitis without fibrosis (MASH-NF), MASH with fibrosis (MASH-F), or without MASLD (control subjects, CS) were identified by presence of steatosis, portal and lobular inflammation, and fibrosis. SIBO was determined by standardized lactulose breath tests. Results: A total of 59 patients with MASLD, 16 with MASL, 20 with MASH-NF, 23 with MASH-F, and 14 CS were recruited. Higher percentages of SIBO were observed in MASLD patients (44.2%) compared to CS (14.2%; $p = 0.0363$). Interestingly, MASH-F showed higher percentages of SIBO (65.2%) in comparison to non-fibrotic MASLD (33.3%; $p = 0.0165$). The presence of SIBO was not correlated with the level of hepatic steatosis in MASLD patients. Conclusions: A positive correlation between MASLD and SIBO in obese patients was principally explained by the presence of liver fibrosis. Our findings suggest a pathogenic role of intestinal dysbiosis in the progression of MASLD. Future research will elucidate the underlying mechanisms of SIBO in MASLD advancement.

## GENÉTICA

**EPIGENOMICS. 2024 MAR;16(6):419-426. DOI: 10.2217/EPI-2023-0357.**

NEURAL TUBE DEFECTS AND EPIGENETICS: ROLE OF HISTONE POST-TRANSLATIONAL HISTONE MODIFICATIONS

Rosa Pardo V, Richard H Finnell, M Elizabeth Ross, Pablo Alarcón, José Suazo

Neural tube defects (NTDs) are the most common congenital anomalies of the CNS. It is widely appreciated that both genetic and environmental factors contribute to their etiology. The inability to ascribe clear genetic patterns of inheritance to various NTD phenotypes suggests it is possible that epigenetic mechanisms are involved in the etiology of NTDs. In this context, the contribution of DNA methylation as an underlying contributing factor to the etiology of NTDs has been extensively reviewed. Here, an updated accounting of the evidence linking post-translational histone modifications to these birth defects, relying heavily upon studies in humans, and the possible molecular implications inferred from reports based on cellular and animal models, are presented.

**ANDES PEDIATR. 2024 APR;95(2):196-201. DOI: 10.32641/ANDESPEDIATR.V95I2.4820.**

SÍNDROME DE ALAGILLE POR DELECIÓN DEL GEN JAG1. UNA CAUSA POCO FRECUENTE

Diana Avila-Jaque, Catherine Díaz, Rosa Pardo

Alagille syndrome (ALGS) is an autosomal dominant, multisystem disorder that typically presents with cholestasis, cardiac, ocular, skeletal, vascular and renal abnormalities, and distinct facial features. Most cases are due to variants in the JAG1 gene, with only a small percentage involving a complete gene deletion. Objective: to contribute to the phenotype delineation and interpretation of a microdeletion not previously described in the literature on chromosome 20. Clinical case: A 4-month-old female patient was diagnosed with a heart murmur. An echocardiogram revealed pulmonary artery stenosis, which, combined with a prominent forehead observed on physical examination, determined her referral to clinical genetics. Because ALGS was suspected, complementary studies were performed, revealing butterfly vertebras and a genetic panel identified a pathogenic heterozygous deletion, encompassing the entire coding sequence of the JAG1 gene. To rule out a more extensive deletion, a chromosome microarray was performed, confirming a pathogenic microdeletion on chromosome 20 of 378 kb (arr[GRCh37] 20p12.2(10414643_10792802)x1). Conclusions: A targeted sequencing panel followed by confirmation with a chromosome microarray allowed the identification and delineation of a pathogenic microdeletion not previously reported in the literature, including the complete JAG1 gene in a Chilean patient whose phenotype is consistent with ALGS.

**ECANCERMEDICALSCIENCE. 2024 MAY 10:18:1701. DOI: 10.3332/ECANCER.2024.1701. ECOLLECTION 2024.**

MULTILOCUS INHERITED NEOPLASIA ALLELE SYNDROME: REPORT OF UNCOMMON COMBINATIONS BETWEEN CHEK2/ATM AND BRCA1/CDKN2A GENES

Ricardo Ubilla, Michelle Zeppelin, Fernanda Martin

Background: Multilocus inherited neoplasia allelic syndrome (MINAS) is a recently coined term that describes the coexistence of two or more pathogenic variants (PVs) in cancer susceptibility genes (CSGs) in a single individual. Case presentation: This article presents two cases of MINAS due to rare CSG combinations. The first was a 37-year-old woman carrying PVs in the mutated ataxia telangiectasia (ATM) and CHEK2 genes, with HER-2 positive unilateral breast cancer at 29. The second was a 53-year-old woman carrying PVs in the BRCA1 and CDKN2A genes, who presented with triple-negative breast cancer at 51. We describe their family history and treatment, where the lack of evidence for personalised management becomes evident. Conclusion: Predicting the phenotypic effect of harbouring two variants in CSG is challenging. It is essential to encourage the notification of other cases and carry out functional studies to establish specific risks for affected individuals to develop personalised follow-up guidelines to reduce the associated morbimortality.

**ECANCERMEDICALSCIENCE. 2024 MAR 21:18:1683. DOI: 10.3332/ECANCER.2024.1683. ECOLLECTION 2024.**

VARIANTS IN BRCA1/2 IN A HOSPITAL-BASED COHORT IN CHILE AND NATIONAL LITERATURE REVIEW

Fernanda J Martin, Isabel M Saffie, Mabel A Hurtado, Diana Avila-Jaque, Rodrigo A Lagos, Carolina A Selman, Jonathan Z Huserman, Valentina A Castillo, Badir J Chahuán

Purpose: The aim was to assess the diagnostic yield of next generation sequencing (NGS) multi-gene panels for breast and ovarian cancer in a high-complexity cancer centre in Chile. Additionally, our goal was to broaden the genotypic spectrum of BRCA variants already identified in Chilean families. Methods: Retrospective analysis was conducted on the genetic test results of 722 individuals from Fundación Arturo López Pérez's genetic counselling unit between 2016 and 2021. A comprehensive literature review encompassing articles analysing the frequency of germinal pathogenic variants in BRCA1/2 within the Chilean population was undertaken. Results: 23.5% of the panels had positive results, with 60% due to pathogenic variants in the BRCA1/2 genes. Seven previously unreported variants in BRCA1 from Chilean studies were identified.One or more variants of uncertain significance were detected in 31% of the results, and 11.5% of the families in this cohort presented copy number variants (CNVs) in BRCA1/2.8 studies analysed the frequency of pathogenic variants in BRCA1/2 in the Chilean population between 2006 and 2023, with a frequency between 7.1% and 17.1%.51 BRCA1 variants in 149 families have been reported in Chile and 38 BRCA2 variants in 132 families. Nine founder pathogenic variants identified by one study were present in 51.9% of the total Chilean families reported. Conclusion: Our findings advocate for the integration of NGS multi-gene panel testing as a primary strategy within our population. This approach allows for the comprehensive assessment of single nucleotide variants and CNVs in BRCA1/2, alongside other high and moderately penetrant genes associated with breast and ovarian cancer.

**WORLD NEUROSURG. 2024 MAY:185:135-140. DOI: 10.1016/J.WNEU.2024.01.089.**

GLOBAL NEUROSURGERY AT THE 76TH WORLD HEALTH ASSEMBLY (2023): FIRST NEUROSURGERY-DRIVEN RESOLUTION CALLS FOR MICRONUTRIENT FORTIFICATION TO PREVENT SPINA BIFIDA

Martina Gonzalez Gomez, Anastasia Arynchyna-Smith, Kemel A Ghotme, Roxanna Garcia, Walter D Johnson, Frederick A Boop, Kee B Park, Adrian Caceres, Rosa A Pardo Vargas y otros

Since 2018, a neurosurgery delegation has been actively engaged and consistently present at the World Health Assembly. Recognizing the growing impact of neurosurgical diseases, the neurosurgery delegation participated in the 76th World Health Assembly in May 2023, advocating for timely, safe, and affordable global neurosurgical care. The delegation focused on forging new collaborations, strengthening the World Health Organization-World Federation of Neurosurgical Societies official relations, and actively supporting resolutions that impact the neurosurgical patients. However, there is a long advocacy journey ahead to address unmet neurosurgical needs. Patient-centered advocacy is an inherent task of our profession and the essence of the Global Neurosurgery Bogota Declaration of 2016. The highlight of the 76th World Health Assembly was the adoption of the first neurosurgery-driven resolution calling for micronutrient fortification to prevent spina bifida and other micronutrient deficiencies. For the last 4 years, the Global Alliance for Prevention of Spina Bifida, a group spearheaded by neurosurgeons, advocated for spina bifida prevention. This Alliance collaborated with many stakeholders, notably, the Colombian government to promote the resolution: "Accelerating efforts for preventing micronutrient deficiencies and their consequences, including spina bifida and other neural tube defects, through safe and effective food fortification." This is a proud milestone for the neurosurgical profession. There are many strategies available for neurosurgeons, when working together with elected leaders, other stakeholders, and allied professionals, to implement initiatives that can prevent future cases of spina bifida and other neurological disorders and reduce the burden of neurosurgical disease.

**CEREBELLUM. 2024 AUG;23(4):1727-1732. DOI: 10.1007/S12311-023-01654-X.**

THE PHENOTYPIC SPECTRUM OF SPINOCEREBELLAR ATAXIA TYPE 19 IN A SERIES OF LATIN AMERICAN PATIENTS

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Spinocerebellar ataxia 19 (SCA19) represents a rare autosomal dominant genetic disorder resulting in progressive ataxia and cerebellar atrophy. SCA19 is caused by variants in the KCND3 gene, which encodes a voltage-gated potassium channel subunit essential for cerebellar Purkinje cell function. We describe six cases from Chile and Mexico, representing the largest report on SCA19 in Latin America. These cases encompass a range of clinical presentations, highlighting the phenotypic variability within SCA19 from an early-onset, severe disease to a late-onset, slowly progressive condition with normal lifespan. While some patients present with pure ataxia, others also show cognitive impairment, dystonia, and other neurological symptoms. The correlations between specific KCND3 variants and phenotypic outcomes are complex and warrant further investigation. As the genomic landscape of spinocerebellar ataxias evolves, comprehensive genetic testing is becoming pivotal in improving diagnostic accuracy. This study contributes to a better understanding of the clinical spectrum of SCA19, laying the groundwork for further genotype-phenotype correlations and functional studies to elucidate the underlying pathophysiology.

## GERIATRÍA

**MECH AGEING DEV. 2024 DEC:222:111997. DOI: 10.1016/J.MAD.2024.111997.**

DECIPHERING OSTEOSARCOPENIA THROUGH THE HALLMARKS OF AGING

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Osteosarcopenia is a major driver of functional loss and a risk factor for falls, fractures, disability and mortality in older adults, urgently requiring the development of effective interventions to address it. The hallmarks of aging provide a theoretical and practical framework that allows for the structured organization of current knowledge and the planning of new development lines. This article comprehensively reviews the currently available literature on the role of the hallmarks of aging in the development of osteosarcopenia, thereby offering a panoramic view of the state of the art and knowledge gaps in this field.

**ALZHEIMERS DEMENT. 2024 FEB;20(2):1298-1308. DOI: 10.1002/ALZ.13522.**

THE FIRST GENOME-WIDE ASSOCIATION STUDY IN THE ARGENTINIAN AND CHILEAN POPULATIONS IDENTIFIES SHARED GENETICS WITH EUROPEANS IN ALZHEIMER'S DISEASE

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Introduction: Genome-wide association studies (GWAS) are fundamental for identifying loci associated with diseases. However, they require replication in other ethnicities. Methods: We performed GWAS on sporadic Alzheimer's disease (AD) including 539 patients and 854 controls from Argentina and Chile. We combined our results with those from the European Alzheimer and Dementia Biobank (EADB) in a meta-analysis and tested their genetic risk score (GRS) performance in this admixed population. Results: We detected apolipoprotein E ε4 as the single genome-wide significant signal (odds ratio = 2.93 [2.37-3.63], P = 2.6 × 10-23). The meta-analysis with EADB summary statistics revealed four new loci reaching GWAS significance. Functional annotations of these loci implicated endosome/lysosomal function. Finally, the AD-GRS presented a similar performance in these populations, despite the score diminished when the Native American ancestry rose. Discussion: We report the first GWAS on AD in a population from South America. It shows shared genetics modulating AD risk between the European and these admixed populations. Highlights: This is the first genome-wide association study on Alzheimer's disease (AD) in a population sample from Argentina and Chile. Trans-ethnic meta-analysis reveals four new loci involving lysosomal function in AD. This is the first independent replication for TREM2L, IGH-gene-cluster, and ADAM17 loci. A genetic risk score (GRS) developed in Europeans performed well in this population. The higher the Native American ancestry the lower the GRS values.

## HEMATOLOGÍA

### REV MED CHIL. 2024 JAN;152(1):119-123. DOI: 10.4067/S0034-98872024000100119.

MANEJO DE EMBARAZADA CON DEFICIENCIA DE FACTOR VII. A PROPÓSITO DE UN CASO

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Tissue Factor-Factor VII complex is essential in coagulation activation. Congenital factor VII deficiency is a rare disorder that has an autosomal recessive inheritance. Clinical presentations are heterogeneous, ranging from asymptomatic carriers to severe bleeding phenotypes with factor VII replacement therapy requirements. Treatments options are plasma derived and recombinants FVII concentrates or fresh frozen plasma in case that first options are not available. In pregnancy factor VII levels increase in women with mild and moderate deficiencies but not in severe deficiency. The management of pregnant women with factor FVII deficiency must be done by a multidisciplinary team of hematologist, obstetrics and anesthetist and should be guided by the women bleeding history, the coagulations test, levels of factor FVII and rout of delivery. We present the case of a 31-year-old pregnant woman who, due to an alteration in prothrombin time, is diagnosed with Factor VII deficiency and its respective obstetric management.

## INMUNOLOGÍA

### MEDICINE (BALTIMORE). 2024 JUL 26;103(30):E38288. DOI: 10.1097/MD.0000000000038288.

THE CHALLENGES OF CHILE TO ACHIEVE CONTROL THE HIV/AIDS PANDEMIC THE YEAR 2030: A REVIEW

Pablo Ferrer Campos

Chile is contending with the highest rates of new human immunodeficiency virus (HIV) cases in both Latin America and globally, despite substantial ongoing investments in treatment. This comprehensive study, derived from PUBMED and Google searches, ANID data, and various organizational reports, highlights key areas for improvement. Over the past decade, Chile's annual infection rate has risen, signaling an urgent need for detailed analysis and effective solutions. The study includes 44 references, comprising 32 scientific articles and 12 reports from entities like the WHO and the Pan American Health Organization. Data was meticulously collected through diverse means, such as scientific congresses, meetings with authorities, and direct data requests. Fourteen critical points are identified for addressing the HIV epidemic in Chile, spanning from legislative reforms to enhanced prevention campaigns. Key recommendations include universal diagnosis, decentralized healthcare, the availability of self-tests, and a focus on mental health and the impact of migration. Despite Chile's strong economic indicators, factors such as inadequate sexual education, outdated legislation, and centralized diagnostic processes contribute to the persistent increase in new cases. The study underscores the pressing need for enhanced investment in prevention policies. Chile faces significant challenges in meeting the 90/90/90 targets, yet there is optimism in aiming for the 95/95/95 strategy by 2030. Achieving success requires a global commitment, an emphasis on prevention, and collaborative efforts among authorities, healthcare providers, and patients. Overcoming these identified barriers is essential for Chile to reach its ambitious goal and ultimately end the HIV epidemic.

### LANCET HIV. 2024 JUN;11(6):E369-E379. DOI: 10.1016/S2352-3018(24)00031-6.

SWITCH TO FIXED-DOSE DORAVIRINE (100 MG) WITH ISLATRAVIR (0·75 MG) ONCE DAILY IN VIROLOGICALLY SUPPRESSED ADULTS WITH HIV-1 ON ANTIRETROVIRAL THERAPY: 48-WEEK RESULTS OF A PHASE 3, RANDOMISED, OPEN-LABEL, NON-INFERIORITY TRIAL

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Background: Doravirine and islatravir is an investigational, once-daily, single-tablet regimen with high antiviral potency, favourable safety and tolerability, and low propensity for resistance. We report week 48 results from a phase 3 trial evaluating switch from stable, oral antiretroviral therapy (ART) to the fixed combination of doravirine (100 mg) and islatravir (0·75 mg). Methods: This phase 3, multicentre, randomised, active-controlled, open-label, non-inferiority trial was conducted at 77 research, community, and hospital-based clinics in 15 countries. Adults aged 18 years or older with fewer than 50 HIV-1 RNA copies per mL on any oral, two-drug or three-drug ART regimen for at least 3 months, and no history of previous virological failure on any past or current regimen were randomly assigned (1:1) by a computer-generated randomisation schedule to switch to doravirine (100 mg) and islatravir (0·75 mg) or to continue their baseline ART regimen. Block randomisation was based on a block size of four, and randomisation was stratified by baseline regimen (ie, protease inhibitor, integrase inhibitor, or other). Participants in the doravirine and islatravir group were instructed to take one tablet at approximately the same time each day, and participants in the baseline ART group continued to take the medication according to the locally approved label. HIV-1 RNA and safety evaluations were done at baseline and weeks 4, 12, 24, 36, and 48. CD4 cell counts were measured at baseline, week 24, and week 48. The primary endpoint was proportion of participants with greater than or equal to 50 HIV-1 RNA copies per mL at week 48 in the full analysis set (ie, all participants who received at least one dose of study drug) using the US Food and Drug Administration snapshot approach

and prespecified non-inferiority margin of 4%. This study is registered with ClinicalTrials.gov (NCT04223778) and is completed. Findings: Between Feb 18 and Oct 2, 2020, 740 individuals were screened for eligibility, of whom 672 (90·8%) participants (249 [37·1%] women and 423 [62·9%] men; median CD4 count of 678 cells per µL [IQR 496-868]) were randomly assigned to doravirine (100 mg) and islatravir (0·75 mg; n=336) or to continue baseline ART (n=336). The last follow-up visit occurred on Sept 8, 2021. At week 48, zero of 336 participants in the doravirine and islatravir group versus five (1·5%) of 336 participants in the baseline ART group had greater than or equal to 50 HIV-1 RNA copies per mL (difference -1·5, 95% CI -3·4 to -0·3). The per-protocol analysis showed consistent results. Headache was the most common adverse event in both groups (35 [10·4%] of 336 participants in the doravirine and islatravir group, 16 [4·8%] of 336 in the baseline ART group), infection rates were similar (113 [33·6%] in both groups), and discontinuations due to adverse events were low (seven [2·1%] vs one [0·3%]). 66 (19·6%) of 336 participants had treatment-related adverse events in the doravirine and islatravir group compared with 30 (8·9%) of 336 in the baseline ART group. In the islatravir and doravirine group, CD4 cell counts (mean change -30·3 cells per µL) and total lymphocyte counts (mean change -0·26 × 109/L) were decreased at 48 weeks. Interpretation: Switching to single-tablet doravirine (100 mg) and islatravir (0·75 mg) maintained viral suppression up to week 48 and was non-inferior to antiretroviral combinations used in clinical practice for adults with HIV-1; however, decreases in CD4 cell and total lymphocyte counts do not support further development of once-daily doravirine (100 mg) and islatravir (0·75 mg).

**LANCET HIV. 2024 FEB;11(2):E75-E85. DOI: 10.1016/S2352-3018(23)00258-8.**

SAFETY AND EFFICACY OF DORAVIRINE AS FIRST-LINE THERAPY IN ADULTS WITH HIV-1: WEEK 192 RESULTS FROM THE OPEN-LABEL EXTENSIONS OF THE DRIVE-FORWARD AND DRIVE-AHEAD PHASE 3 TRIALS

Chloe Orkin, Jean-Michel Molina, Pedro Cahn, Johannes Lombaard, Khuanchai Supparatpinyo, Sushma Kumar, Havilland Campbell, Hong Wan, Valerie Teal, Zhi Jin Xu, Ernest Asante-Appiah, Peter Sklar, Hedy Teppler, Rima Lahoulou, DRIVE-FORWARD and DRIVE-AHEAD collaborators

Background: In two phase 3 trials for first-line therapy in adults with HIV-1, doravirine showed non-inferior efficacy, a favourable safety profile, and a superior lipid profile to darunavir and efavirenz through to 48 and 96 weeks. Here we report 192-week results from both studies. Methods: DRIVE-FORWARD and DRIVE-AHEAD are multicentre, double-blind, randomised, active comparator-controlled, phase 3 trials of first-line antiretroviral treatment in adults with HIV-1. Eligible participants (aged ≥18 years) were naive to antiretroviral therapy, had plasma HIV-1 RNA 1000 copies per mL or more at screening, had no known resistance to any of the trial drugs, and had creatinine clearance 50 mL per min or more. DRIVE-FORWARD was conducted at 125 sites in 15 countries and compared doravirine (100 mg) with ritonavir-boosted darunavir (ritonavir [100 mg] and darunavir [800 mg]), each administered orally once daily with two nucleoside or nucleotide reverse transcriptase inhibitors (tenofovir disoproxil fumarate [300 mg] and emtricitabine [200 mg] or abacavir sulfate [600 mg] and lamivudine [300 mg]). DRIVE-AHEAD was conducted at 126 sites in 23 countries and compared doravirine (100 mg), lamivudine (300 mg), and tenofovir disoproxil fumarate (300 mg) with that of efavirenz (600 mg), emtricitabine (200 mg), and tenofovir disoproxil fumarate (300 mg), all administered orally once daily. DRIVE-FORWARD enrolment was between Dec 1, 2014, and June 1, 2020, and DRIVE-AHEAD enrolment was between June 10, 2015, and Aug 10, 2020. After the 96-week double-blind phase, eligible participants could enter an open-label extension and either continue doravirine or switch from comparator to doravirine for an additional 96 weeks. Efficacy (HIV-1 RNA <50 copies per mL) and safety assessments (adverse events and changes in laboratory parameters) were pooled. The DRIVE-FORWARD and DRIVE-AHEAD trials were registered with ClinicalTrials.gov, NCT02275780 and NCT02403674. Findings: Of 1494 participants treated in the double-blind phase (1261 [84%] male and 233 [16%] female), 550 continued doravirine and 502 switched to doravirine in the extension. Using the FDA snapshot approach, HIV-1 RNA less than 50 copies per mL was maintained in 457 (83%) of 550 participants who continued doravirine and 404 (80%) of 502 participants who switched to doravirine. Protocol-defined virological failure and development of resistance were low, occurring mainly before week 96. Two (<1%) of 550 participants who continued doravirine reported serious drug-related adverse events, and three (1%) who continued doravirine and one (<1%) of 502 who switched to doravirine discontinued due to drug-related adverse events. Participants continuing or switching to doravirine showed generally favourable lipid profiles, little weight gain, and small decreases in estimated glomerular filtration rates, with no discontinuations due to increased creatinine or renal adverse events. Interpretation: Favourable efficacy and safety profiles for doravirine at week 96 were maintained through to week 192 in participants who continued or switched to doravirine, supporting use of doravirine for long-term first-line HIV-1 treatment and for virologically suppressed adults switching therapy.

**J ALLERGY CLIN IMMUNOL PRACT. 2024 OCT;12(10):2648-2668.E2. DOI: 10.1016/J.JAIP.2024.06.040.**

CONCEPTS FOR THE DEVELOPMENT OF PERSON-CENTERED, DIGITALLY ENABLED, ARTIFICIAL INTELLIGENCE-ASSISTED ARIA CARE PATHWAYS (ARIA 2024)

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The traditional healthcare model is focused on diseases (medicine and natural science) and does not acknowledge patients' resources and abilities to be experts in their own lives based on their lived experiences. Improving healthcare safety, quality,

and coordination, as well as quality of life, is an important aim in the care of patients with chronic conditions. Person-centered care needs to ensure that people's values and preferences guide clinical decisions. This paper reviews current knowledge to develop (1) digital care pathways for rhinitis and asthma multimorbidity and (2) digitally enabled, person-centered care.1 It combines all relevant research evidence, including the so-called real-world evidence, with the ultimate goal to develop digitally enabled, patient-centered care. The paper includes (1) Allergic Rhinitis and its Impact on Asthma (ARIA), a 2-decade journey, (2) Grading of Recommendations, Assessment, Development and Evaluation (GRADE), the evidence-based model of guidelines in airway diseases, (3) mHealth impact on airway diseases, (4) From guidelines to digital care pathways, (5) Embedding Planetary Health, (6) Novel classification of rhinitis and asthma, (7) Embedding real-life data with population-based studies, (8) The ARIA-EAACI (European Academy of Allergy and Clinical Immunology) strategy for the management of airway diseases using digital biomarkers, (9) Artificial intelligence, (10) The development of digitally enabled, ARIA person-centered care, and (11) The political agenda. The ultimate goal is to propose ARIA 2024 guidelines centered around the patient to make them more applicable and sustainable.

**REV. CHILENA. INFECTOL. [INTERNET]. 2024 DEC. 12 [CITED 2025 JUN. 4];41(6). DOI: 10.4067/S0716-10182024000600162**

GUÍA CLÍNICAVERSIÓN IN PRESS ID 2179ORIENTACIONES PARA EL USO DE TERAPIA ANTIRRETROVIRAL EN PERSONAS QUE VIVEN CON VIH EN CHILE

Ceballos ME, Bernal F, Herrera P, Pérez C. C, Muñoz R, Afani A, Araya A. X, Piñera M. C, Silva M.

La terapia antirretroviral ha mejorado significativamente el pro-nóstico de las personas que viven con el virus de la inmunodeficiencia humana. Sin embargo, su beneficio estará determinado por la correcta utilización de la misma, por lo que estas guías entregan orientaciones para la elección de los esquemas de tratamiento en adultos y niños, con consideraciones para diferentes comorbilidades y estados fisiológicos como grupos de edad o embarazo. Se indican los posibles cambios de terapia por simplificaciones o interacciones y los ajustes de esquemas en casos de fallo virológico. Estas recomendaciones reflejan la posi-ción de sus autores y no necesariamente de sociedades científicas o de la autoridad sanitaria nacional.

## MEDICINA INTERNA

**REV MED CHIL. 2024 MAY;152(5):621-626. DOI: 10.4067/S0034-98872024000500621.**

REPORTE DE CASO: SÍNDROME DE GUILLAIN-BARRÉ CON DOLOR DE DIFÍCIL MANEJO Y RETENCIÓN URINARIA PERSISTENTE

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El síndrome de Guillain-Barré (SGB) es una polirradiculoneuropatía inflamatoria aguda que compromete el sistema nervioso periférico y afecta predominantemente la función motora. El dolor, tanto somático como neuropático, se reporta en el 89% de los casos y es refractario a analgésicos de primera línea en la mayoría de estos. Presentamos el caso de una mujer de 75 años con un cuadro agudo de tetraparesia flácida arrefléctica compatible con SGB; recibe tratamiento con inmunoglobulina endovenosa (IgIV) con lo que mejora el componente motor, pero asocia dolor refractario a antiinflamatorios no esteroidales y pregabalina además de retención urinaria persistente con intentos frustros de retiro de catéter urinario. Se indica fentanilo transdérmico con buena respuesta y tolerancia, además de tamsulosina y cateterismo intermitente, logrando retirar el catéter al cabo de seis semanas. En base al caso, se sugiere la evaluación individualizada del dolor y de la retención urinaria en SGB, considerando el uso de opioides transdérmicos y medidas de vaciamiento vesical no invasivas respectivamente.

**REV MED CHILE 2024; 152(11): 1176-1180. DOI: 10.4067/S0034-98872024001101176.**

UN CASO DE HEMORRAGIA VARICEAL RECURREUN CASO DE HEMORRAGIA VARICEAL RECURRENTE SECUNDARIA A ENFERMEDAD VASCULAR PORTOSINUSOIDAL

Nicolás Ortiz-López, Juan Pablo Roblero, Jaime Poniachik, Álvaro Urzúa, Laura Carreño

La hipertensión portal es un síndrome caracterizado por la elevación de la presión en el sistema venoso portal, con consecuencias graves. La cirrosis es la causa más común, pero existen otras causas menos frecuentes, incluyendo la hipertensión portal idiopática, recientemente definida como enfermedad vascular portosinusoidal (EVPS) que afecta las vénulas portales y los sinuoides hepáticos. Se presenta el caso de un hombre de 68 años con antecedentes de hipertensión portal y hemorragia variceal recurrente. A pesar del tratamiento médico y procedimientos endoscópicos, las hemorragias persistieron. Se realizó una derivación portosistémica intrahepática transyugular (TIPS, transjugular intrahepatic portosystemic shunt) para su manejo. La elastografía hepática mostró una rigidez hepática inusualmente baja para la cirrosis, lo que llevó a la realización de una biopsia hepática. Los hallazgos histológicos respaldaron el diagnóstico de EVPS. En cuanto al tratamiento, no existen terapias específicas para la EVPS, y el enfoque se centra en tratar las complicaciones asociadas a la hipertensión portal. La EVPS es una entidad poco común que puede ser una causa subyacente de hipertensión portal no cirrótica. Este caso subraya la importancia de la concienciación para un diagnóstico temprano y un manejo adecuado. La investigación continua es esencial para comprender mejor esta rara condición y mejorar la calidad de vida de los pacientes.

## MEDICINA NUCLEAR

### INT J CARDIOL HEART VASC. 2024 APR 4:52:101404. DOI: 10.1016/J.IJCHA.2024.101404.

CARDIOVASCULAR TESTING RECOVERY IN LATIN AMERICA ONE YEAR INTO THE COVID-19 PANDEMIC: AN ANALYSIS OF DATA FROM AN INTERNATIONAL LONGITUDINAL SURVEY

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Background: The COVID-19 pandemic disproportionately impacted Latin America (LATAM), significantly disrupting cardiovascular testing. This study evaluated cardiac procedure recovery in LATAM one year after the outbreak. Methods: The International Atomic Energy Agency (IAEA) surveyed 669 centers in 107 countries worldwide, including 135 facilities in 19 LATAM countries, to assess cardiovascular procedure volumes in March 2019, April 2020, and April 2021, and changes in center practices and staffing conditions one year into the COVID-19 pandemic. Findings: LATAM centers reported a 21 % decrease in procedure volumes in April 2021 from pre-pandemic-baseline, vs. a 0 % change in the rest of the world (RoW), and greater volume reductions for almost all procedure types. Centers in Central America and Mexico reported the largest procedure reductions (47 % reduction) compared to the Caribbean (15 %), and South America (14 %, p = 0.01), and this LATAM region was a significant predictor of lower procedure recovery in multivariable regression. More LATAM centers reported reduced salaries and increased layoffs of clinical staff compared to RoW, and LATAM respondents estimated that half of physician and non-physician staff experienced excess psychological stress related to the pandemic, compared to 25 % and 30 % in RoW (p < 0.001). Conclusions: Cardiovascular testing recovery in LATAM trailed behind RoW for most procedure types, with centers in Central America and Mexico reporting the greatest volume reductions. This study found lasting impacts of COVID-19 on cardiovascular care in LATAM and the need for mental health support for LATAM healthcare workers in current and future pandemics.

## NEFROLOGÍA

### REV. MÉD. CHILE 2024 VOL.152 NO.2 SANTIAGO FEB. 2024. DOI: 10.4067/S0034-98872024000200244

CONSENSO MULTIDISCIPLINARIO SOBRE EL USO DE INHIBIDORES DE SGLT-2 (ISGLT-2) EN LA PRÁCTICA CLÍNICA CHILENA MEDIANTE METODOLOGÍA GRADE

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El consenso chileno sobre el uso de inhibidores de SGLT-2 (iSGLT-2) en la práctica clínica, elaborado conjuntamente por las sociedades Chilenas de Cardiología, Diabetes, Medicina Familiar y Nefrología, recomienda fuertemente el uso de estos fármacos en personas con insuficiencia cardíaca y fracción de eyección reducida, diabetes mellitus tipo 2 para prevención de eventos cardiovasculares y evitar la progresión de enfermedad renal crónica. En insuficiencia cardíaca con fracción de eyección conservada o levemente reducida, y enfermedad renal crónica sin diabetes, el consenso sugiere el uso de iSGLT-2. Se destaca la importancia de combinar iSGLT-2 con IECAs o ARA-II en enfermedad renal crónica, y se recomienda su uso en reemplazo de sulfonilureas como segunda línea para control glicémico en diabetes tipo 2. El consenso enfatiza la necesidad de estrategias para optimizar el diagnóstico, mejorar la adherencia y educar sobre los beneficios más allá del control glicémico. Se discuten consideraciones de seguridad y costo-efectividad para una implementación priorizada según la evidencia. El documento resalta la importancia de la colaboración multidisciplinaria y la generación de evidencia local para aprovechar al máximo el potencial de estos fármacos en el manejo de condiciones cardiometabólicas complejas en Chile.

### REV NEFROL DIAL TRASPL. 2024;44(2):91-98

COVID-19 EN TRASPLANTADOS RENALES HOSPITALIZADOS: ANÁLISIS DEL REGISTRO MULTICÉNTRICO DURANTE LA PRIMERA OLA DE LA PANDEMIA EN CHILE

Jacqueline Pefaur, Luis Toro, Ximena Badilla, Leopoldo Ardiles, Andrés Boltansky, Pía Rosatti, Beatriz Tapia, Ximena Rocca, Paola Mur, Alicia Fernández, Álvaro Castillo, Carolina Díaz, Leticia Elgueta, Francisco García, Hans Müller, Rodrigo Mansilla, Carolina Muñoz, Marcelo Salvatici, María Esperanza Selame, Marcela Valenzuela, Daniela Zamora, Giovanni Enciso, Rita Panace, Sebastián Cabrera, Ana Mireya Ortiz, Sandra Mardones, Carolina Oshiro, Juan Eduardo Sánchez, Eduardo Lorca, Rubén Torres

Introducción: La evolución de la infección por COVID-19 se ha demostrado grave en los pacientes trasplantados de riñón. Objetivos: Conocer datos epidemiológicos, clínicos y determinar predictores de mal pronóstico en los albores de la epidemia. Material y Métodos: estudio nacional semiprospectivo, multicéntrico, en sujetos con injerto funcionante, infectados durante la primera ola de la pandemia, entre el 1 de marzo y el 31 de septiembre de 2020 en Chile. Resultados: registramos la hospitalización de 97 adultos con injerto funcionante a través de todo el territorio nacional con edad promedio 52.5 años, 62% hombres, 45% hipertensos, 11% coronarios, 10% diabéticos, y 5% con enfermedad pulmonar obstructiva crónica, con un seguimiento post-trasplante promedio de 7.2 años y función renal previa promedio de 47.7 ml/min/1.7m2 (fórmula CKD-EPI). Entre el inicio de los

síntomas y el diagnóstico hubo un periodo promedio de 4.8 días, predominando la tos (44%), disnea (42%) y fiebre (42%). Un 34% desarrolló injuria renal aguda y de ellos un 36% requirió soporte dialítico. La letalidad fue de un 30%, predominando en aquellos con falla orgánica múltiple 80% y quienes requirieron ventilación mecánica invasiva (52%). En el análisis multivariado, los mejores predictores de mortalidad fueron la mayor edad (OR: 2,92) y vivir en una comuna de bajos ingresos (OR: 2,35). Conclusiones: la información generada por este proyecto de la Sociedad Chilena de Nefrología permitió monitorizar la evolución inicial de la pandemia y proponer estrategias de vacunación prioritarias, ajustes de inmunosupresión y diseñar aspectos logísticos para reducir los riesgos de nuestros pacientes trasplantados.

### REV. MÉD. CHILE VOL.152 NO.4 SANTIAGO APR. 2024 DOI: /10.4067/S0034-98872024000400460

DISMINUCIÓN DE LA FUNCIÓN RENAL CON LA EDAD EN CHILE: DIFERENCIAS DE GÉNERO Y EFECTO DE COMORBILIDADES

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de filtración glomerular estimada (VFGe) mediante creatinina sérica es ampliamente utilizada para evaluar la función renal. Su disminución con la edad y en presencia de enfermedades crónicas como diabetes, hipertensión y obesidad es bien conocido, sin embargo, no existen datos representativos en la población chilena. Estimar la disminución de VFGe con la edad según género y presencia de enfermedades crónicas en población adulta chilena. Métodos: Estudio transversal en 5.638 participantes ≥18 años de la Encuesta Nacional de Salud 2009 y 2017. Se estimó VFGe mediante CKD-EPI a partir de creatinina sérica. Se comparó la disminución de VFGe por género y presencia de enfermedades crónicas (diabetes, hipertensión, dislipidemia y/u obesidad). Resultados: La VFGe disminuyó con la edad en ambos géneros, con mayor pendiente en mujeres (-0,88 vs -0,78 mL/min/1,73 m2/año, p<0,01). La VFGe disminuyó temprana y homo-géneamente a partir de los 18 años. En presencia de enfermedades crónicas la pendiente fue significativamente mayor (-0,94 vs -0,83 mL/min/1,73 m2/ año, p<0,001). Las mujeres con enfermedades crónicas tuvieron la mayor disminución (-1,00 mL/min/1,73 m2/año). Conclusión: La VFGe disminuyó progresivamente con la edad en población chilena, observándose una disminución temprana a partir de los 18 años, acentuándose en mujeres y presencia de enfermedades crónicas. Nuestros hallazgos entregan informa-ción poblacional relevante para la interpretación de la VFGe en distintos grupos etarios y de riesgo.

## ONCOLOGÍA

### J GERIATR ONCOL. 2024 APR;15(3):101642. DOI: 10.1016/J.JGO.2023.101642.

DEVELOPMENT OF GERIATRIC ONCOLOGY IN LATIN AMERICA: A REPORT FROM THE LATIN AMERICAN COOPERATIVE ONCOLOGY GROUP

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Population aging represents a critical issue for global cancer care, notably in low- and middle-income countries (LMIC). Latin America is a large region composed of 21 countries with notable diversity in both human development and access to quality healthcare. Thus, it is necessary to understand how care for older individuals is being delivered in such large and diverse regions of the world. This review describes the recent advances made in Mexico, Brazil, and Chile, focusing on the creation and implementation of educational, research, and clinical activities in geriatric oncology. These initiatives intend to change healthcare professionals' perceptions about the care for older adults and to improve the way older patients are being treated.

### CANCERS (BASEL). 2024 DEC 17;16(24):4195. DOI: 10.3390/CANCERS16244195.

INBREEDING AND GALLBLADDER CANCER RISK: HOMOZYGOSITY ASSOCIATIONS ADJUSTED FOR INDIGENOUS AMERICAN ANCESTRY, BMI, AND GENETIC RISK OF GALLSTONE DISEASE

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Latin Americans have a rich genetic make-up that translates into heterogeneous fractions of the autosomal genome in runs of homozygosity (FROH) and heterogeneous types and proportions of indigenous American ancestry. While autozygosity has been linked to several human diseases, very little is known about the relationship between inbreeding, genetic ancestry, and cancer risk in Latin Americans. Chile has one of the highest incidences of gallbladder cancer (GBC) in the world, and we investigated the association between inbreeding, GBC, gallstone disease (GSD), and body mass index (BMI) in 4029 genetically admixed Chileans. We calculated individual FROH above 1.5 Mb and weighted polygenic risk scores for GSD, and applied multiple logistic regression to assess the association between homozygosity and GBC risk. We found that homozygosity was due to a heterogeneous mixture of genetic drift and consanguinity in the study population. Although we found no association between homozygosity and overall GBC risk, we detected interactions of FROH with sex, age, and

genetic risk of GSD that affected GBC risk. Specifically, the increase in GBC risk per 1% FROH was 19% in men (p-value = 0.002), 30% in those under 60 years of age (p-value = 0.001), and 12% in those with a genetic risk of GSD above the median (p-value = 0.01). The present study highlighted the complex interplay between inbreeding, genetic ancestry, and genetic risk of GSD in the development of GBC. The applied methodology and our findings underscored the importance of considering the population-specific genetic architecture, along with sex- and age-specific effects, when investigating the genetic basis of complex traits in Latin Americans.

**BMC CANCER. 2024 AUG 3;24(1):951. DOI: 10.1186/S12885-024-12737-1.**

BEYOND TOBACCO: GENOMIC DISPARITIES IN LUNG CANCER BETWEEN SMOKERS AND NEVER-SMOKERS

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Background: Tobacco use is one of the main risk factors for Lung Cancer (LC) development. However, about 10-20% of those diagnosed with the disease are never-smokers. For Non-Small Cell Lung Cancer (NSCLC) there are clear differences in both the clinical presentation and the tumor genomic profiles between smokers and never-smokers. For example, the Lung Adenocarcinoma (LUAD) histological subtype in never-smokers is predominately found in young women of European, North American, and Asian descent. While the clinical presentation and tumor genomic profiles of smokers have been widely examined, never-smokers are usually underrepresented, especially those of a Latin American (LA) background. In this work, we characterize, for the first time, the difference in the genomic profiles between smokers and never-smokers LC patients from Chile. Methods: We conduct a comparison by smoking status in the frequencies of genomic alterations (GAs) including somatic mutations and structural variants (fusions) in a total of 10 clinically relevant genes, including the eight most common actionable genes for LC (EGFR, KRAS, ALK, MET, BRAF, RET, ERBB2, and ROS1) and two established driver genes for malignancies other than LC (PIK3CA and MAP2K1). Study participants were grouped as either smokers (current and former, n = 473) or never-smokers (n = 200) according to self-report tobacco use at enrollment. Results: Our findings indicate a higher overall GA frequency for never-smokers compared to smokers (58 vs. 45.7, p-value < 0.01) with the genes EGFR, KRAS, and PIK3CA displaying the highest prevalence while ERBB2, RET, and ROS1 the lowest. Never-smokers present higher frequencies in seven out of the 10 genes; however, smokers harbor a more complex genomic profile. The clearest differences between groups are seen for EGFR (15.6 vs. 21.5, p-value: < 0.01), PIK3CA (6.8 vs 9.5) and ALK (3.2 vs 7.5) in favor of never-smokers, and KRAS (16.3 vs. 11.5) and MAP2K1 (6.6 vs. 3.5) in favor of smokers. Alterations in these genes are comprised almost exclusively by somatic mutations in EGFR and mainly by fusions in ALK, and only by mutations in PIK3CA, KRAS and MAP2K1. Conclusions: We found clear differences in the genomic landscape by smoking status in LUAD patients from Chile, with potential implications for clinical management in these limited-resource settings.

## REUMATOLOGÍA

**J RHEUMATOL. 2024 JUN 1;51(6):563-576. DOI: 10.3899/JRHEUM.2023-1172.**

PAN AMERICAN LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY RECOMMENDATIONS FOR THE TREATMENT OF PSORIATIC ARTHRITIS

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Objective: Psoriatic arthritis (PsA) is chronic disease that compromises multiple domains and might be associated with progressive joint damage, increased mortality, functional limitation, and considerably impaired quality of life. Our objective was to generate evidence-based recommendations on the management of PsA in Pan American League of Associations for Rheumatology (PANLAR) countries. Methods: We used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)-ADOLOPMENT approach to adapt the 2019 recommendations of the European Alliance of Associations for Rheumatology. A working group consisting of rheumatologists from various countries in Latin America identified relevant topics for the treatment of PsA in the region. The methodology team updated the evidence and synthesized the information used to generate the final recommendations. These were then discussed and defined by a panel of 31 rheumatologists from 15 countries. Results: Theses guidelines report 15 recommendations addressing therapeutic targets, use of antiinflammatory agents and corticosteroids, treatment with disease-modifying antirheumatic drugs (conventional synthetic, biologic, and targeted synthetic), therapeutic failure, optimization of biologic therapy, nonpharmacological interventions, assessment tools, and follow-up of patients with PsA. Conclusion: Here we present a set of recommendations to guide decision making in the treatment of PsA in Latin America, based on the best evidence available, considering resources, medical expertise, and the patient's values and preferences. The successful implementation of these recommendations should be based on clinical practice conditions, healthcare settings in each country, and a tailored evaluation of patients.

**CLIN EXP RHEUMATOL. 2024 FEB;42(2):277-287. DOI: 10.55563/CLINEXPRHEUMATOL/S14ZQ8.**

AGREEMENT BETWEEN LOCAL AND CENTRAL ANTI-SYNTHETASE ANTIBODIES DETECTION: RESULTS FROM THE CLASSIFICATION CRITERIA OF ANTI-SYNTHETASE SYNDROME PROJECT BIOBANK

Aravinthan Loganathan, Giovanni Zanframundo, Akira Yoshida, Sara Faghihi-Kashani, Iazsmin Bauer Ventura, Eduardo Dourado, Francisca Bozan, Gianluca Sambataro y otros

Objectives: The CLASS (Classification Criteria of Anti-Synthetase Syndrome) project is a large international multicentre study that aims to create the first data-driven anti-synthetase syndrome (ASSD) classification criteria. Identifying anti-aminoacyl tRNA synthetase antibodies (anti-ARS) is crucial for diagnosis, and several commercial immunoassays are now available for this purpose. However, using these assays risks yielding false-positive or false-negative results, potentially leading to misdiagnosis. The established reference standard for detecting anti-ARS is immunoprecipitation (IP), typically employed in research rather than routine autoantibody testing. We gathered samples from participating centers and results from local anti-ARS testing. As an "ad-interim" study within the CLASS project, we aimed to assess how local immunoassays perform in real-world settings compared to our central definition of anti-ARS positivity. Methods: We collected 787 serum samples from participating centres for the CLASS project and their local anti-ARS test results. These samples underwent initial central testing using RNA-IP. Following this, the specificity of ARS was reconfirmed centrally through ELISA, line-blot assay (LIA), and, in cases of conflicting results, protein-IP. The sensitivity, specificity, positive likelihood ratio and positive and negative predictive values were evaluated. We also calculated the inter-rater agreement between central and local results using a weighted $\kappa$ co-efficient. Results: Our analysis demonstrates that local, real-world detection of anti-Jo1 is reliable with high sensitivity and specificity with a very good level of agreement with our central definition of anti-Jo1 antibody positivity. However, the agreement between local immunoassay and central determination of anti-non-Jo1 antibodies varied, especially among results obtained using local LIA, ELISA and "other" methods. Conclusions: Our study evaluates the performance of real-world identification of anti-synthetase antibodies in a large cohort of multi-national patients with ASSD and controls. Our analysis reinforces the reliability of real-world anti-Jo1 detection methods. In contrast, challenges persist for anti-non-Jo1 identification, particularly anti-PL7 and rarer antibodies such as anti-OJ/KS. Clinicians should exercise caution when interpreting anti-synthetase antibodies, especially when commercial immunoassays test positive for non-anti-Jo1 antibodies.

**J CLIN RHEUMATOL. 2024 MAR 1;30(2):52-57. DOI: 10.1097/RHU.0000000000002052.**

PERFORMANCE OF THE 2019 AMERICAN COLLEGE OF RHEUMATOLOGY/EUROPEAN LEAGUE AGAINST RHEUMATISM CLASSIFICATION CRITERIA FOR IGG4-RELATED DISEASE IN A LATIN AMERICAN COHORT

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Background/objective: The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria (2019 AECC) for IgG4-related disease (IgG4-RD) is considered a significant advancement in the study of this condition. Most studies evaluating their performance have focused on White and Asian patients, leaving a knowledge gap regarding Latin American populations. Therefore, this study aimed to assess the performance of the 2019 AECC for IgG4-RD in a cohort of Latin American patients. Methods: A multicenter medical records review study was conducted, involving centers from Argentina, Chile, Mexico, Peru, and Uruguay. Data on IgG4-RD patients and mimicker conditions were collected through a standardized online form. The criterion standard for diagnosing IgG4-RD was based on the fulfillment of the Comprehensive Diagnostic Criteria for IgG4-RD and/or the Consensus Statement on Pathology. The 2019 AECC was retrospectively applied. Results: We included 300 patients, with 180 (60%) having IgG4-RD and 120 (40%) having mimicker conditions. The 2019 AECC had a sensitivity of 66.7% and a specificity of 100%. Sensitivity increased to 73.3% when disease-specific autoantibody items were removed, without affecting specificity. The true-positive cases had more involved organs, a higher availability of biopsy results, and were more likely to belong to the Mikulicz/systemic and proliferative phenotypes. Conclusions: The use of the 2019 AECC for IgG4-RD in a Latin American population confirms its high specificity in excluding those without the disease. The presence of concomitant autoimmune diseases and clinically nonsignificant disease-specific autoantibodies excludes a significant number of patients from fulfilling the criteria.

**RHEUMATOL ADV PRACT. 2024 MAR 12;8(2):RKAE041. DOI: 10.1093/RAP/RKAE041.**

GASTRIC DYSRHYTHMIAS IN PATIENTS WITH EARLY SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

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Objectives: Gastric involvement in patients with early systemic sclerosis (SSc) has not been previously investigated. We aim to evaluate the association of gastric dysrhythmias with gastrointestinal (GI) symptoms and nailfold video capillaroscopy (NVC). Methods: Cross-sectional study. Patients with early SSc, completed the UCLA GIT 2.0 questionnaire, performed an NVC, and a surface Electrogastrography (EGG). Descriptive statistics was used for demographic and clinical characteristics and Fisher and Kendall Tau tests were used for association analysis. Results: 75 patients were screened, 30 patients were consecutively

enrolled, 29 performed the EGG and 1 patient had a non-interpretable NVC. 29/30 were female with a mean age of 48.7 years (25-72). The mean disease duration from the first non-RP symptom was 22.6 +/-10.8 months and most of the patients had limited disease (76.6%). Total GIT 2.0 score symptoms were moderate-severe in 63% of the participants and 28/29 had an abnormal EGG. Bradygastria was the most common pattern present in 70% of the participants. NVC patterns: 17% early, 34% active, 28% scleroderma-like, 14% non-specific, and 2 patients had a normal NVC. There was no association between severe GI symptoms or NVC patterns and severely abnormal EGG, but the presence of bradygastria was associated with severe impairment in the social functioning area (p 0.018). Conclusions: Gastric dysmotility is common in early SSc and there is a lack of correlation between GI symptoms and NVC scleroderma patterns. EGG is a sensitive, cheap, and non-invasive exam, that may be an alternative to early diagnosis of GI involvement.

## SERVICIO MEDICINA FÍSICA Y REHABILITACIÓN

### JAMA NETW OPEN. 2024 JAN 2;7(1):E2350301. DOI: 10.1001/JAMANETWORKOPEN.2023.50301.

HYBRID CARDIAC REHABILITATION PROGRAM IN A LOW-RESOURCE SETTING: A RANDOMIZED CLINICAL TRIAL

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Importance: While effective, cardiovascular rehabilitation (CR) as traditionally delivered is not well implemented in lower-resource settings. Objective: To test the noninferiority of hybrid CR compared with traditional CR in terms of cardiovascular events. Design, setting, and participants: This pragmatic, multicenter, parallel arm, open-label randomized clinical trial (the Hybrid Cardiac Rehabilitation Trial [HYCARET]) with blinded outcome assessment was conducted at 6 referral centers in Chile. Adults aged 18 years or older who had a cardiovascular event or procedure, no contraindications to exercise, and access to a mobile telephone were eligible and recruited between April 1, 2019, and March 15, 2020, with follow-up until July 29, 2021. Interventions: Participants were randomized 1:1 in permuted blocks to the experimental arm, which received 10 center-based supervised exercise sessions plus counseling in 4 to 6 weeks and then were supported at home via telephone calls and text messages through weeks 8 to 12, or the control arm, which received the standard CR of 18 to 22 sessions with exercises and education in 8 to 12 weeks. Main outcomes and measures: The primary outcome was cardiovascular events or mortality. Secondary outcomes were quality of life, return to work, and lifestyle behaviors measured with validated questionnaires; muscle strength and functional capacity, measured through physical tests; and program adherence and exercise-related adverse events, assessed using checklists. Results: A total of 191 participants were included (mean [SD] age, 58.74 [9.80] years; 145 [75.92%] male); 93 were assigned to hybrid CR and 98 to standard CR. At 1 year, events had occurred in 5 unique participants in the hybrid CR group (5.38%) and 9 in the standard CR group (9.18%). In the intention-to-treat analysis, the hybrid CR group had 3.80% (95% CI, -11.13% to 3.52%) fewer cardiovascular events than the standard CR group, and relative risk was 0.59 (95% CI, 0.20-1.68) for the primary outcome. In the per-protocol analysis at different levels of adherence to the intervention, all 95% CIs crossed the noninferiority boundary (eg, 20% adherence: absolute risk difference, -0.35% [95% CI, -7.56% to 6.85%]; 80% adherence: absolute risk difference, 3.30% [95% CI, -3.70% to 10.31%]). No between-group differences were found for secondary outcomes except adherence to supervised CR sessions (79.14% [736 of 930 supervised sessions] in the hybrid CR group vs 61.46% [1201 of 1954 sessions] in the standard CR group). Conclusions and relevance: The results suggest that a hybrid CR program is noninferior to standard center-based CR in a low-resource setting, primarily in terms of recurrent cardiovascular events and potentially in terms of intermediate outcomes. Hybrid CR may induce superior adherence to supervised exercise. Clinical factors and patient preferences should inform CR model allocation.

### J HAND THER. 2024 JUL-SEP;37(3):397-404. DOI: 10.1016/J.JHT.2023.08.010.

EXERCISE-BASED INTERVENTION AS A NONSURGICAL TREATMENT FOR PATIENTS WITH CARPAL INSTABILITY: A CASE SERIES

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Background: Although the important roles of proprioception and neuromuscular control in carpal instabilities under laboratory conditions have been recognized, only a few studies have translated this knowledge into a routine clinical practice. Purpose: This study aimed to evaluate the results of a personalized rehabilitation in patients with carpal instability on functionality and pain intensity. Study design: This was a case series study. Methods: This case series included 39 adults (mean age: 38.2 ± 14.0 years; 16/23 females/males) diagnosed with carpal instability (radial or ulnar) with indication for orthopedic treatment. The disabilities of the arm, shoulder, and hand questionnaire was used to assess upper limb functionality. Pain perception was assessed using a visual analog scale. Exercise-based physiotherapy interventions were performed according to the clinical needs of the patients for at least 6 weeks (2-3 sessions per week). For the treatment of radial instability (n = 13), strengthening exercises of the abductor pollicis longus, extensor carpi radialis longus, flexor carpi radialis, and pronator quadratus muscles were prescribed. For the treatment of ulnar instability (n = 24), extensor carpi ulnaris and pronator quadratus were trained.

All patients underwent proprioceptive training in open kinetic chain and closed kinetic chain, as well as strengthening of the unaffected hand. Changes before and after treatment were compared using the nonparametric Wilcoxon signed rank test. Results: A significant improvement with a large effect size in disabilities of the arm, shoulder, and hand ($P < .001$; $d = 2.9$) and visual analog scale ($P < .001$; $d = 3.2$) scores were obtained after treatment. Moreover, the changes were greater than the minimal clinically important difference of 10.8 and 1.4, respectively. Similar results were found when patients with radial instability and ulnar instability were analyzed separately. Conclusions: Personalized training with specific proprioception and strengthening exercises produces improvements in functionality and pain perception in our cohort of people with carpal instability. These results highlight the importance of multicomponent exercise in the treatment of wrist instability. Future randomized clinical trials should further investigate the effectiveness of this protocol.

**REV MED CHIL. 2024 JUL;152(7):776-786. DOI: 10.4067/S0034-98872024000700776.**

ASOCIACIÓN ENTRE TRASTORNOS DEL EQUILIBRIO, SEVERIDAD DE FIBROMIALGIA Y CONFIANZA EN EL EQUILIBRIO: UN ESTUDIO OBSERVACIONAL SOBRE FIBROMIALGIA

Daniela Sandoval Navarrete, Michelle Levenier Gonzalez, Ariel Castro Lara, Antonia Elgueta Rosales

La fibromialgia es un síndrome de dolor crónico generalizado asociado a fatiga, trastornos del sueño y una amplia gama de síntomas adicionales, entro los cuales los trastornos de equilibrio son una queja frecuente. Objetivo: Determinar la existencia de una correlación entre trastornos del equilibrio y la severidad de la fibromialgia. Metodología: Se llevó a cabo un estudio observacional de corte transversal en la Unidad de Tratamiento del Dolor (UTD) del Hospital Clínico Universidad de Chile (HCUCH). Se utilizó la Escala de Berg (BBS) para evaluar los trastornos del equilibrio, el Fibromyalgia Impact Questionnaire (FIQ) para medir la severidad de la fibromialgia, y el Activities Specific Balance Confidence (ABC-16) para evaluar la confianza en el equilibrio. Resultados: Se reclutaron un total de 35 pacientes (97.14% mujeres), con una edad media de 50.97 años. El 97.14% de los pacientes presentó un impacto moderado a severo en el FIQ-R. La puntuación media obtenida en la Escala de Berg fue de 49.57 puntos, revelando una correlación negativa significativa entre el FIQ y el BBS (rPearson= −0.64; −0.70). La puntuación media obtenida en el ABC-16 fue del 47%, presentando una correlación moderada con la puntuación de la BBS (rPearson= 0.54). El 54.29% de los pacientes informó haber experimentado una o más caídas en los últimos 6 meses. Conclusión: Se encontró una correlación inversa significativa entre los trastornos de equilibrio y la severidad del impacto de la fibromialgia. Además, se observó una correlación moderada entre la confianza en el equilibrio y los puntajes de la Escala de Berg.

## DEPARTAMENTO NEUROLOGÍA Y NEUROCIRUGÍA

**AMYOTROPH LAT SCL FR. 2024 AUG;25(5-6):528-532. DOI: 10.1080/21678421.2024.2329706.**

INCIDENCE OF AMYOTROPHIC LATERAL SCLEROSIS IN CHILE

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Objective: This study aimed to estimate amyotrophic lateral sclerosis (ALS) incidence and survival rates in the Metropolitan region of Chile. Methods: We conducted a cohort study of ALS cases in the Metropolitan Region from 2016 to 2019. A total of 219 ALS patients were recruited from Corporación ELA-Chile registry, in collaboration with neurologists from Sociedad de Neurología, Psiquiatría y Neurocirugía de Chile. We calculated incidence rates by sex and age and determined median survival from onset and diagnosis. Survival analysis used the Kaplan-Meier statistic, estimating hazard ratios for age, sex, time from symptom onset and from diagnosis using a Weibull regression model. All analyses were done using R 4.1.0. Results: Overall, ALS diagnosis incidence was 0.97 cases per 100,000 inhabitants, peaking in the 70-79 age group and declining thereafter. The male-to-female ratio was 1.23. The median time to death from diagnosis was 2.3 years (95% confidence interval [CI]: 1.9-2.5), and from the first symptom, it was 3.1 years (95% CI: 2.8-3.5). Conclusions: This is the first population-based study reporting ALS incidence and survival rates in Chile's Metropolitan region. Incidence resembled other Latin American studies. Median survival from diagnosis and from the first symptom were in line with previous findings. Our results corroborated lower ALS rates in Latin America, consistent with prior research.

**FRONT GENET. 2024 NOV 29:15:1477291. DOI: 10.3389/FGENE.2024.1477291.**

DETECTION OF GENE VARIANTS ASSOCIATED WITH RECESSIVE LIMB-GIRDLE MUSCULAR WEAKNESS AND POMPE DISEASE IN A GLOBAL COHORT OF PATIENTS THROUGH THE APPLICATION OF NEXT-GENERATION SEQUENCING ANALYSIS

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Introduction: Hereditary myopathies arise due to numerous pathogenic variants occurring in distinct genes, which amount to several hundred. Limb-girdle muscular dystrophies (LGMDs) constitute a heterogeneous group of neuromuscular disorders

involving more than 30 genes. Clinically, LGMD is characterized by limb-girdle muscular weakness (LGMW). Late-onset Pompe disease is an important disorder with a differential diagnosis for LGMD, where next-generation sequencing (NGS) plays a crucial role in accurate and prompt diagnosis. The sensitivity and specificity of a 10-gene NGS panel have been previously evaluated for the prevalent forms of recessive LGMD (LGMD-R) and Pompe disease in Latin American patients with LGMW of unknown cause. This project aims to identify the regional relative prevalence of frequent LGMD-R subtypes and Pompe disease in a larger geographic area and to diagnose patients with LGMW by identifying genetic variants of LGMD-R and Pompe disease. Methods and results: This 21-country multicentric analysis enrolled 2,372 patients with LGMW from 2017 to 2018. Sequencing analysis was performed using the Illumina NextSeq 500 system, and variant interpretation was performed according to the American College of Medical Genetics and Genomics guidelines. Pathogenic or likely pathogenic variants were seen in 11% of patients (n = 261). Among the positive cases, NGS effectively diagnosed 86.2% and 13.8% of patients with LGMD and Pompe disease, respectively. The most prevalent pathogenic acid $\alpha$-glucosidase (GAA) variant identified was c.-32-13T > G. Conclusion: The study adds to the knowledge of the relative occurrence of various subtypes of LGMD worldwide. The inclusion of GAA in the NGS panel to investigate patients with LGMW is a powerful diagnostic approach to screen for late-onset Pompe disease.

**NAT MED. 2024 DEC;30(12):3646-3657. DOI: 10.1038/S41591-024-03209-X.**

BRAIN CLOCKS CAPTURE DIVERSITY AND DISPARITIES IN AGING AND DEMENTIA ACROSS GEOGRAPHICALLY DIVERSE POPULATIONS

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Brain clocks, which quantify discrepancies between brain age and chronological age, hold promise for understanding brain health and disease. However, the impact of diversity (including geographical, socioeconomic, sociodemographic, sex and neurodegeneration) on the brain-age gap is unknown. We analyzed datasets from 5,306 participants across 15 countries (7 Latin American and Caribbean countries (LAC) and 8 non-LAC countries). Based on higher-order interactions, we developed a brain-age gap deep learning architecture for functional magnetic resonance imaging (2,953) and electroencephalography (2,353). The datasets comprised healthy controls and individuals with mild cognitive impairment, Alzheimer disease and behavioral variant frontotemporal dementia. LAC models evidenced older brain ages (functional magnetic resonance imaging: mean directional error = 5.60, root mean square error (r.m.s.e.) = 11.91; electroencephalography: mean directional error = 5.34, r.m.s.e. = 9.82) associated with frontoposterior networks compared with non-LAC models. Structural socioeconomic inequality, pollution and health disparities were influential predictors of increased brain-age gaps, especially in LAC ($R^2$ = 0.37, $F^2$ = 0.59, r.m.s.e. = 6.9). An ascending brain-age gap from healthy controls to mild cognitive impairment to Alzheimer disease was found. In LAC, we observed larger brain-age gaps in females in control and Alzheimer disease groups compared with the respective males. The results were not explained by variations in signal quality, demographics or acquisition methods. These findings provide a quantitative framework capturing the diversity of accelerated brain aging.

**CUREUS. 2024 OCT 10;16(10):E71231. DOI: 10.7759/CUREUS.71231.**

CHONDROMATOSIS OF THE LUMBAR SPINE: MINIMALLY INVASIVE SPINE SURGERY FOR THIS RARE CONDITION

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Synovial chondromatosis (SC) is a rare, benign disease. It usually occurs in large joints such as the hip and knee. Few cases have been reported in the spine, especially in the lumbar spine. It is characterized by the presence of clusters of chondrocytes within the joints and free in the joint cavity. The main symptom is pain. Diagnosis requires a high level of suspicion, and malignancy must always be ruled out. Surgical management is a challenge. We present the case of a patient with an extensive spinal tumor that was managed under the principles of minimal spinal invasion. The exeresis was performed in three different surgical times, achieving the total exeresis of the tumor with low morbidity.

**EPILEPSIA OPEN. 2024 APR;9(2):776-784. DOI: 10.1002/EPI4.12900.**

CAUSES AND PROGNOSIS OF ADULTS EXPERIENCING A FIRST SEIZURE IN ADULTHOOD: A PILOT COHORT STUDY CONDUCTED IN FIVE COUNTRIES IN LATIN AMERICA

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There are limited data on first seizure (FS) among adults in low and middle-income countries. We describe findings from a prospective cohort study involving 180 adults presenting with seizures in emergency departments in five Latin American countries. Overall, 102 participants (56.7%) had acute symptomatic seizures (ASyS) while 78 (43.3%) had unprovoked seizures (UPS). Among patients with ASyS, 55 (53.9%) had structural causes, with stroke (n = 24, 23.5%), tumor (n = 10, 9.8%), and trauma (n = 3, 3%) being the most frequent. Nineteen patients (18.6%) had infectious causes, including four (4%) with meningoencephalitis, three (3%)

neurocysticercosis, and two (2%) bacterial meningoencephalitis. Twenty patients (19.6%) had metabolic/toxic evidence, including four (4%) with uremic encephalopathy, two (2%) hyponatremia, and three (3%) acute alcohol intoxication. Immune dysfunction was present in seven (7%) patients and neurodegenerative in two (2%). Among participants with UPS, 45 (57.7%) had unknown etiology, 24 (30.7%) had evidence of structural disorders (remote symptomatic), four (5%) were related to infectious etiology (>7 days before the seizure), and five (6.4%) had genetic causes. During the 3- and 6-month follow-up, 29.8% and 14% of patients with UPS, respectively, experienced seizure recurrence, while 23.9% and 24.5% of patients with ASyS had seizure recurrence. Longer follow-up is necessary to assess seizure recurrence for patients with ASyS after the acute cause is resolved and to determine the 10-year risk of recurrence, which is part of the definition of epilepsy. PLAIN LANGUAGE SUMMARY: We monitored 180 adults who presented with their first seizure in emergency departments across five Latin American countries. Among these patients, 57% had acute symptomatic seizures, with structural causes such as stroke (23%), infection (17%), or tumor (10%) being more prevalent. Among the 43% with unprovoked seizures, 58% showed no identifiable acute cause, while 6.4% were due to genetics. Within 3 months after their initial seizure, 26.6% of individuals experienced a second seizure, with 11.9% continuing to have seizures in Months 3-6. Between Months 3 and 6, an additional 20% of patients encountered a second seizure. Research is needed to better understand the cause and prognosis of these patients to improve outcomes.

**NEUROSCI. 2024 OCT 12;5(4):462-484. DOI: 10.3390/NEUROSCI5040034.**

EXPLORING NEUROPROTECTION AGAINST RADIATION-INDUCED BRAIN INJURY: A REVIEW OF KEY COMPOUNDS

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Brain radiation is a crucial tool in neuro-oncology for enhancing local tumor control, but it can lead to mild-to-profound and progressive impairments in cognitive function. Radiation-induced brain injury is a significant adverse effect of radiotherapy for cranioencephalic tumors, primarily caused by indirect cellular damage through the formation of free radicals. This results in late neurotoxicity manifesting as cognitive impairment due to free radical production. The aim of this review is to highlight the role of different substances, such as drugs used in the clinical setting and antioxidants such as ascorbate, in reducing the neurotoxicity associated with radiation-induced brain injury. Currently, there is mainly preclinical and clinical evidence supporting the benefit of these interventions, representing a cost-effective and straightforward neuroprotective strategy.

**J PERS MED. 2024 MAY 28;14(6):578. DOI: 10.3390/JPM14060578.**

SELF-REPORTED SLEEP DURATION IS A USEFUL TOOL TO PREDICT SARCOPENIA IN CHILEAN OLDER ADULTS: EVIDENCE FROM THE ALEXANDROS LONGITUDINAL STUDY

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Age-related sleep disorders share common pathways with sarcopenia. Prospective data from Latin American populations are scarce, and the association between sleep disorders and sarcopenia in Chileans remains unknown. Thus, we aimed to study the longitudinal association between sleep disorders and sarcopenia in a cohort study of 1116 community-dwelling Chilean older people ≥60 years old from the ALEXANDROS cohorts. After the exclusion criteria, 318 subjects were followed. Sociodemographic data, self-reported chronic diseases, sedentarism, sleep characteristics, anthropometric measurements, handgrip strength, and muscle performance were assessed. Results indicated that at baseline, the prevalence of sarcopenia was 24.10% without gender differences, and the prevalence of self-reported sleep problems was 23.3%, higher in women (26.46% versus 17.15% in men). The adjusted Cox regression models for sarcopenia showed an association between sarcopenia, sleep disorders (HR = 2.08, 95% IC 1.14-3.80), and long sleep duration (HR = 2.42, 95% IC 1.20-4.91). After 8.24 years of follow-up, there were 2.2 cases of sarcopenia per 100 person-years. This study demonstrates that sleep disorders are an independent risk factor for sarcopenia in Chilean older people. The identification of sleep disorders through self-reported data provides an opportunity for early identification of risk and cost-effective sarcopenia prevention.

**TRENDS CANCER. 2024 DEC;10(12):1161-1173. DOI: 10.1016/J.TRECAN.2024.09.011.**

THE UPRISING CONNECTION BETWEEN ENDOPLASMIC RETICULUM STRESS AND THE TUMOR MICROENVIRONMENT

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The tumor microenvironment (TME) represents a dynamic network of cancer cells, stromal cells, immune mediators, and extracellular matrix components, crucial for cancer progression. Stress conditions such as oncogene activation, nutrient deprivation, and hypoxia disrupt the endoplasmic reticulum (ER), activating the unfolded protein response (UPR), the main adaptive mechanism to restore ER function. The UPR regulates cancer progression by engaging cell-autonomous and cell-non-autonomous mechanisms, reprogramming the stroma and promoting immune evasion, angiogenesis, and invasion. This review explores the role of UPR beyond cancer cells, focusing on how ER stress signaling reshapes the TME, supporting tumor growth. The therapeutic potential of targeting the UPR is also discussed.

**EPILEPSY BEHAV REP. 2024 AUG 8:27:100703. DOI: 10.1016/J.EBR.2024.100703.**

OPERCULAR MYOCLONIC-ANARTHRIC STATUS (OMASE) SECONDARY TO ANTI-HU PARANEOPLASTIC NEUROLOGICAL SYNDROME

César Romero, Alonso Quijada, Gabriel Abudinén, Catherine Céspedes, Ledda Aguilera

Focal Opercular Myoclonic - Anarthric Status Epilepticus (OMASE) is a rare form of focal motor status epilepticus caused by several etiologies. It is characterized by fluctuating dysarthria and epileptic myoclonus involving the bilateral glossopharyngeal musculature. We present the case of a 52-year-old woman who experienced gradual and progressive paralysis and myoclonus of facial and bulbar muscles; additional tests revealed the presence of right breast ductal adenocarcinoma and positive serum anti-Hu and anti-GAD65 antibodies. High doses of steroid pulses, anti-seizure therapy, and rituximab partially controlled myoclonus; the tumor resection improved dysphagia and dysarthria.

**FRONT NEUROL. 2024 SEP 23;15:1481563. DOI: 10.3389/FNEUR.2024.1481563.**

CORRIGENDUM: DIRECT ORAL ANTICOAGULANTS FOR THE TREATMENT OF CEREBRAL VENOUS THROMBOSIS - A PROTOCOL OF AN INTERNATIONAL PHASE IV STUDY.

Van de Munckhof A, Sánchez van Kammen M, Krzywicka K, Aaron S, Aguiar de Sousa D, Antochi F, Arauz A, Barboza MA, Conforto AB, Dentali F, Galdames Contreras D *et al*.

Introduction: Current guidelines recommend that patients with cerebral venous thrombosis (CVT) should be treated with vitamin K antagonists (VKAs) for 3-12 months. Direct oral anticoagulants (DOACs), however, are increasingly used in clinical practice. An exploratory randomized controlled trial including 120 patients with CVT suggested that the efficacy and safety profile of dabigatran (a DOAC) is similar to VKAs for the treatment of CVT, but large-scale prospective studies from a real-world setting are lacking. Methods: DOAC-CVT is an international, prospective, observational cohort study comparing DOACs to VKAs for the prevention of recurrent venous thrombotic events after acute CVT. Patients are eligible if they are 18 years or older, have a radiologically confirmed CVT, and have started oral anticoagulant treatment (DOAC or VKA) within 30 days of CVT diagnosis. Patients with an absolute contra-indication for DOACs, such as pregnancy or severe renal insufficiency, are excluded from the study. We aim to recruit at least 500 patients within a three-year recruitment period. The primary endpoint is a composite of recurrent venous thrombosis and major bleeding at 6 months of follow-up. We will calculate an adjusted odds ratio for the primary endpoint using propensity score inverse probability treatment weighting. Discussion: DOAC-CVT will provide real-world data on the comparative efficacy and safety of DOACs versus VKAs for the treatment of CVT.

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**REVISTA ESPAÑOLA DE LINGÜÍSTICA APLICADA, VOLUME 37, ISSUE 2, MAY 2024, P. 720 – 746. DOI: 10.1075/RESLA.22033.MEZ**

ESTUDIO CORRELACIONAL DEL GÉNERO FICHA CLÍNICA UN ANÁLISIS MULTIDIMENSIONAL E INTERDISCIPLINARIO

Paulina Meza, Fernando Lillo-Fuentes, Erlantz Velasco, Carlos Silva-Rosas

Nuestro objetivo es relacionar los rasgos lingüísticos, la calidad lingüístico-discursiva, la evaluación disciplinar y la percepción de autoeficacia en escritura en el género Ficha Clínica. En este estudio correlacional, se analizó un corpus de 52 Fichas Clínicas, producidas por estudiantes de Medicina de una universidad chilena, quienes, además, respondieron un cuestionario

de percepción de autoeficacia en escritura. La evaluación disciplinar se obtuvo a partir de la calificación del texto por parte de médicos-docentes. Para el análisis de la calidad lingüístico-discursiva se diseñó y validó un instrumento específico (Rúbrica para Evaluar la Calidad Lingüístico-Discursiva de Textos Disciplinares en Medicina). Los resultados muestran correlaciones estadísticamente significativas entre la evaluación realizada por los médicos y la calidad lingüístico-discursiva. La percepción de autoeficacia no presenta correlaciones significativas con ninguna de estas variables. En conclusión, la investigación representa un avance importante en la descripción del género Ficha Clínica desde una perspectiva multidimensional e interdisciplinaria.

# DEPARTAMENTO OBSTETRICIA Y GINECOLOGÍA

**EUR J OBSTET GYNECOL REPROD BIOL. 2024 DEC:303:116-122. DOI: 10.1016/J.EJOGRB.2024.10.025.**

LAPAROSCOPIC CERVICO-ISTHMIC CERCLAGE: A "NEEDLE-FREE" APPROACH FOR MANAGING CERVICAL INSUFFICIENCY IN PREGNANT AND NON-PREGNANT PATIENTS

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This video-article describes a laparoscopic cervico-isthmic cerclage technique for managing cervical insufficiency in both pregnant and non-pregnant patients, utilizing a port-site closure device for precise suture placement. Two cases-one non-pregnant and one at 12 weeks gestation-underwent the procedure, with details on trocar placement, dissection, and suture passage documented. Both surgeries were completed successfully, with minimal blood loss and no complications. The use of the port-site closure device allowed for precise suture placement near the uterine vessels, contributing to favorable postoperative outcomes. This laparoscopic approach offers a minimally invasive alternative to the open technique in specialized centers.

**CLIMACTERIC. 2024 JUN;27(3):269-274. DOI: 10.1080/13697137.2024.2306278.**

GENITOURINARY SYMPTOMS AND SEXUAL FUNCTION IN WOMEN WITH PRIMARY OVARIAN INSUFFICIENCY

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Objective: There are limited studies on urogenital symptoms in women who experience menopause before the age of 40 years due to primary ovarian insufficiency (POI) or bilateral oophorectomy (surgical POI). This study aimed to compare the urogenital symptoms, including sexuality, of women with POI to those without the condition. Methods: This cross-sectional study conducted was in seven Latin American countries, in which postmenopausal women (with POI and non-POI) were surveyed with a general questionnaire, the Menopause Rating Scale (MRS) and the six-item Female Sexual Function Index (FSFI-6). The association of premature menopause with more urogenital symptoms and lower sexual function was evaluated with logistic regression analysis. Results: Women with POI experience more urogenital symptoms (MRS urogenital score: 3.54 ± 3.16 vs. 3.15 ± 2.89, $p < 0.05$) and have lower sexual function (total FSFI-6 score: 13.71 ± 7.55 vs. 14.77 ± 7.57 $p < 0.05$) than women who experience menopause at a normal age range. There were no significant differences in symptoms when comparing women based on the type of POI (idiopathic or surgical). After adjusting for covariates, our logistic regression model determined that POI is associated with more urogenital symptoms (odds ratio [OR]: 1.38, 95% confidence interval [CI] 1.06-1.80) and lower sexual function (OR: 1.67, 95% CI 1.25-2.25). Conclusion: POI, whether idiopathic or secondary to bilateral oophorectomy, is associated with symptoms that affect vaginal and sexual health.

**PEDIATR CARDIOL. 2024 DEC;45(8):1729-1740. DOI: 10.1007/S00246-023-03265-Z.**

EARLY-ONSET FETAL GROWTH RESTRICTION INCREASES LEFT VENTRICULAR SPHERICITY IN ADOLESCENTS BORN VERY PRETERM

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Left ventricular shape alterations predict cardiovascular outcomes and have been observed in children born preterm and after fetal growth restriction (FGR). The aim was to investigate whether left ventricular shape is altered in adolescents born very preterm and if FGR has an additive effect. Adolescents born very preterm due to verified early-onset FGR and two control groups with birthweight appropriate for gestational age (AGA), born at similar gestational age and at term, respectively, underwent cardiac MRI. Principal component analysis was applied to find the modes of variation best explaining shape variability for end-diastole, end-systole, and for the combination of both, the latter indicative of function. Seventy adolescents were included (13-16 years; 49% males). Sphericity was increased for preterm FGR versus term AGA for end-diastole (36[0-60] vs - 42[- 82-8]; $p = 0.01$) and the combined analysis (27[- 23-94] vs - 51[- 119-11]; $p = 0.01$), as well as for preterm AGA versus term AGA for end-diastole (30[- 56-115] vs - 42[- 82-8]; $p = 0.04$), for end-systole (57[- 29-89] vs - 30[- 79-34]; $p = 0.03$), and the combined analysis (44[- 50-145] vs - 51[- 119-11]; $p = 0.02$). No group differences were observed for left ventricular mass or ejection fraction (all $p \geq 0.33$). Sphericity was increased after very preterm birth and exacerbated by early-onset FGR, indicating an additive effect to that of very preterm

birth on left ventricular remodeling. Increased sphericity may be a prognostic biomarker of future cardiovascular disease in this cohort that as of yet shows no signs of cardiac dysfunction using standard clinical measurements.

**MENOPAUSE. 2024 JUL 1;31(7):641-646. DOI: 10.1097/GME.0000000000002367.**

ASSOCIATION OF MUSCLE DISORDERS IN LATE POSTMENOPAUSAL WOMEN ACCORDING TO THE TYPE OF EXPERIENCED MENOPAUSE

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Objective: Musculoskeletal disorders frequently affect postmenopausal women. This study aims to compare muscle disorders between women according to the type of experienced menopause: premature (PM) or normal age of menopause (NAM). Methods: This was a cross-sectional study conducted in nine Latin American countries in which late postmenopausal women (55 to 70 years) were surveyed with a general questionnaire, the Menopause Rating Scale (MRS: item #4 exploring musculoskeletal discomfort), and strength, assistance with walking, rising from a chair, climbing stairs, and falling questionnaire (risk of sarcopenia). Results: A total of 644 women were included: 468 who had NAM, and 176 who had PM (116 spontaneous and 60 surgical). The overall mean age of the participants was 60.9 ± 4.2 years. Women who had PM experienced more musculoskeletal discomfort (33.5% vs 20.9%, P < 0.001) and a higher likelihood of sarcopenia (35.2% vs 19.9%, P < 0.001) than women who had a NAM. Women who had surgical PM exhibited a higher prevalence of severe musculoskeletal discomfort (46.7% vs 29.3%, P < 0.02) and a higher likelihood of sarcopenia (45.0% vs 27.6%, P < 0.02) than women who had a NAM. After adjusting for covariates (age, body mass index, menopausal hormone therapy use, physical activity, education, cigarette consumption, use of antidepressants, sexual activity, comorbidities, and having a partner), our logistic regression model determined that spontaneous PM was not associated with higher odds of musculoskeletal discomfort and higher odds of sarcopenia. On the other hand, women who had surgical PM were more likely to experience musculoskeletal discomforts (odds ratio: 2.26; 95% confidence interval: 1.22-4.17) and higher odds for sarcopenia (odds ratio: 2.05; 95% confidence interval: 1.16-3.65) as compared to women who experienced a NAM. Conclusions: Women experiencing surgical PM have a higher likelihood of developing muscle disorders. This underscores the potential significance of hormonal levels in influencing musculoskeletal health during postmenopause.

**LANCET. 2024 FEB 10;403(10426):545-553. DOI: 10.1016/S0140-6736(23)02228-6.**

TERM PLANNED DELIVERY BASED ON FETAL GROWTH ASSESSMENT WITH OR WITHOUT THE CEREBROPLACENTAL RATIO IN LOW-RISK PREGNANCIES (RATIO37): AN INTERNATIONAL, MULTICENTRE, OPEN-LABEL, RANDOMISED CONTROLLED TRIAL

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Background: The cerebroplacental ratio is associated with perinatal mortality and morbidity, but it is unknown whether routine measurement improves pregnancy outcomes. We aimed to evaluate whether the addition of cerebroplacental ratio measurement to the standard ultrasound growth assessment near term reduces perinatal mortality and severe neonatal morbidity, compared with growth assessment alone. Methods: RATIO37 was a randomised, open-label, multicentre, pragmatic trial, conducted in low-risk pregnant women, recruited from nine hospitals over six countries. The eligibility criteria were designed to be broad; participants were required to be 18 years or older, with an ultrasound-dated confirmed singleton pregnancy in the first trimester, an alive fetus with no congenital malformations at the routine second-trimester ultrasound, an absence of adverse medical or obstetric history, and the capacity to give informed consent. Women were randomly assigned in a 1:1 ratio (block size 100) using a web-based system to either the concealed group or revealed group. In the revealed group, the cerebroplacental ratio value was known by clinicians, and if below the fifth centile, a planned delivery after 37 weeks was recommended. In the concealed group, women and clinicians were blinded to the cerebroplacental ratio value. All participants underwent ultrasound at 36 + 0 to 37 + 6 weeks of gestation with growth assessment and Doppler evaluation. In both groups, planned delivery was recommended when the estimated fetal weight was below the tenth centile. The primary outcome was perinatal mortality from 24 weeks' gestation to infant discharge. The study is registered at ClinicalTrials.gov (NCT02907242) and is now closed. Findings: Between July 29, 2016, and Aug 3, 2021, we enrolled 11 214 women, of whom 9492 (84·6%) completed the trial and were eligible for analysis (4774 in the concealed group and 4718 in the revealed group). Perinatal mortality occurred in 13 (0·3%) of 4774 pregnancies in the concealed group and 13 (0·3%) of 4718 in the revealed group (OR 1·45 [95% CI 0·76-2·76]; p=0·262). Overall, severe neonatal morbidity occurred in 35 (0·73%) newborns in the concealed group and 18 (0·38%) in the revealed group (OR 0·58 [95% CI 0·40-0·83]; p=0·003). Severe neurological morbidity occurred in 13 (0·27%) newborns in the concealed group and nine (0·19%) in the revealed group (OR 0·56 [95% CI 0·25-1·24]; p=0·153). Severe non-neurological morbidity occurred in 23 (0·48%) newborns in the concealed group and nine (0·19%) in the revealed group (0·58 [95% CI 0·39-0·87]; p=0·009). Maternal adverse events were not collected. Interpretation: Planned delivery at term based on ultrasound fetal growth assessment and cerebroplacental ratio at term was not followed by a reduction of perinatal mortality although significantly reduced severe neonatal morbidity compared with fetal growth assessment alone. Funding: La Caixa foundation, Cerebra Foundation for the Brain Injured Child, Agència per la Gestió d'Ajuts Universitaris i de Recerca, and Instituto de Salud Carlos III.

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SEVERE MENOPAUSAL SYMPTOMS LINKED TO COGNITIVE IMPAIRMENT: AN EXPLORATORY STUDY

Andrés Calle, Juan E Blümel, Peter Chedraui, María S Vallejo, Alejandra Belardo, Maribel Dextre, Alejandra Elizalde-Cremonte, Carlos Escalante, María T Espinoza, Gustavo Gómez-Tabares, Álvaro Monterrosa-Castro, Mónica Ñañez, Eliana Ojeda, Claudia Rey, Doris Rodríguez, Marcio A Rodrigues, Carlos Salinas, Konstantinos Tserotas, Sócrates Aedo

Objective: To evaluate the association between menopausal symptoms and cognitive decline in postmenopausal women. Methods: This was a subanalysis of a cross-sectional, observational study conducted among women attending gynecological consultations across nine Latin American countries. The survey involved late postmenopausal women who were asked to complete a general questionnaire and the Menopause Rating Scale (MRS) to assess menopausal symptoms, with the Montreal Cognitive Assessment used to evaluate cognitive function as an outcome. A Montreal Cognitive Assessment score of less than 21 was used to define women with mild cognitive impairment (MCI). Results: The study included 1,287 postmenopausal women with a mean age of 55.5 years and a mean body mass index of 26.3 kg/m 2 . On average, participants had 13.8 years of education and 2.3 ± 1.8 children, with 72.8% reporting having a partner. Additionally, 36.7% ever used menopausal hormone therapy. Regarding lifestyle factors, 50.3% engaged in a sedentary lifestyle, whereas 70.5% had never smoked. 15.3% of women had MCI exhibited significantly more intense menopausal symptoms compared with those without MCI (MRS total score 15.24 ± 12.58 vs 10.53 ± 8.84, respectively, P < 0.001). Logistic regression analysis revealed a significant association between severe menopausal symptoms (MRS total score ≥14 points) and MCI (odds ratio [OR], 1.74; 95% CI, 1.25-2.42). Conversely, a lower body mass index (OR, 0.96; 95% CI, 0.95-0.98), sexual activity (OR, 0.70; 95% CI, 0.51-0.96), physical exercise (OR, 0.55; 95% CI, 0.39-0.76), menopausal hormone therapy use (OR, 0.36; 95% CI, 0.24-0.55), and higher educational level (OR, 0.31; 95% CI, 0.21-0.46) were associated with lower odds for MCI. Conclusion: Severe menopausal symptoms in postmenopausal women were associated with cognitive impairment. This study highlights the intricate interplay between hormonal, lifestyle, and sociodemographic factors and cognitive health.

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ASSOCIATION BETWEEN TYPE OF MENOPAUSE AND MILD COGNITIVE IMPAIRMENT: THE REDLINC XII STUDY

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Objective: To evaluate the association between type of menopause (spontaneous or surgical) and mild cognitive impairment (MCI). Study design: This study was a cross-sectional, observational, and sub-analytical investigation conducted within gynecological consultations across nine Latin American countries. Method: We assessed sociodemographic, clinical, and anthropometric data, family history of dementia, and the presence of MCI using the Montreal Cognitive Assessment (MoCA) tool. Results: The study involved 1185 postmenopausal women with a mean age of 55.3 years and a body mass index of 26.4 kg/m2. They had an average of 13.3 years of education, and 37 % were homemakers. Three hundred ninety-nine experienced menopause before 40, including 136 with surgical menopause (bilateral oophorectomy). Out of the 786 women who experienced menopause at 40 or more years, 110 did so due to bilateral oophorectomy. There were no differences in MoCA scores among women who experienced menopause before or after the age of 40. However, lower MoCA scores were observed in women with surgical menopause than in those with spontaneous menopause (23.8 ± 4.9 vs. 25.0 ± 4.3 points, respectively, p < 0.001). Our logistic regression model with clustering of patients within countries found a significant association between MCI and surgical menopause (OR 1.47, 95 % CI: 1.01-2.16), use (ever) of menopausal hormone therapy (OR 0.33, 95 % CI: 0.21-0.50), and having >12 years of education (OR 0.21, 95 % CI: 0.14-0.30). Conclusion: When comparing women who experience spontaneous menopause over the age of 40 with those who undergo it before this age, there was no observed increased risk of developing MCI, while those with surgical menopause, independent of age, are more prone to cognitive decline. Women who have ever used menopausal hormone therapy have a lower MCI risk. Further research is warranted to delve deeper into this topic.

## LABORATORIO ENDOCRINOLOGÍA Y BIOLOGÍA DE LA REPRODUCCIÓN

**CELLS. 2024 SEP 19;13(18):1578. DOI: 10.3390/CELLS13181578.**

EPSTEIN-BARR VIRUS BARF1 IS EXPRESSED IN LUNG CANCER AND IS ASSOCIATED WITH CANCER PROGRESSION

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Background: Epstein-Barr virus (EBV) is involved in the development of lymphomas, nasopharyngeal carcinomas (NPC), and a subgroup of gastric carcinomas (GC), and has also been detected in lung carcinomas, even though the role of the virus in this malignancy has not yet been established. BamH1-A Rightward Frame 1 (BARF1), a suggested exclusive epithelial EBV oncoprotein, is detected in both EBV-associated GCs (EBVaGC) and NPC. The expression and role of BARF1 in lung cancer is unknown. Methods: A total of 158 lung carcinomas including 80 adenocarcinomas (AdCs) and 78 squamous cell carcinomas (SQCs) from Chilean

patients were analyzed for EBV presence via polymerase chain reaction (PCR), Immunohistochemistry (IHC), or chromogenic in situ hybridization (CISH). The expression of BARF1 was evaluated using Reverse Transcription Real-Time PCR (RT-qPCR). Additionally, A549 and BEAS-2B lung epithelial cells were transfected with a construct for ectopic BARF1 expression. Cell proliferation, migration, invasion, and epithelial-mesenchymal transition (EMT) were evaluated. Results: We found that EBV was present in 37 out of 158 (23%) lung carcinomas using PCR. Considering EBV-positive specimens using PCR, IHC for Epstein-Barr nuclear antigen 1 (EBNA1) detected EBV in 24 out of 30 (80%) cases, while EBERs were detected using CISH in 13 out of 16 (81%) cases. Overall, 13 out of 158 (8%) lung carcinomas were shown to be EBV-positive using PCR/IHC/CISH. BARF1 transcripts were detected in 6 out of 13 (46%) EBV-positive lung carcinomas using RT qPCR. Finally, lung cells ectopically expressing BARF1 showed increased migration, invasion, and EMT. Conclusions: EBV is frequently found in lung carcinomas from Chile with the expression of BARF1 in a significant subset of cases, suggesting that this viral protein may be involved in EBV-associated lung cancer progression.

**BIOLOGY (BASEL). 2024 DEC 20;13(12):1078. DOI: 10.3390/BIOLOGY13121078.**

GENES ASSOCIATED WITH THE IMMUNE SYSTEM AFFECTED BY IONIZING RADIATION AND ESTROGEN IN AN EXPERIMENTAL BREAST CANCER MODEL

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Breast cancer is a global health issue that, when in the metastasis stage, is characterized by the lack of estrogen receptor-$\alpha$, the progesterone receptor, and human epidermal growth receptor expressions. The present study analyzed the differential gene expression related to the immune system affected by ionizing radiation and estrogen in cell lines derived from an experimental breast cancer model that was previously developed; where the immortalized human breast epithelial cell line MCF-10F, a triple-negative breast cancer cell line, was exposed to low doses of high linear energy transfer $\alpha$ particle radiation (150 keV/µm), it subsequently grew in the presence or absence of 17$\beta$-estradiol. Results indicated that interferon-related developmental regulator 1 gene expression was affected in the estrogen-treated cell line; this interferon, as well as the Interferon-Induced Transmembrane protein 2, and the TNF alpha-induced Protein 6 gene expression levels were higher than the control in the Alpha3 cell line. Furthermore, the interferon-related developmental regulator 1, the Interferon-Induced Transmembrane protein 2, the TNF alpha-induced Protein 6, the Nuclear Factor Interleukin 3-regulated, and the Interferon-Gamma Receptor 1 showed high expression levels in the Alpha5 cell line, and the Interferon Regulatory Factor 6 was high in the Tumor2 cell line. Additionally, to further strengthen these data, publicly available datasets were analyzed. This analysis was conducted to assess the correlation between estrogen receptor alpha expression and the genes mentioned above in breast cancer patients, the differential gene expression between tumor and normal tissues, the immune infiltration level, the ER status, and the survival outcome adjusted by the clinical stage factor. It can be concluded that the genes of the interferon family and Tumor Necrosis factors can be potential therapeutic targets for breast cancer, since they are active before tumor formation as a defense of the body under radiation or estrogen effects.

## SERVICIO OFTALMOLOGÍA

**OCUL IMMUNOL INFLAMM. 2024 OCT;32(8):1819-1831. DOI: 10.1080/09273948.2023.2296030.**

NON-INFECTIOUS UVEITIS AND PREGNANCY, IS THERE AN OPTIMAL TREATMENT? UVEITIS COURSE AND SAFETY OF UVEITIS TREATMENT IN PREGNANCY

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In pregnancy, a plethora of factors causes changes in maternal immunity. Uveitis flare-ups are more frequent in the first trimester and in undertreated patients. Management of non-infectious uveitis during pregnancy remains understudied. A bibliographic review to consolidate existing evidence was performed by a multidisciplinary group of Ophthalmologists, Gynaecologists and Rheumatologists. Our group recommends initial management with minimum-required doses of corticosteroids, preferably locally, to treat intraocular inflammation whilst ensuring good neonatal outcomes. If ineffective, clinicians should consider addition of Cyclosporine, Azathioprine or Certolizumab pegol, which are seemingly safe in pregnancy. Other therapies (such as Methotrexate, Mycophenolate Mofetil and alkylating agents) are teratogenic or have a detrimental effect on the foetus. Furthermore, careful multidisciplinary preconception discussions and close follow-up are recommended, monitoring for flare-ups and actively tapering medication doses, with a primary endpoint focused on protecting ocular tissues from inflammation, whilst giving minimal risk of poor pregnancy and foetal outcomes.

**PLOS ONE. 2024 NOV 11;19(11):E0311811. DOI: 10.1371/JOURNAL.PONE.0311811.**

INTERPRETABLE MULTIMODAL CLASSIFICATION FOR AGE-RELATED MACULAR DEGENERATION DIAGNOSIS

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Explainable Artificial Intelligence (XAI) is an emerging machine learning field that has been successful in medical image analysis. Interpretable approaches are able to “unbox” the black-box decisions made by AI systems, aiding medical doctors to justify their

diagnostics better. In this paper, we analyze the performance of three different XAI strategies for medical image analysis in ophthalmology. We consider a multimodal deep learning model that combines optical coherence tomography (OCT) and infrared reflectance (IR) imaging for the diagnosis of age-related macular degeneration (AMD). The classification model is able to achieve an accuracy of 0.94, performing better than other unimodal alternatives. We analyze the XAI methods in terms of their ability to identify retinal damage and ease of interpretation, concluding that grad-CAM and guided grad-CAM can be combined to have both a coarse visual justification and a fine-grained analysis of the retinal layers. We provide important insights and recommendations for practitioners on how to design automated and explainable screening tests based on the combination of two image sources.

**CASE REP OPHTHALMOL. 2024 MAR 19;15(1):238-245. DOI: 10.1159/000537707.**

MAXILLARY AMELOBLASTOMA WITH LOCAL RECURRENCE, ORBITAL INVASION, AND SYSTEMIC METASTASES: A CASE REPORT AND REVIEW OF THE LITERATURE

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Introduction: Maxillary ameloblastoma is a rare, slow-growing odontogenic tumor that can recur after surgical excision, be locally aggressive, and rarely develop systemic metastases. We describe the course and management of a patient with recurrent maxillary ameloblastoma with orbital invasion and systemic metastases, the fourth case of its kind to be described in the literature. Case presentation: A 50-year-old female presented with left hyperglobus. A diagnosis of maxillary ameloblastoma was made based on biopsy and neuroimaging with MRI and CT. Surgical management included partial maxillectomy with orbital floor reconstruction, given the orbital invasion. Three years later, left hyperglobus recurred, and the patient was found to have orbital recurrence and lung metastases on PET imaging. The lung and orbital lesions have responded well to chemoradiation therapy without surgical intervention. Conclusion: Maxillary ameloblastoma is a rare tumor that typically arises from odontogenic tissues. Though considered benign, they can recur and in the case of our patient, metastasize. Complete surgical excision with wide surgical margins is associated with a shorter average time to recurrence and a lower incidence of metastasis. Cases of metastasis are managed with chemotherapy with or without adjuvant radiotherapy. Precision medicine may play a role in managing this entity in the future, given the discovery of differing profiles of maxillary ameloblastoma compared to mandibular. Ophthalmologists should be aware of this tumor as it can invade the orbit, resulting in significant ocular morbidity and mortality.

**J CLIN MED. 2024 MAY 11;13(10):2835. DOI: 10.3390/JCM13102835.**

QUANTITATIVE MICROVASCULAR CHANGE ANALYSIS USING A SEMI-AUTOMATED SOFTWARE IN MACULA-OFF RHEGMATOGENOUS RETINAL DETACHMENT ASSESSED BY SWEPT-SOURCE OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

Pablo Díaz-Aljaro, Javier Zarranz-Ventura, Laura Broc-Iturralde, Nevena Romanic-Bubalo, Ignacio Díaz-Aljaro, Zhongdi Chu, Ruikang K Wang, Xavier Valldeperas

Objective: To analyze the performance of custom semi-automated software for quantitative analysis of retinal capillaries in eyes with macula-off rhegmatogenous retinal detachment (RRD) and the role of these microvascular measures as potential biomarkers of postoperative visual outcomes. Methods: A prospective, observational, and single-center study was conducted on consecutive patients who underwent 25G pars-plana vitrectomy for primary uncomplicated macula-off RRD. Optical coherence tomography angiography (OCTA) was performed in the fellow and RRD eyes before surgery and in months 1, 3, and 6 after surgery. The preoperative values of the fellow eyes were used as surrogates of macula-off ones. The primary endpoints were the mean vessel diameter index (VDI); vessel area density (VAD); and vessel skeleton density (VSD) at month 6. Results: Forty-four eyes (44 patients) were included in the study. Considering the fellow eyes as a surrogate of preoperative values of macula-off eyes, VDI in superficial (SCP) and deep (DCP) capillary plexuses was significantly reduced at month 6 ($p = 0.0087$ and $p = 0.0402$, respectively); whereas VSD in SCP increased significantly from preoperative values ($p = 0.0278$). OCTA built-in software parameters were significantly reduced from month 1 to month 6 in both SCP and DCP (p values ranged between 0.0235 and <0.0001). At month 6, 25 (56.8%) eyes achieved a best-corrected visual acuity BCVA ≥ 0.3 (LogMAR). The greater the preoperative BCVA, the greater the probability of achieving good visual outcomes (Odds ratio: 11.06; $p = 0.0037$). However, none of the OCTA parameters were associated with the probability of achieving a BCVA improvement ≥ 0.3. Conclusions: Quantitative evaluation of capillary density and morphology through OCTA and semi-automated software represents a valuable tool for clinical assessment and managing the disease comprehensively.

**INT HEALTH. 2024 JUL 2;16(4):468-470. DOI: 10.1093/INTHEALTH/IHAD079.**

HETEROGENOUS PATHOGEN PROFILE ASSOCIATED WITH ACUTE CONJUNCTIVITIS IN NEPAL

Chaudhary M; Sitaula S; Ruder K; Chen C; Zhong LN; Lu YH; Abraham T; Yu D; Hinterwirth A; Lietman TM; Doan T; Seitzman GD; Urzua CA; Vega F; Salgado F; Cuitino L.

Background: Infectious conjunctivitis is common in Nepal. Materials and methods: This prospective study recruited 60 patients with presumed acute infectious conjunctivitis from the B.P. Koirala Lions Center for Ophthalmic Studies in Kathmandu, Nepal. Swabs from the conjunctiva and anterior nares were processed for metagenomic RNA deep sequencing (RNA-seq). Results:

Pathogens were identified in 55% of cases. RNA viruses were the most common pathogen class identified. Severe acute respiratory syndrome coronavirus 2 was the most common RNA virus identified. Conclusions: Acute infectious conjunctivitis varies by location. Contrary to expectations, RNA viruses predominated. Repeat surveillance may be useful and RNA-seq allows for detection of the unexpected pathogen including RNA viruses.

**INT J INFECT DIS. 2024 SEP:146:107133. DOI: 10.1016/J.IJID.2024.107133.**

COXSACKIEVIRUS A24 CAUSING ACUTE CONJUNCTIVITIS IN A 2023 OUTBREAK IN VIETNAM

Huy Tran, Thao Ha, Linh Hoang, Yen Tran, Kevin Ruder, Lina Zhong, Cindi Chen, YuHeng Liu, Danny Yu, Thomas Abraham, Armin Hinterwirth, Michael Deiner, Travis C Porco, Thomas M Lietman, Thuy Doan, Gerami D Seitzman; SCORPIO Study Group

Objectives: To determine the associated pathogen during the 2023 conjunctivitis outbreak in Vietnam METHODS: RNA-sequencing was used to identify pathogens before and during the outbreak. Results: 24 patients with infectious conjunctivitis between March and October 2023 from Hai Yen Vision Institute in Vietnam were swabbed. Coxsackievirus A24v was the most common pathogen identified. Phylogenetic analysis of these strains demonstrates similarities to the Coxsackievirus identified in the 2022 India outbreak. Human adenovirus D was also circulating. Ocular findings of tearing, purulence, and itching were common in this outbreak. Conclusions: Multiple viruses can co-circulate during conjunctivitis outbreaks. Hemorrhagic conjunctivitis, commonly associated with coxsackievirus conjunctivitis, was not a common clinical sign in this outbreak. Repeat genetic surveillance, with the notable inclusion of RNA virus detection strategies, is important for outbreak detection.

## SERVICIO OTORRINOLARINGOLOGÍA

**ALZHEIMERS DEMENT (AMST). 2024 FEB 1;16(1):E12467. DOI: 10.1002/DAD2.12467.**

COCHLEAR DYSFUNCTION AS AN EARLY BIOMARKER OF COGNITIVE DECLINE IN NORMAL HEARING AND MILD HEARING LOSS

Vicente Medel, Paul H Delano, Chama Belkhiria, Alexis Leiva, Cristina De Gatica, Victor Vidal, Carlos F Navarro, Simon San Martín, Melissa Martínez, Christine Gierke, Ximena García, Mauricio Cerda, Rodrigo Vergara, Carolina Delgado, Gonzalo A Farías

Introduction: Age-related hearing loss is an important risk factor for cognitive decline. However, audiogram thresholds are not good estimators of dementia risk in subjects with normal hearing or mild hearing loss. Here we propose to use distortion product otoacoustic emissions (DPOAEs) as an objective and sensitive tool to estimate the risk of cognitive decline in older adults with normal hearing or mild hearing loss. Methods: We assessed neuropsychological, brain magnetic resonance imaging, and auditory analyses on 94 subjects > 64 years of age. Results: We found that cochlear dysfunction, measured by DPOAEs-and not by conventional audiometry-was associated with Clinical Dementia Rating Sum of Boxes (CDR-SoB) classification and brain atrophy in the group with mild hearing loss (25 to 40 dB) and normal hearing (<25 dB). discussion: Our findings suggest that DPOAEs may be a non-invasive tool for detecting neurodegeneration and cognitive decline in the older adults, potentially allowing for early intervention.

**FRONT NEURAL CIRCUITS. 2024 JAN 4:17:1301962. DOI: 10.3389/FNCIR.2023.1301962.**

THE CORTICOFUGAL OSCILLATORY MODULATION OF THE COCHLEAR RECEPTOR DURING AUDITORY AND VISUAL ATTENTION IS PRESERVED IN TINNITUS

Rodrigo Donoso-San Martín, Alexis Leiva, Constantino D Dragicevic, Vicente Medel, Paul H Delano

Introduction: The mechanisms underlying tinnitus perception are still under research. One of the proposed hypotheses involves an alteration in top-down processing of auditory activity. Low-frequency oscillations in the delta and theta bands have been recently described in brain and cochlear infrasonic signals during selective attention paradigms in normal hearing controls. Here, we propose that the top-down oscillatory activity observed in brain and cochlear signals during auditory and visual selective attention in normal subjects, is altered in tinnitus patients, reflecting an abnormal functioning of the corticofugal pathways that connect brain circuits with the cochlear receptor. Methods: To test this hypothesis, we used a behavioral task that alternates between auditory and visual top-down attention while we simultaneously measured electroencephalogram (EEG) and distortion-product otoacoustic emissions (DPOAE) signals in 14 tinnitus and 14 control subjects. Results: We found oscillatory activity in the delta and theta bands in cortical and cochlear channels in control and tinnitus patients. There were significant decreases in the DPOAE oscillatory amplitude during the visual attention period as compared to the auditory attention period in tinnitus and control groups. We did not find significant differences when using a between-subjects statistical approach comparing tinnitus and control groups. On the other hand, we found a significant cluster in the delta band in tinnitus when using within-group statistics to compare the difference between auditory and visual DPOAE oscillatory power. Conclusion: These results confirm the presence of top-down infrasonic low-frequency cochlear oscillatory activity in the delta and theta bands in tinnitus patients, showing that the corticofugal suppression of cochlear oscillations during visual and auditory attention in tinnitus patients is preserved.

**AUDIOL NEUROTOL. 2024;29(4):253-262. DOI: 10.1159/000533683.**

SUPRA-THRESHOLD LS CE-CHIRP AUDITORY BRAINSTEM RESPONSE IN THE ELDERLY

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Introduction: Aging deteriorates peripheral and central auditory structures and functions. In elders, for an accurate audiological evaluation, it is important to explore beyond the cochlear receptor. Audiograms provide an estimation of hearing thresholds, while the amplitudes and latencies of supra-threshold auditory brainstem response (ABR) can offer noninvasive measures of the auditory pathways functioning. Regarding ABR, in young populations, level-specific chirp (LS CE-chirp) stimulus has been proposed as an alternative synchronizing method to obtain larger ABR responses than those evoked by clicks. However, the supra-threshold characteristics of chirp evoked ABR, and their association to hearing thresholds is relatively unknown in the elderly. The aim of this study was to evaluate supra-threshold LS CE-chirp ABRs in an aged population by comparing their features with click ABRs, and evaluating their relationship with audiometric hearing thresholds. Methods: We carried out a cross-sectional study to characterize the hearing of 125 adults aged over 65 years. We determined the audiometric hearing thresholds and supra-threshold ABRs elicited by LS CE-chirp and click stimuli at 80 dB nHL. We evaluated associations by means of partial correlations and covariate adjustment. We performed specific frequencies' analysis and subgroup analysis per hearing level. Results: Wave V responses had significantly shorter latencies and larger amplitudes when elicited by LS CE-chirp as compared to click-evoked responses. Audiometric hearing thresholds correlated with age, but ABR characteristics did not. We found mild correlations between hearing thresholds and ABR characteristics, predominantly at higher frequencies and with chirp. We found scarce evidence of correlation between ABR characteristics and the average of behavioral hearing thresholds between 0.5 to 4 kHz (0.5-4 kHz PTA). After subgroup analysis according to the hearing level, no stronger or more significant correlations were found between ABR characteristics and 0.5-4 kHz PTA. Discussion: In this study, we found that supra-threshold LS CE-chirp ABR presented some of the previously described similitudes and differences with supra-threshold click ABR in younger populations. Although, the average amplitude and latency of wave V evoked by LS CE-chirp were larger and faster than those evoked by clicks, these results should be taken with caution at the individual level, and further studies are required to state that LS CE-chirp ABRs are better than click ABRs in elders for clinical evaluations. We did not find consistent associations between hearing thresholds and supra-threshold wave V features, suggesting that these measures should be considered independently in the elderly.

**PLOS ONE. 2024 MAR 7;19(3):E0299911. DOI: 10.1371/JOURNAL.PONE.0299911.**

A FREQUENCY PEAK AT 3.1 KHZ OBTAINED FROM THE SPECTRAL ANALYSIS OF THE COCHLEAR IMPLANT ELECTROCOCHLEOGRAPHY NOISE

Javiera Herrada, Vicente Medel, Constantino Dragicevic, Juan C Maass, Carlos E Stott, Paul H Delano

Introduction: The functional evaluation of auditory-nerve activity in spontaneous conditions has remained elusive in humans. In animals, the frequency analysis of the round-window electrical noise recorded by means of electrocochleography yields a frequency peak at around 900 to 1000 Hz, which has been proposed to reflect auditory-nerve spontaneous activity. Here, we studied the spectral components of the electrical noise obtained from cochlear implant electrocochleography in humans. Methods: We recruited adult cochlear implant recipients from the Clinical Hospital of the Universidad de Chile, between the years 2021 and 2022. We used the AIM System from Advanced Bionics® to obtain single trial electrocochleography signals from the most apical electrode in cochlear implant users. We performed a protocol to study spontaneous activity and auditory responses to 0.5 and 2 kHz tones. Results: Twenty subjects including 12 females, with a mean age of 57.9 ± 12.6 years (range between 36 and 78 years) were recruited. The electrical noise of the single trial cochlear implant electrocochleography signal yielded a reliable peak at 3.1 kHz in 55% of the cases (11 out of 20 subjects), while an oscillatory pattern that masked the spectrum was observed in seven cases. In the other two cases, the single-trial noise was not classifiable. Auditory stimulation at 0.5 kHz and 2.0 kHz did not change the amplitude of the 3.1 kHz frequency peak. Conclusion: We found two main types of noise patterns in the frequency analysis of the single-trial noise from cochlear implant electrocochleography, including a peak at 3.1 kHz that might reflect auditory-nerve spontaneous activity, while the oscillatory pattern probably corresponds to an artifact.

**HEAR RES. 2024 SEP 15:451:109093. DOI: 10.1016/J.HEARES.2024.109093.**

WIRELESS ELECTROCOCHLEOGRAPHY IN AWAKE CHINCHILLAS: A MODEL TO STUDY CROSSMODAL MODULATIONS AT THE PERIPHERAL LEVEL

Catherine Pérez-Valenzuela, Sergio Vicencio-Jiménez, Mia Caballero, Paul H Delano, Diego Elgueda

The discovery and development of electrocochleography (ECochG) in animal models has been fundamental for its implementation in clinical audiology and neurotology. In our laboratory, the use of round-window ECochG recordings in chinchillas has allowed a better understanding of auditory efferent functioning. In previous works, we gave evidence of the corticofugal modulation of auditory-nerve and cochlear responses during visual attention and working memory. However, whether these cognitive top-down mechanisms to the most peripheral structures of the auditory pathway are also active during audiovisual crossmodal stimulation

is unknown. Here, we introduce a new technique, wireless ECochG to record compound-action potentials of the auditory nerve (CAP), cochlear microphonics (CM), and round-window noise (RWN) in awake chinchillas during a paradigm of crossmodal (visual and auditory) stimulation. We compared ECochG data obtained from four awake chinchillas recorded with a wireless ECochG system with wired ECochG recordings from six anesthetized animals. Although ECochG experiments with the wireless system had a lower signal-to-noise ratio than wired recordings, their quality was sufficient to compare ECochG potentials in awake crossmodal conditions. We found non-significant differences in CAP and CM amplitudes in response to audiovisual stimulation compared to auditory stimulation alone (clicks and tones). On the other hand, spontaneous auditory-nerve activity (RWN) was modulated by visual crossmodal stimulation, suggesting that visual crossmodal simulation can modulate spontaneous but not evoked auditory-nerve activity. However, given the limited sample of 10 animals (4 wireless and 6 wired), these results should be interpreted cautiously. Future experiments are required to substantiate these conclusions. In addition, we introduce the use of wireless ECochG in animal models as a useful tool for translational research.

**INFECT AGENTS CANCER. 2024 SEP 27;19(1):47. DOI: 10.1186/S13027-024-00609-Z.**

CIAP-2 PROTEIN IS UPREGULATED BY HUMAN PAPILLOMAVIRUS IN OROPHARYNGEAL CANCERS: ROLE IN RADIORESISTANCE IN VITRO

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Background: High-risk human papillomaviruses are the causal agents of a subset of head and neck cancers. A previous transcriptomic analysis showed that cIAP2 protein, involved in cell survival and apoptosis, is upregulated in OKF6 oral cells that express HPV16 E6/E7. In addition, cIAP2 promotes radioresistance, a very important concern in HNC treatment. However, cIAP2 increase has not yet been evaluated in oropharyngeal carcinomas (OPCs), nor has been the role of cIAP2 in HNC radioresistance. Methods: We carried out a descriptive-analytical retrospective study in 49 OPCs from Chilean patients. We determined the expression of cIAP2 at transcript and proteins levels using reverse-transcriptase -polymerase chain reaction and immunohistochemistry, respectively. HPV and p16 expression were previously analyzed in these specimens. In addition, SCC-143 HNC cells ectopically expressing HPV16 E6/E7 were analyzed for cIAP2 expression and after transfection with a siRNA for HPV16 E6/E7 knocking down. Results: We found a statistically significant association between HPV presence and cIAP2 expression ($p = 0.0032$ and $p = 0.0061$, respectively). An association between p16 and cIAP2 levels was also found ($p = 0.038$). When SCC-143 cells were transfected with a construct expressing HPV16 E6/E7, the levels of cIAP2 were significantly increased ($p = 0.0383$ and $p = 0.0115$, respectively). Conversely, HPV16 E6 and E7 knocking down resulted in a decrease of cIAP2 levels ($p = 0.0161$ and $p = 0.006$, respectively). Finally, cIAP2 knocking down in HPV16 E6/E7 cells resulted in increased apoptosis after exposure to radiation at 4 and 8 Gy ($p = 0.0187$ and $p = 0.0061$, respectively). Conclusion: This study demonstrated for the first time a positive relationship between HPV presence and cIAP2 levels in OPCs. Additionally, cIAP2 knocking down sensitizes HNC cells to apoptosis promoted by radiation. Therefore, cIAP2 is a potential therapeutic target for radiation in HPV-driven HNC.

**AUDIOL RES. 2024 AUG 14;14(4):701-713. DOI: 10.3390/AUDIOLRES14040059.**

CLINICAL PROFILE, TRENDS, AND MANAGEMENT IN PEDIATRIC PATIENTS WITH AUDIOVESTIBULAR DISORDERS: CAN WE PREDICT EMOTIONAL DISABILITY IN PEDIATRIC PATIENTS WITH EPISODES OF VERTIGO AND DIZZINESS?

Joan Lorente-Piera, Nicolás Pérez-Fernández, Melissa Blanco-Pareja, Raquel Manrique-Huarte, Pia Michael Larenas, Valeria Serra, Manuel Manrique

Background: Audiovestibular disorders in childhood occur with considerable frequency. However, the difficulty of obtaining medical history, the nonspecificity of symptoms, and the lack of cooperation during complementary tests often contribute significantly to diagnostic biases, attributing clinical presentations to psychosomatic disorders. The objectives of this work are, firstly, to characterize, from an auditory and vestibular perspective, the most frequent causes of vertigo in childhood and a possible relationship with emotional symptoms. On the other hand, to propose the usefulness of the MSSQ-Short questionnaire as a predictive variable in the evolution of children diagnosed with recurrent vertigo of childhood (RVC). Methods: An observational cross-sectional study was designed with retrospective data collection at three tertiary hospitals. Results: Among the 117 patients recruited between 2016 and 2024, 32 patients (27.35%) were diagnosed with an anxious-depressive syndrome prior to audiovestibular testing. The mean age was 11.19 ± 5.61 years and the most frequent final diagnoses were vestibular migraine (VM) with 41.03% and RVC with 23.93%. Patients with VM, compared with RVC, are approximately 1.12 times more likely to have psychosomatic pathology (CI 0.39 to 3.25). The most sensitive and frequently altered test was VEMPS (39.32%), with statistical significance in VM and otic capsule dehiscence, while regarding the MSSQ-Short questionnaire, the linear regression of 0.28 indicates an increase in clinical duration with high questionnaire scores. Conclusions: Vestibular disorders causing dizziness and vertigo are challenging to diagnose, often due to lack of cooperation and/or symptom nonspecificity. A thorough medical history and complementary tests, including audiovestibular and imaging studies, are advisable, thus avoiding systematically attributing children's complaints to other psychosomatic disorders.

## DEPARTAMENTO PSIQUIATRÍA Y SALUD MENTAL

### REV MED CHIL. 2024 APR;152(4):476-482. DOI: 10.4067/S0034-98872024000400476.

CARACTERÍSTICAS DE PERSONAS DEPRIMIDAS CON HIPERTENSIÓN Y/O DIABETES MELLITUS EN CENTROS ATENCIÓN PRIMARIA DE SALUD EN SANTIAGO DE CHILE

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Eighty percent of depressed patients in Primary Health Care (PHC) have a comorbidity. It is essential to contribute local evidence on the characteristics of patients with physical and psychiatric comorbidities to better address clinical practice. Aim: To characterize depressed patients from the cardiovascular program (PCV) of eight family health centers (CESFAM) in two communes of the Metropolitan Region. Material and methods: Secondary analysis of data from a cluster-randomized clinical trial recruiting 359 program enrollees aged 18 years or older with a Patient Health Questionnaire 9-item (PHQ-9) score greater than or equal to 15. The inclusion criteria for participants were to be 18 years of age or older, to have a score on the Patient Health Questionnaire 9-item (PHQ-9) greater than or equal to 15, and to be enrolled in the cardiovascular program of the respective health center. Results: These are mainly women users of the cardiovascular program with depressive symptoms of moderate to severe intensity with a previous depressive history (60.39%), previously treated in a (75.69%). Only 17.7% were using antidepressant drugs at the time of the interview.97.1% of the interviewees were using drugs for hypertension and/or diabetes. Conclusions: These are people with depressive episode, hypertension and/or diabetes who, having a personal and family history of depression, are not receiving pharmacological treatment for depression, which probably affects their quality of life. Better adherence to clinical guidelines for the treatment of depression is required.

### LANCET PSYCHIATRY. 2024 JUL;11(7):536-544. DOI: 10.1016/S2215-0366(24)00134-2.

WORLDWIDE INCIDENCE OF SUICIDES IN PRISON: A SYSTEMATIC REVIEW WITH META-REGRESSION ANALYSES

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Background: Suicide is a leading cause of death during imprisonment. This systematic review aimed to synthesise available evidence of prison suicide incidence worldwide. Methods: We systematically searched the scientific literature, data repositories, and prison system reports, supplemented by correspondence with prison administrations. We included reports on people living in prison but excluded studies in preselected groups (by age or offence type). Absolute numbers and incidence rates of suicide mortality per 100 000 person-years by sex and country were extracted from 2000 to 2021. IQRs were used to describe the suicide incidence in different world regions. Incidence rate ratios comparing suicides of people living in prison with age-standardised general populations were calculated. We conducted meta-regression analyses on national-level and prison-level factors to examine heterogeneity. The study protocol was pre-registered with PROSPERO, CRD42021296819. Findings: We included three scientific studies, 124 official reports, and 11 datasets from email correspondence. Between 2000 and 2021, there were 29 711 reported suicides during 91·2 million person-years of imprisonment in 82 jurisdictions worldwide (sex-specific data available for 13 289 individuals: 12 544 [94·4%] male and 745 [5·6%] female individuals). There were large variations between countries, with most studies reporting suicide rates in the range of 24-89 per 100 000 person-years in both sexes (22-86 in male individuals and 25-107 in female individuals). In meta-regression analyses, Europe (vs other regions), high-income countries (vs low-income and middle-income countries), and countries with lower incarceration rates (vs those with higher incarceration rates) had higher suicide rates. Incidence rate ratios between people who are incarcerated and age-standardised general populations in the same jurisdictions were typically in the range of 1·9-6·0 in male and 10·4-32·4 in female individuals. Interpretation: Prison services worldwide, and particularly in Europe, should prioritise suicide prevention. Assessment and management of suicide risk in female individuals living in prison need particular attention due to excess mortality relative to community-based populations. Interpretation of synthesised data needs to be done with caution due to high heterogeneity between jurisdictions.

### PSYCHOL MED. 2024 SEP 26;54(14):1-14. DOI: 10.1017/S0033291724002307.

NEED ESTIMATES OF PSYCHIATRIC BEDS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Adrian P Mundt, Enzo Rozas-Serri, Francesco D Fritz, Sabine Delhey, Mathias Siebenförcher, Stefan Priebe

This study aimed to review and synthesize the need estimates for psychiatric beds, explore how they changed over time and compare them against the prevalence of actually existing beds. We searched PubMed, Embase classic and Embase, PsycINFO and PsycIndex, Open Grey, Google Scholar, Global Health EBSCO and Proquest Dissertations, from inception to September 13, 2022. Publications providing estimates for the required number of psychiatric inpatient beds were included. Need estimates, length of stay, and year of the estimate were extracted. Need estimates were synthesized using medians and interquartile ranges (IQRs). We also computed prevalence ratios of the need estimates and the existing bed capacities at the same time and place. Sixty-five publications with 98 estimates were identified. Estimates for bed needs were trending lower until 2000, after which they stabilized. The twenty-six most recent estimates after 2000 were submitted to data synthesis (n = 15 for beds with unspecified length of stay, n = 7 for short-stay, and n = 4 for long-stay beds). Median estimates per 100 000 population were 47 (IQR: 39 to 50) beds with unspecified length of stay, 28 (IQR: 23 to 31) beds for short-stay, and 10 (IQR: 8 to 11) for long-stay beds. The median prevalence ratio of need estimates and the actual bed prevalence

was 1.8 (IQR: 1.3 to 2.3) from 2000 onwards. Historically, the need estimates for psychiatric beds have decreased until about 2000. In the past two decades, they were stable over time and consistently higher than the actual bed numbers provided.

**HEALTH PROMOT PRACT. 2024 SEP;25(5):836-844. DOI: 10.1177/15248399231201551.**

FACILITATING FACTORS AND BARRIERS TO THE IMPLEMENTATION OF THE ICELANDIC PREVENTION MODEL OF ADOLESCENT SUBSTANCE USE IN CHILE: A FOCUS GROUP STUDY

Carolina Sepúlveda, Carlos Ibáñez, Nicolás Libuy, Viviana Guajardo, Ana María Araneda, Lorena Contreras, Paula Donoso, Adrian P Mundt

The use of alcohol and other drugs is a major public health problem in adolescence. The implementation of evidence-based prevention strategies is still scarce in the global south. This study aimed to evaluate facilitators and barriers to the implementation of the Icelandic prevention model of adolescent substance use (IPM) in Chile. We conducted a qualitative study of stakeholders during the implementation process of the IPM in six municipalities of the Metropolitan Region of Santiago, Chile. We convened six focus groups with parents and professionals from schools and municipal prevention teams (38 participants). Recordings were transcribed and submitted to a six-step thematic analysis. The following facilitators emerged: Participants valued the contribution of the IPM to articulate existing programs and teams, its community focus, and the local data obtained through the survey. There were also several barriers: Those included resistance to adopting a foreign model, the tension between generating local strategies and looking for measures to ensure the fidelity of the implementation, socioeconomic differences between and within municipalities, low-risk perception and supervision of parents in Chile, and a culture that generally does not discourage adolescent substance use. Implementation of the IPM was largely accepted by the stakeholders who agreed with the community approach of the model. The main barriers to consider were related to cultural and socioeconomic factors that need to be addressed in further research and may limit the effects of the model in Chile.

**PREV SCI. 2024 FEB;25(2):245-255. DOI: 10.1007/S11121-023-01539-9.**

COMMUNITY-BASED PREVENTION OF SUBSTANCE USE IN ADOLESCENTS: OUTCOMES BEFORE AND DURING THE COVID-19 PANDEMIC IN SANTIAGO, CHILE

Nicolás Libuy, Carlos Ibáñez, Ana María Araneda, Paula Donoso, Lorena Contreras, Viviana Guajardo, Adrian P Mundt

A primary community prevention approach in Iceland was associated with strong reductions of substance use in adolescents. Two years into the implementation of this prevention model in Chile, the aim of this study was to assess changes in the prevalence of adolescent alcohol and cannabis use and to discuss the impact of the COVID-19 pandemic on the substance use outcomes. In 2018, six municipalities in Greater Santiago, Chile, implemented the Icelandic prevention model, including structured assessments of prevalence and risk factors of substance use in tenth grade high school students every 2 years. The survey allows municipalities and schools to work on prevention with prevalence data from their own community. The survey was modified from an on-site paper format in 2018 to an on-line digital format in a shortened version in 2020. Comparisons between the cross-sectional surveys in the years 2018 and 2020 were performed with multilevel logistic regressions. Totally, 7538 participants were surveyed in 2018 and 5528 in 2020, nested in 125 schools from the six municipalities. Lifetime alcohol use decreased from 79.8% in 2018 to 70.0% in 2020 ($X2 = 139.3$, $p < 0.01$), past-month alcohol use decreased from 45.5 to 33.4% ($X2 = 171.2$, $p < 0.01$), and lifetime cannabis use decrease from 27.9 to 18.8% ($X2 = 127.4$, $p < 0.01$). Several risk factors improved between 2018 and 2020: staying out of home after 10 p.m. ($X2 = 105.6$, $p < 0.01$), alcohol use in friends ($X2 = 31.8$, $p < 0.01$), drunkenness in friends ($X2 = 251.4$, $p < 0.01$), and cannabis use in friends ($X2 = 217.7$, $p < 0.01$). However, other factors deteriorated in 2020: perceived parenting ($X2 = 63.8$, $p < 0.01$), depression and anxiety symptoms ($X2 = 23.5$, $p < 0.01$), and low parental rejection of alcohol use ($X2 = 24.9$, $p < 0.01$). The interaction between alcohol use in friends and year was significant for lifetime alcohol use ($\beta = 0.29$, $p < 0.01$) and past-month alcohol use ($\beta = 0.24$, $p < 0.01$), and the interaction between depression and anxiety symptoms and year was significant for lifetime alcohol use ($\beta = 0.34$, $p < 0.01$), past-month alcohol use ($\beta = 0.33$, $p < 0.01$), and lifetime cannabis use ($\beta = 0.26$, $p = 0.016$). The decrease of substance use prevalence in adolescents was attributable at least in part to a reduction of alcohol use in friends. This could be related to social distancing policies, curfews, and homeschooling during the pandemic in Chile that implied less physical interactions between adolescents. The increase of depression and anxiety symptoms may also be related to the COVID-19 pandemic. The factors rather attributable to the prevention intervention did not show substantial changes (i.e., sports activities, parenting, and extracurricular activities).

**INQUIRY. 2024 JAN-DEC:61:469580241273187. DOI: 10.1177/00469580241273187.**

EFFECTS OF ANXIETY, STRESS AND PERCEIVED SOCIAL SUPPORT ON DEPRESSION AND LONELINESS AMONG OLDER PEOPLE DURING THE COVID-19 PANDEMIC: A CROSS-SECTIONAL PATH ANALYSIS

Maryam Farhang, Izaskun Álvarez-Aguado, Javier Celis Correa, Maria Cecilia Toffoletto, Miguel Rosello-Peñaloza, Claudia Miranda-Castillo

During the COVID-19 pandemic, older people were exposed to high levels of anxiety and stress leading to loneliness and depressive disorders. The purpose of the present study was to investigate the effects of anxiety, positive coping, perceived social support, and perceived stress on depression and loneliness among older people during the COVID-19 pandemic. This was a cross-sectional online/telephone survey. A non-probability convenience sampling method was used. Participants were 112 people aged 60 years

and above, without cognitive impairment, who experienced confinement (from March 2020 onward) and had access to the internet or telephone. A path analysis model showed a direct significant effect of anxiety on both, depression (β = .68, P < .001) and perceived stress (β = .65, P < .001), as well as an indirect effect of anxiety on loneliness via perceived stress (β = .65) * (β = .40); and social support (β = -.21) * (β = -.20). The model showed adequate fit $\chi 2$(df = 4) =5.972, P = .201; RMSEA = 0.066 (0.000, 0.169), CFI = 0.992; TLI = 0.970. Anxiety had a significant effect on depressive symptoms as well as on loneliness via perceived social support and perceived stress. According to our findings, in order to reduce depressive symptoms and perceived loneliness, it is essential to develop timely interventions that decrease levels of anxiety and stress and increase levels of perceived social support in older people, particularly when there are any restrictions, physical or contextual, that prevent face-to-face contact. This can be achieved by implementing preventive community-based programs, enhancing accessibility to mental health services, and collaborating with local support groups, among others.

**INT J MOL SCI. 2024 OCT 18;25(20):11204. DOI: 10.3390/IJMS252011204.**

BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) AS A PREDICTOR OF TREATMENT RESPONSE IN SCHIZOPHRENIA AND BIPOLAR DISORDER: A SYSTEMATIC REVIEW

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Brain-derived neurotrophic factor (BDNF) is a potential biomarker of response to treatment in psychiatric disorders. As it plays a role in the pathophysiological development of schizophrenia and bipolar disorder, it is of interest to study its role in predicting therapeutic responses in both conditions. We carried out a systematic review of the literature, looking for differences in baseline BDNF levels and the Val66Met BDNF polymorphism in these disorders between responders and non-responders, and found information showing that the Val/Val genotype and higher baseline BDNF levels may be present in patients that respond successfully to pharmacological and non-pharmacological treatments. However, there is still limited evidence to support the role of the Val66Met polymorphism and baseline BDNF levels as predictors of treatment response.

**SCHIZOPHR RES COGN. 2024 AUG 15:38:100324. DOI: 10.1016/J.SCOG.2024.100324.**

FIXATIONAL EYE MOVEMENTS AND THEIR ASSOCIATED EVOKED POTENTIALS DURING NATURAL VISION ARE ALTERED IN SCHIZOPHRENIA

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Background: Visual exploration is abnormal in schizophrenia; however, few studies have investigated the physiological responses during selecting objectives in more ecological scenarios. This study aimed to demonstrate that people with schizophrenia have difficulties observing the prominent elements of an image due to a deficit mechanism of sensory modulation (active sensing) during natural vision. Methods: An electroencephalogram recording with eye tracking data was collected on 18 healthy individuals and 18 people affected by schizophrenia while looking at natural images. These had a prominent color element and blinking produced by changes in image luminance. Results: We found fewer fixations when all images were scanned, late focus on prominent image areas, decreased amplitude in the eye-fixation-related potential, and decreased intertrial coherence in the SCZ group. Conclusions: The decrease in the visual attention response evoked by the prominence of visual stimuli in patients affected by schizophrenia is generated by a reduction in endogenous attention mechanisms to initiate and maintain visual exploration. Further work is required to explain the relationship of this decrease with clinical indicators.

**SCHIZOPHR RES COGN. 2024 JAN 29:36:100302. DOI: 10.1016/J.SCOG.2024.100302.**

MONTREAL COGNITIVE ASSESSMENT (MOCA) AS A SCREENING TOOL FOR COGNITIVE IMPAIRMENT IN EARLY STAGES OF PSYCHOSIS

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Background: Cognitive alterations have been reported in early stages of psychosis including people with First Episode Psychosis (FEP), Clinical High-Risk Mental State (CHR), and Psychotic-Like Experience (PLE). This study aimed to compare the cognitive function in early stages of psychosis using the Montreal Cognitive Assessment (MoCA), a low-cost and brief assessment tool of cognitive functions. Methods: A total of 154 individuals, including 35 with FEP, 38 CHR, 44 PLE, and 37 healthy controls (HC), were evaluated with the MoCA in Santiago, Chile. We calculated the mean total score of the MoCA and the standard deviation of the mean. Groups were assessed for a trend to lower scores in a pre-determined sequence (HC > PLE > CHR > FEP) using the Jonckheere-Terpstra test (TJT). Results: The mean total MoCA scores were 24.8 ± 3.3 in FEP, 26.4 ± 2.4 in CHR, 26.4 ± 2.3 in PLE, and 27.2 ± 1.8 in HC. The analyses revealed a significant trend (p < 0.05) toward lower MoCA individual domain scores and MoCA total scores in the following order: HC > PLE > CHR > FEP. The mean total scores of all groups were above the cut-off for cognitive impairment (22 points). Conclusions: The MoCA describes lower scores in cognition across early stages of psychosis and may be a useful low-cost assessment instrument in early intervention centers of poorly resourced settings.

**JAMA NETW OPEN. 2024 NOV 4;7(11):E2429630. DOI: 10.1001/JAMANETWORKOPEN.2024.29630.**

DATA-DRIVEN CUTOFF SELECTION FOR THE PATIENT HEALTH QUESTIONNAIRE-9 DEPRESSION SCREENING TOOL

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Importance: Test accuracy studies often use small datasets to simultaneously select an optimal cutoff score that maximizes test accuracy and generate accuracy estimates. Objective: To evaluate the degree to which using data-driven methods to simultaneously select an optimal Patient Health Questionnaire-9 (PHQ-9) cutoff score and estimate accuracy yields (1) optimal cutoff scores that differ from the population-level optimal cutoff score and (2) biased accuracy estimates. Design, setting, and participants: This study used cross-sectional data from an existing individual participant data meta-analysis (IPDMA) database on PHQ-9 screening accuracy to represent a hypothetical population. Studies in the IPDMA database compared participant PHQ-9 scores with a major depression classification. From the IPDMA population, 1000 studies of 100, 200, 500, and 1000 participants each were resampled. Main outcomes and measures: For the full IPDMA population and each simulated study, an optimal cutoff score was selected by maximizing the Youden index. Accuracy estimates for optimal cutoff scores in simulated studies were compared with accuracy in the full population. Results: The IPDMA database included 100 primary studies with 44 503 participants (4541 [10%] cases of major depression). The population-level optimal cutoff score was 8 or higher. Optimal cutoff scores in simulated studies ranged from 2 or higher to 21 or higher in samples of 100 participants and 5 or higher to 11 or higher in samples of 1000 participants. The percentage of simulated studies that identified the true optimal cutoff score of 8 or higher was 17% for samples of 100 participants and 33% for samples of 1000 participants. Compared with estimates for a cutoff score of 8 or higher in the population, sensitivity was overestimated by 6.4 (95% CI, 5.7-7.1) percentage points in samples of 100 participants, 4.9 (95% CI, 4.3-5.5) percentage points in samples of 200 participants, 2.2 (95% CI, 1.8-2.6) percentage points in samples of 500 participants, and 1.8 (95% CI, 1.5-2.1) percentage points in samples of 1000 participants. Specificity was within 1 percentage point across sample sizes. Conclusions and relevance: This study of cross-sectional data found that optimal cutoff scores and accuracy estimates differed substantially from population values when data-driven methods were used to simultaneously identify an optimal cutoff score and estimate accuracy. Users of diagnostic accuracy evidence should evaluate studies of accuracy with caution and ensure that cutoff score recommendations are based on adequately powered research or well-conducted meta-analyses.

## SERVICIO TRAUMATOLOGÍA Y ORTOPEDIA

**CUREUS. 2024 SEP 21;16(9):E69853. DOI: 10.7759/CUREUS.69853.**

WOMAC, KUJALA SCORE, AND KNEE INJURY AND OSTEOARTHRITIS OUTCOME SCORE FOR QUALITY OF LIFE THRESHOLDS FOR PREDICTING INCREASED AND DECREASED LIKELIHOOD OF FAILURE TO IMPROVE QUALITY OF LIFE AFTER TOTAL KNEE REPLACEMENT

Maximiliano Barahona, Macarena A Barahona, Camila Amstein

Background Improvement in quality of life is the primary goal following total knee arthroplasty (TKA). Patient-reported outcome measures (PROMs) have become the standard for evaluating TKA results, capturing the patient's perspective. However, PROMs face challenges such as inconsistent presurgery data collection and ambiguity in determining clinical significance. Establishing reliable thresholds for success and failure is crucial for comparing outcomes. Purpose To determine cutoff values for the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Kujala score, and Knee Injury and Osteoarthritis Outcome Score for Quality of Life (KOOS-QL) that significantly change the likelihood of success (TIS) or failure (TIF) to improve self-reported quality of life one year after TKA compared to the baseline probability of the studied cohort. Methods A retrospective study was conducted to evaluate PROMs following conventional cruciate-retaining (CR) TKA without patellar replacement. Patients were evaluated during 2022 and 2023, with a minimum one-year follow-up. A total of 161 successful evaluations were identified, representing 81% of all CR TKA procedures without patellar replacement performed between January 2018 and June 2022 at a single university hospital. Assessments included the three dimensions of the WOMAC scale (pain, stiffness, and function), Kujala score, and KOOS-QL. The primary outcome was to determine the threshold value of each PROM that significantly reduced or increased the likelihood of "same or worse" self-perceived improvement in quality of life compared to the cohort. Logistic regression with 200 iterations was used for statistical analysis. Results The threshold for improvement success was <4 for WOMAC-Pain, <1 for WOMAC-Stiffness, <15 for WOMAC-Function, >70 for Kujala, and >62 for KOOS-QL. Meanwhile, the threshold for increased failure was >7 for WOMAC-Pain, >3 for WOMAC-Stiffness, >26 for WOMAC-Function, <55 for Kujala, and <41 for KOOS-QL. Conclusions The study successfully established significant thresholds for success and failure in improving quality of life following CR TKA without patellar replacement. The identified thresholds for WOMAC-Pain, WOMAC-Function, and Kujala scores have good-excellent discrimination and can be confidently used to estimate sample sizes and compare quality of life improvements post-TKA.

**J ARTHROPLASTY. 2024 SEP;39(9S2):S171-S178. DOI: 10.1016/J.ARTH.2024.02.006.**

DEVELOPMENT OF A MACHINE-LEARNING MODEL FOR ANTERIOR KNEE PAIN AFTER TOTAL KNEE ARTHROPLASTY WITH PATELLAR PRESERVATION USING RADIOLOGICAL VARIABLES

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Background: Anterior knee pain (AKP) following total knee arthroplasty (TKA) with patellar preservation is a common complication that significantly affects patients' quality of life. This study aimed to develop a machine-learning model to predict the likelihood of developing AKP after TKA using radiological variables. Methods: A cohort of 131 anterior stabilized TKA cases (105 patients) without patellar resurfacing was included. Patients underwent a follow-up evaluation with a minimum 1-year follow-up. The primary outcome was AKP, and radiological measurements were used as predictor variables. There were 2 observers who made the radiological measurement, which included lower limb dysmetria, joint space, and coronal, sagittal, and axial alignment. Machine-learning models were applied to predict AKP. The best-performing model was selected based on accuracy, precision, sensitivity, specificity, and Kappa statistics. Python 3.11 with Pandas and PyCaret libraries were used for analysis. Results: A total of 35 TKA had AKP (26.7%). Patient-reported outcomes were significantly better in the patients who did not have AKP. The Gradient Boosting Classifier performed best for both observers, achieving an area under the curve of 0.9261 and 0.9164, respectively. The mechanical tibial slope was the most important variable for predicting AKP. The Shapley test indicated that high/low mechanical tibial slope, a shorter operated leg, a valgus coronal alignment, and excessive patellar tilt increased AKP risk. Conclusions: The results suggest that global alignment, including sagittal, coronal, and axial alignment, is relevant in predicting AKP after TKA. These findings provide valuable insights for optimizing TKA outcomes and reducing the incidence of AKP.

**RES SPORTS MED. 2024 JUL-AUG;32(4):556-566. DOI: 10.1080/15438627.2022.2163395.**

CROSS-CULTURAL ADAPTATION AND VALIDATION OF THE SHORT MUSCULOSKELETAL FUNCTION ASSESSMENT (SMFA) INTO SPANISH (CHILE)

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The purpose of this protocol was to adapt and validate the English version of the Short Musculoskeletal Function Assessment (SMFA) into Chilean Spanish according to the World Health Organisation guidelines. This is a cross-sectional study of 897 surveys of patients with non-traumatic surgical orthopaedic pathologies. We analysed internal consistency, validity, and acceptability, including correlation with the short form 36 (SF-36) medical score. The validation included 900 participants with a response rate of 99,66%, with excellent internal consistency (Cronbach's $\alpha$ = 0.962). The Dysfunction and Bother Index items showed a value of 0.952 and 0.884 respectively, eliminating one item in the Dysfunction sub-scale. The principal component analysis was forced to four factors explaining 55.5% of the variance. SMFA-CL sub-scales are significantly correlated with SF-36 components and subcomponents. The first version of the SMFA-CL version (Spanish-Chilean) scale is reported. This culturally adapted score demonstrated a high rate of reliability, validity, and ability to objectively evaluate foot and ankle pathologies.

## UNIDAD PACIENTES CRÍTICOS

**MEDICINA (B AIRES). 2024;84(1):148-152.**

PHYSIOLOGICAL EFFECT OF HIGH FLOW OXYGEN THERAPY MEASURED BY ELECTRICAL IMPEDANCE TOMOGRAPHY IN SINGLE-LUNG TRANSPLANTATION

Ignacio Fernández Ceballos, Emilio Steinberg, Joaquin Ems, Juan Martín Nuñez Silveira, Matías Madorno, Indalecio Carboni Bisso, Marcos Las Heras, Rodrigo Cornejo

In patients with chronic obstructive pulmonary disease (COPD), single lung transplantation (SLT) is sometimes performed as an alternative to bilateral lung transplantation due to limited organ availability. However, the postoperative management of SLT presents challenges, including complications related to the distinct compliance of each lung. This case report presents the case of a 65-year-old male patient who underwent SLT and was in the weaning period from mechanical ventilation. High-flow oxygen therapy (HFOT) was administered, and the physiological effects were measured using electrical impedance tomography (EIT). The results demonstrated that the application of HFOT increased air trapping and overdistention in the native lung without benefiting the transplanted lung. HFOT through a tracheostomy tube or nasal cannula resulted in a more heterogeneous distribution of ventilation, with increased end expiratory lung impedance, prolonged expiratory time constants, and an increase in silent spaces. The drop in tidal impedance after applying HFOT did not indicate hypoventilation

but rather overdistention and air trapping in the native lung, while the transplanted lung showed evidence of hypoventilation. These findings suggest that HFOT may not be beneficial for SLT patients and could potentially worsen outcomes. However, due to the limited scope of this case report, further prospective studies with larger patient cohorts are needed to confirm these results.

**PLOS ONE. 2024 OCT 25;19(10):E0301948. DOI: 10.1371/JOURNAL.PONE.0301948. ECOLLECTION 2024.**

EARLY HIGH-SENSITIVITY TROPONIN ELEVATION IN PREDICTING SHORT-TERM MORTALITY IN SEPSIS: A PROTOCOL FOR A SYSTEMATIC REVIEW WITH META-ANALYSIS

Santiago Ferrière-Steinert, Joaquín Valenzuela Jiménez, Sebastián Heskia Araya, Thomas Kouyoumdjian, José Ramos-Rojas, Abraham I J Gajardo

Background: Sepsis is a common admission diagnosis in the intensive care unit (ICU). The Sepsis-3 consensus associates sepsis diagnosis with acute organ dysfunction. In these patients troponin elevation is a well-established phenomenon, but its clinical significance is not settled, as no systematic review has addressed the prognostic significance of the increasingly prevalent high-sensitivity troponin assays in acute organ dysfunction setting. This study aims to clarify the association between early serum troponin levels in high-sensitivity assays with short-term mortality risk in septic patients with acute organ dysfunction. Methods: We will systematically search PubMed, Scopus and Embase for original articles; additionally, a manual search will be carried out through relevant literature. Generally, studies will be deemed eligible for inclusion if they evaluate the association between high-sensitivity troponin in the first 24 hours of admission and ICU, 30-days, or In-hospital mortality; in patients with septic shock or sepsis related to acute organ dysfunction. Two reviewers will independently select studies and extract the data. A meta-analysis for mortality outcome will be performed for comparative data regarding two effect measures: Odd ratios and Standardized Mean differences. Discussion: This study will provide further evidence about the role of high-sensitivity troponin assays in predicting mortality in septic patients; potentially helping to guide further research and yielding valuable information for patient assessment. Conclusion about the certainty of evidence will be presented in a ´Summary of findings´ table.

**J INTENSIVE CARE MED. 2024 SEP 19:8850666241286484. DOI: 10.1177/08850666241286484.**

EFFECT OF EXTENDED PRONE POSITIONING IN INTUBATED COVID-19 PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME, A REVISION LETTER

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The systematic review and meta-analysis performed by Kang *et al* about the effect of extended prone positioning in intubated COVID-19 patients with ARDS presents valuable findings on the effectiveness and safety of extended prone positioning, but also raises several concerns which require clarifications. The inclusion of observational studies without any control group, the use of crude rather than adjusted estimates in key variables from observational studies, an error in data extraction from randomized clinical trials, and the employment of odds ratios rather than risk ratios, may mislead interpretations of the aforementioned intervention.

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SAFETY AND PHARMACOKINETICS OF A COMBINED ANTIOXIDANT THERAPY AGAINST MYOCARDIAL REPERFUSION INJURY: A PHASE 1 RANDOMIZED CLINICAL TRIAL IN HEALTHY HUMANS

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Myocardial reperfusion injury (MRI) accounts for up to 50% of the final size in acute myocardial infarction and other conditions associated with ischemia-reperfusion. Currently, there is still no therapy to prevent MRI, but it is well known that oxidative stress has a key role in its mechanism. We previously reduced MRI in rats through a combined antioxidant therapy (CAT) of ascorbic acid, N-acetylcysteine, and deferoxamine. This study determines the safety and pharmacokinetics of CAT in a Phase I clinical trial. Healthy subjects (n = 18) were randomized 2:1 to CAT or placebo (NaCl 0.9% i.v.). Two different doses/infusion rates of CATs were tested in a single 90-minute intravenous infusion. Blood samples were collected at specific times for 180 minutes to measure plasma drug concentrations (ascorbic acid, N-acetylcysteine, and deferoxamine) and oxidative stress biomarkers. Adverse events were registered during infusion and followed for 30 days. Both CAT1 and CAT2 significantly increased the CAT drug concentrations compared to placebo ($P < .05$). Most of the pharmacokinetic parameters were similar between CAT1 and CAT2. In total, 6 adverse events were reported, all nonserious and observed in CAT1. The ferric-reducing ability of plasma (an antioxidant biomarker) increased in both CAT groups compared to placebo ($P < .001$). The CAT is safe in humans and a potential treatment for patients with acute myocardial infarction undergoing reperfusion therapy.

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SPECIFIC TRAINING IMPROVES THE DETECTION AND MANAGEMENT OF PATIENT-VENTILATOR ASYNCHRONY

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Background: Patient-ventilator asynchrony is common in patients undergoing mechanical ventilation. The proportion of health-care professionals capable of identifying and effectively managing different types of patient-ventilator asynchronies is limited. A few studies have developed specific training programs, but they mainly focused on improving patient-ventilator asynchrony detection without assessing the ability of health-care professionals to determine the possible causes. Methods: We conducted a 36-h training program focused on patient-ventilator asynchrony detection and management for health-care professionals from 20 hospitals in Latin America and Spain. The training program included 6 h of a live online lesson during which 120 patient-ventilator asynchrony cases were presented. After the 6-h training lesson, health-care professionals were required to complete a 1-h training session per day for the subsequent 30 d. A 30-question assessment tool was developed and used to assess health-care professionals before training, immediately after the 6-h training lecture, and after the 30 d of training (1-month follow-up). Results: One hundred sixteen health-care professionals participated in the study. The median (interquartile range) of the total number of correct answers in the pre-training, post-training, and 1-month follow-up were significantly different (12 [8.75-15], 18 [13.75-22], and 18.5 [14-23], respectively). The percentages of correct answers also differed significantly between the time assessments. Study participants significantly improved their performance between pre-training and post-training (P < .001). This performance was maintained after a 1-month follow-up (P = .95) for the questions related to the detection, determination of cause, and management of patient-ventilator asynchrony. Conclusions: A specific 36-h training program significantly improved the ability of health-care professionals to detect patient-ventilator asynchrony, determine the possible causes of patient-ventilator asynchrony, and properly manage different types of patient-ventilator asynchrony.

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STROKE IN CRITICALLY ILL PATIENTS WITH RESPIRATORY FAILURE DUE TO COVID-19: DISPARITIES BETWEEN LOW-MIDDLE AND HIGH-INCOME COUNTRIES

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Purpose: We aimed to compare the incidence of stroke in low-and middle-income countries (LMICs) versus high-income countries (HICs) in critically ill patients with COVID-19 and its impact on in-hospital mortality. Methods: International observational study conducted in 43 countries. Stroke and mortality incidence rates and rate ratios (IRR) were calculated per admitted days using Poisson regression. Inverse probability weighting (IPW) was used to address the HICs vs. LMICs imbalance for confounders. Results: 23,738 patients [20,511(86.4 %) HICs vs. 3,227(13.6 %) LMICs] were included. The incidence stroke/1000 admitted-days was 35.7 (95 %CI = 28.4-44.9) LMICs and 17.6 (95 %CI = 15.8-19.7) HICs; ischemic 9.47 (95 %CI = 6.57-13.7) LMICs, 1.97 (95 %CI = 1.53, 2.55) HICs; hemorrhagic, 7.18 (95 %CI = 4.73-10.9) LMICs, and 2.52 (95 %CI = 2.00-3.16) HICs; unspecified stroke type 11.6 (95 %CI = 7.75-17.3) LMICs, 8.99 (95 %CI = 7.70-10.5) HICs. In regression with IPW, LMICs vs. HICs had IRR = 1.78 (95 %CI = 1.31-2.42, p < 0.001). Patients from LMICs were more likely to die than those from HICs [43.6% vs 29.2 %; Relative Risk (RR) = 2.59 (95 %CI = 2.29-2.93), p < 0.001)]. Patients with stroke were more likely to die than those without stroke [RR = 1.43 (95 %CI = 1.19-1.72), p < 0.001)]. Conclusions: Stroke incidence was low in HICs and LMICs although the stroke risk was higher in LMICs. Both LMIC status and stroke increased the risk of death. Improving early diagnosis of stroke and redistribution of healthcare resources should be a priority.

## SERVICIO UROLOGÍA

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POSTVOID RESIDUAL VOLUME CORRELATES WITH BLADDER OUTLET OBSTRUCTION AND NOT WITH DETRUSOR CONTRACTION STRENGTH PARAMETERS IN WOMEN: A MATCHED CASE-CONTROL STUDY

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Purpose: To compare voiding parameters in women with and without increased postvoid residual (PVR) volume, to correlate these parameters with PVR volume and PVR percentage, and to describe their ability to predict an increased PVR volume. Methods: Retrospective cross-sectional study of urodynamics data prospectively acquired from consecutive symptomatic women over a 5-year period. Patients with spinal cord disorders and with abdominal straining during voiding (abdominal pressure ≥10 cm H2O over baseline at maximum flow rate [Qmax]) were excluded. Increased PVR volume was defined as ≥50 mL. Patients with and without increased PVR volume were matched by age, presence of urodynamic stress urinary incontinence and premicturition

bladder volume. Female bladder outlet obstruction (BOO) index (female-BOOI), urethral resistance (UR), projected isovolumetric pressure 1 (PIP1), and relative BOO indexes (female-BOOI/PIP1 and UR/PIP1 ratios) were calculated. Linear regression analysis was applied to correlate the voiding indexes with PVR volume and PVR percentage. The area under the curve (AUC) of the receiver operating characteristic (ROC) analysis was calculated to describe diagnostic accuracy of these indexes for increased PVR volume. Results: One-hundred ten women with mean age 65.9±13.7 (range, 20-87) years were included. All voiding parameters were significantly different between women with and without increased PVR volume, except for PIP1. Female-BOOI showed the best correlation with increased PVR volume (R2=0.2509, P<0.001) and PVR percentage (R2=0.3677, P<0.001). PIP1 showed no correlation. Relative BOOI indexes did not improve these correlations. ROC curve analyzes confirmed that female-BOOI and UR had good ability to predict increased PVR volume (AUC=0.841 and AUC=0.856, respectively). Conclusion: PVR volume and PVR percentage correlated with BOO but not to detrusor contraction strength parameters in symptomatic women that void without abdominal straining. The results of this study contribute to the understanding of the pathophysiology of increased PVR volume in women.

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THE INCIDENCE OF PELVIC AND LOW BACK PAIN IN PATIENTS WITH PELVIC ORGAN PROLAPSE

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Introduction and hypothesis: To define the prevalence and incidence of pelvic/low back pain in patients with pelvic organ prolapse (POP). Methods: Patients presenting for POP to three urogynecology centers in the US, UK, and Chile were enrolled in an IRB-approved cross-sectional study assessing pain, GU, GI and sexual function symptoms. For prevalence, symptoms were noted as present if the participant recorded the symptom and reported the degree of bother as “somewhat,” “a moderate amount,” or “a lot.” For incidence, participants were queried if the symptom’s onset concurred with the POP. We also queried if they perceived the symptom was worsened by their POP. Results: Two hundred five participants were recruited: 100 from the US, 46 from the UK, and 59 from Chile. One US participant was excluded due a missing examination. The prevalence of pelvic pain was 42%. Seventy-three percent of these participants reported the onset of pelvic pain coinciding with prolapse onset, and 81% endorsed worsening pelvic pain with POP. The prevalence of low back pain was 46%, with 30% reporting the onset coincided with the onset of POP and 44% responded that prolapse worsened their pain. Conclusion: A higher proportion of participants than expected endorsed pelvic/low back pain. Among patients with pelvic pain, the majority experienced symptom onset with POP onset and a worsening of pain with POP. While roughly half of participants reported low back pain; a minority correlated this to their POP. These findings highlight a high incidence of pelvic pain, challenging the perception of POP as a painless condition.

## CENTRO INVESTIGACIÓN CLÍNICA AVANZADA

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EDUCATIONAL DISPARITIES IN BRAIN HEALTH AND DEMENTIA ACROSS LATIN AMERICA AND THE UNITED STATES

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Background: Education influences brain health and dementia. However, its impact across regions, specifically Latin America (LA) and the United States (US), is unknown. Methods: A total of 1412 participants comprising controls, patients with Alzheimer’s disease (AD), and frontotemporal lobar degeneration (FTLD) from LA and the US were included. We studied the association of education with brain volume and functional connectivity while controlling for imaging quality and variability, age, sex, total intracranial volume (TIV), and recording type. Results: Education influenced brain measures, explaining 24%-98% of the geographical differences. The educational disparities between LA and the US were associated with gray matter volume and connectivity variations, especially in LA and AD patients. Education emerged as a critical factor in classifying aging and dementia across regions. Discussion: The results underscore the impact of education on brain structure and function in LA, highlighting the importance of incorporating educational factors into diagnosing, care, and prevention, and emphasizing the need for global diversity in research. Highlights: Lower education was linked to reduced brain volume and connectivity in healthy controls (HCs), Alzheimer’s disease (AD), and frontotemporal lobar degeneration (FTLD). Latin American cohorts have lower educational levels compared to the those in the United States. Educational disparities majorly drive brain health differences between regions. Educational differences were significant in both conditions, but more in AD than FTLD. Education stands as a critical factor in classifying aging and dementia across regions.

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EFFECT OF REPEATED EXPOSURE TO SEVOFLURANE ON ELECTROENCEPHALOGRAPHIC ALPHA OSCILLATION IN PEDIATRIC PATIENTS UNDERGOING RADIATION THERAPY: A PROSPECTIVE OBSERVATIONAL STUDY

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Background: Pharmacological tolerance is defined as a decrease in the effect of a drug over time, or the need to increase the dose to achieve the same effect. It has not been established whether repeated exposure to sevoflurane induces tolerance in children. Methods: We conducted an observational study in children younger than 6 years of age scheduled for multiple radiotherapy sessions with sevoflurane anesthesia. To evaluate the development of sevoflurane tolerance, we analyzed changes in electroencephalographic spectral power at induction, across sessions. We fitted individual and group-level linear regression models to evaluate the correlation between the outcomes and sessions. In addition, a linear mixed-effect model was used to evaluate the association between radiotherapy sessions and outcomes. Results: Eighteen children were included and the median number of radiotherapy sessions per child was 28 (interquartile range: 10 to 33). There was no correlation between induction time and radiotherapy sessions. At the group level, the linear mixed-effect model showed, in a subgroup of patients, that alpha relative power and spectral edge frequency 95 were inversely correlated with the number of anesthesia sessions. Nonetheless, this subgroup did not differ from the other subjects in terms of age, sex, or the total number of radiotherapy sessions. Conclusions: Our results suggest that children undergoing repeated anesthesia exposure for radiotherapy do not develop tolerance to sevoflurane. However, we found that a group of patients exhibited a reduction in the alpha relative power as a function of anesthetic exposure. These results may have implications that justify further studies.