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

Resúmenes de publicaciones WOS 2023

DEPARTAMENTO ANESTESIOLOGÍA

METHODSX. 2023 JAN 24:10:102041. DOI: 10.1016/J.MEX.2023.102041. ECOLLECTION 2023.

SAFIDE: DETECTION OF SACCADE AND FIXATION PERIODS BASED ON EYE-MOVEMENT ATTRIBUTES FROM VIDEO-OCULOGRAPHY, SCLERAL COIL OR ELECTROOCULOGRAPHY DATA

Samuel Madariaga, Cecilia Babul, José Ignacio Egaña, Iván Rubio-Venegas, Gamze Güney, Miguel Concha-Miranda, Pedro E Maldonado, Christ Devia

In this work we present SaFiDe, a deterministic method to detect eye movements (saccades and fixations) from eye-trace data. We developed this method for human and nonhuman primate data from video- and coil-recorded eye traces and further applied the algorithm to eye traces computed from electrooculograms. All the data analyzed were from free-exploration paradigms, where the main challenge was to detect periods of saccades and fixations that were uncued by the task. The method uses velocity and acceleration thresholds, calculated from the eye trace, to detect saccade and fixation periods. We show that our fully deterministic method detects saccades and fixations from eye traces during free visual exploration. The algorithm was implemented in MATLAB, and the code is publicly available on a GitHub repository. The algorithm presented is entirely deterministic, simplifying the comparison between subjects and tasks. Thus far, the algorithm presented can operate over video-based eye tracker data, human electrooculogram records, or monkey scleral eye coil data.

J PEDIATR HEMATOL ONCOL. 2023 OCT 1;45(7):377-382. DOI: 10.1097/MPH.0000000000002706.

TECHNIQUES AND COMPLICATIONS OF ANESTHESIA IN PEDIATRIC RADIOTHERAPY: A RETROSPECTIVE COHORT STUDY

Nicolás Villablanca, Nicolás Valls, Roberto González

Background: Anesthesia during pediatric external beam radiation therapy poses a challenge, as radiotherapy rooms are not designed for the administration of anesthesia. Aims: We conducted a retrospective cohort study of children who underwent radiation therapy to describe the anesthetic approach and assess anesthetic-related complications. Materials and methods: Data of all, who underwent radiation therapy under general anesthesia between November 2019 and January 2021, were recorded. Data were obtained from medical records, including demographic characteristics and information, regarding the anesthetic procedure and its associated complications. We describe our protocols for preoperative assessment, anesthetic procedures, and postanesthetic discharge evaluation. Results: Over the reporting period, 739 sessions of general anesthesia were performed. The mean number of radiation therapy rounds per patient was 23.5 sessions. Anesthetic induction was accomplished by sevoflurane inhalation in 639 sessions (86.4%) and intravenous propofol in the remaining 13.6%. General anesthesia was maintained with sevoflurane in all cases. Anesthesia-related complications occurred in 118 sessions (15.7%). The most frequent was nausea in 48 (6.4%) cases, followed by hypotension in 38 (5.1%). Airway-related complications occurred at a low frequency (2.3%), and all were resolved successfully with positive pressure ventilation. No patient hospitalizations were required because of any anesthetic complications. Conclusions: Inhalation anesthesia is reliable and safe for pediatric patients undergoing radiation therapy.

CENTRO DE INVESTIGACIÓN CLÍNICA AVANZADA - CICA

SCI DATA. 2023 DEC 9;10(1):889. DOI: 10.1038/S41597-023-02806-8.

THE BRAINLAT PROJECT, A MULTIMODAL NEUROIMAGING DATASET OF NEURODEGENERATION FROM UNDERREPRESENTED BACKGROUNDS

Pavel Prado, Vicente Medel, Raul Gonzalez-Gomez, Agustín Sainz-Ballesteros, Victor Vidal, Hernando Santamaría-García, Sebastian Moguilner, Jhony Mejia, Andrea Slachevsky, Maria Isabel Behrens y otros

The Latin American Brain Health Institute (BrainLat) has released a unique multimodal neuroimaging dataset of 780 participants from Latin American. The dataset includes 530 patients with neurodegenerative diseases such as Alzheimer's disease (AD), behavioral variant frontotemporal dementia (bvFTD), multiple sclerosis (MS), Parkinson's disease (PD), and 250 healthy controls (HCs). This dataset (62.7 ± 9.5 years, age range 21-89 years) was collected through a multicentric effort across five Latin American countries to address the need for affordable, scalable, and available biomarkers in regions with larger inequities. The BrainLat is the first regional collection of clinical and

cognitive assessments, anatomical magnetic resonance imaging (MRI), resting-state functional MRI (fMRI), diffusion-weighted MRI (DWI), and high density resting-state electroencephalography (EEG) in dementia patients. In addition, it includes demographic information about harmonized recruitment and assessment protocols. The dataset is publicly available to encourage further research and development of tools and health applications for neurodegeneration based on multimodal neuroimaging, promoting the assessment of regional variability and inclusion of underrepresented participants in research.

SCI REP. 2023 OCT 10;13(1):17137. DOI: 10.1038/S41598-023-44203-6.

THE AUTOPHAGY PROTEIN DEF8 IS ALTERED IN ALZHEIMER'S DISEASE AND Aβ42-EXPRESSING DROSOPHILA BRAINS

Sebastián Oyarce-Pezoa, Guilherme Gischkow Rucatti, Francisco Muñoz-Carvajal, Nicole Sanhueza, Wileidy Gomez, Sandra Espinoza, Mario Leiva, Nicolás García, Daniela P Ponce, Carol D SanMartín, Diego Rojas-Rivera, Natalia Salvadores, Maria I Behrens, Ute Woehlbier, Melissa Calegaro-Nassif, Mario Sanhueza

Alzheimer's disease (AD) is the most common neurodegenerative disorder, characterized by protein accumulation in the brain as a main neuropathological hallmark. Among them, Aβ42 peptides tend to aggregate and create oligomers and plaques. Macroautophagy, a form of autophagy characterized by a double-membrane vesicle, plays a crucial role in maintaining neuronal homeostasis by degrading protein aggregates and dysfunctional organelles as a quality control process. Recently, DEF8, a relatively uncharacterized protein, has been proposed as a participant in vesicular traffic and autophagy pathways. We have reported increased DEF8 levels in lymphocytes from mild cognitive impairment (MCI) and early-stage AD patients and a neuronal profile in a murine transgenic AD model. Here, we analyzed DEF8 localization and levels in the postmortem frontal cortex of AD patients, finding increased levels compared to healthy controls. To evaluate the potential function of DEF8 in the nervous system, we performed an in silico assessment of its expression and network profiles, followed by an in vivo evaluation of a neuronal Def8 deficient model using a Drosophila melanogaster model of AD based on Aβ42 expression. Our findings show that DEF8 is an essential protein for maintaining cellular homeostasis in the nervous system, and it is upregulated under stress conditions generated by Aβ42 aggregation. This study suggests DEF8 as a novel actor in the physiopathology of AD, and its exploration may lead to new treatment avenues.

ALZHEIMERS DEMENT. 2023 FEB;19(2):721-735. DOI: 10.1002/ALZ.12757.

BIOMARKERS FOR DEMENTIA IN LATIN AMERICAN COUNTRIES: GAPS AND OPPORTUNITIES

Mario A Parra, Paulina Orellana, Tomas Leon, Cabello G Victoria, Fernando Henriquez, Rodrigo Gomez, Constanza Avalos, Andres Damian, Andrea Slachevsky, Agustin Ibañez, Henrik Zetterberg, Betty M Tijms, Jennifer S Yokoyama, Stefanie D Piña-Escudero, J Nicholas Cochran, Diana L Matallana, Daisy Acosta, Ricardo Allegri, Bianca P Arias-Suárez, Bernardo Barra, Maria Isabel Behrens y otros

Limited knowledge on dementia biomarkers in Latin American and Caribbean (LAC) countries remains a serious barrier. Here, we reported a survey to explore the ongoing work, needs, interests, potential barriers, and opportunities for future studies related to biomarkers. The results show that neuroimaging is the most used biomarker (73%), followed by genetic studies (40%), peripheral fluids biomarkers (31%), and cerebrospinal fluid biomarkers (29%). Regarding barriers in LAC, lack of funding appears to undermine the implementation of biomarkers in clinical or research settings, followed by insufficient infrastructure and training. The survey revealed that despite the above barriers, the region holds a great potential to advance dementia biomarkers research. Considering the unique contributions that LAC could make to this growing field, we highlight the urgent need to expand biomarker research. These insights allowed us to propose an action plan that addresses the recommendations for a biomarker framework recently proposed by regional experts.

FRONT AGING NEUROSCI. 2023 FEB 9:15:1097577. DOI: 10.3389/FNAGI.2023.1097577. ECOLLECTION 2023.

VISUAL-SPATIAL PROCESSING IMPAIRMENT IN THE OCCIPITAL-FRONTAL CONNECTIVITY NETWORK AT EARLY STAGES OF ALZHEIMER'S DISEASE

Iván Plaza-Rosales, Enzo Brunetti, Rodrigo Montefusco-Siegmund, Samuel Madariaga, Rodrigo Hafelin, Daniela P Ponce, María Isabel Behrens, Pedro E Maldonado, Andrea Paula-Lima

Introduction: Alzheimer's disease (AD) is the leading cause of dementia worldwide, but its pathophysiological phenomena are not fully elucidated. Many neurophysiological markers have been suggested to identify early cognitive impairments of AD. However, the diagnosis of this disease remains a challenge for specialists. In the present cross-sectional study, our objective was to evaluate the manifestations and mechanisms underlying visual-spatial deficits at the early stages of AD. Methods: We combined behavioral, electroencephalography (EEG), and eye movement recordings during the performance of a spatial navigation task (a virtual version of the Morris Water Maze adapted to humans). Participants (69-88 years old) with amnesic mild cognitive impairment-Clinical Dementia Rating scale (aMCI-CDR 0.5) were selected as probable early AD (eAD) by a neurologist specialized in dementia. All patients included in this study were evaluated at the CDR 0.5 stage but progressed to probable AD during clinical follow-up. An equal number of matching healthy controls (HCs) were evaluated while performing the navigation task. Data were collected at the Department of Neurology of the Clinical Hospital of the Universidad de Chile and the Department of Neuroscience of the Faculty of Universidad de Chile. Results: Participants with aMCI preceding AD (eAD) showed impaired spatial learning and their visual exploration differed from the control group. eAD group did not clearly prefer regions of interest that could guide solving the task, while controls did. The eAD group showed decreased visual occipital evoked potentials associated with eye fixations, recorded at occipital electrodes. They also showed an alteration of the spatial spread of activity to parietal and frontal regions at the end of the task. The control group presented marked occipital activity in the beta band (15-20 Hz) at early visual processing time. The eAD group showed a reduction in beta band functional connectivity in the prefrontal cortices reflecting poor planning of navigation strategies. Discussion: We found that EEG signals combined with visual-spatial navigation analysis, yielded early and specific features that may underlie the basis for understanding the loss of functional connectivity in AD. Still, our results are clinically promising for early diagnosis required to improve quality of life and decrease healthcare costs.

APPL NEUROPSYCHOL ADULT. 2023 FEB 24:1-17. DOI: 10.1080/23279095.2023.2174438.

THE LIMITATIONS AND CHALLENGES IN THE ASSESSMENT OF EXECUTIVE DYSFUNCTION ASSOCIATED WITH REAL-WORLD FUNCTIONING: THE *OPPORTUNITY OF SERIOUS GAMES*

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Nowadays, there is a broad range of methods for detecting and evaluating executive dysfunction ranging from clinical interview to neuropsychological evaluation. Nevertheless, a critical issue of these assessments is the lack of correspondence of the neuropsychological test's results with real-world functioning. This paper proposes serious games as a new framework to improve the neuropsychological assessment of real-world functioning. We briefly discuss the contribution and limitations of current methods of evaluation of executive dysfunction (paper-and-pencil tests, naturalistic observation methods, and Information and Communications Technologies) to inform on daily life functioning. Then, we analyze what are the limitations of these methods to predict real-world performance: (1) A lack of appropriate instruments to investigate the complexity of real-world functioning, (2) the vast majority of neuropsychological tests assess well-structured tasks, and (3) measurement of behaviors are based on simplistic data collection and statistical analysis. This work shows how serious games offer an opportunity to develop more efficient tools to detect executive dysfunction in everyday life contexts. Serious games provide meaningful narrative stories and virtual or real environments that immerse the user in natural and social environments with social interactions. In those highly interactive game environments, the player needs to adapt his/her behavioral performance to novel and ill-structured tasks which are suited for collecting user interaction evidence. Serious games offer a novel opportunity to develop better tools to improve diagnosis of the executive dysfunction in everyday life contexts. However, more research is still needed to implement serious games in everyday clinical practice.

RES SQ [PREPRINT]. 2023 SEP 18:RS.3.RS-3215728. DOI: 10.21203/RS.3.RS-3215728/V1.

DEVELOPMENTAL TRAJECTORIES OF EEG APERIODIC AND PERIODIC POWER: IMPLICATIONS FOR UNDERSTANDING THE TIMING OF THALAMOCORTICAL DEVELOPMENT DURING INFANCY

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

The development of neural circuits over the first years of life has long-lasting effects on brain function, yet our understanding of early circuit development in humans remains limited. Here, aperiodic and periodic EEG power features 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. Consistent with the transient developmental progression of thalamocortical circuitry, we observe the presence and then absence of periodic alpha and high beta peaks across the three-year period, as well as the emergence of a low beta peak (12-20Hz) after six months of age. We present preliminary evidence that the emergence of the low beta peak is associated with thalamocortical connectivity sufficient for anesthesia-induced alpha coherence. Together, these findings suggest that early age-dependent changes in alpha and beta periodic peaks may reflect the state of thalamocortical network development.

FRONT CELL NEUROSCI. 2023 MAR 21:17:1132121. DOI: 10.3389/FNCEL.2023.1132121. ECOLLECTION 2023.

LONG-TERM POTENTIATION AND SPATIAL MEMORY TRAINING STIMULATE THE HIPPOCAMPAL EXPRESSION OF RYR2 CALCIUM RELEASE CHANNELS

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Introduction: Neuronal Ca2+ signals generated through the activation of Ca2+-induced Ca2+ release in response to activity-generated Ca2+ influx play a significant role in hippocampal synaptic plasticity, spatial learning, and memory. We and others have previously reported that diverse stimulation protocols, or different memory-inducing procedures, enhance the expression of endoplasmic reticulum-resident Ca2+ release channels in rat primary hippocampal neuronal cells or hippocampal tissue. Methods and Results: Here, we report that induction of long-term potentiation (LTP) by Theta burst stimulation protocols of the CA3-CA1 hippocampal synapse increased the mRNA and protein levels of type-2 Ryanodine Receptor (RyR2) Ca2+ release channels in rat hippocampal slices. Suppression of RyR channel activity (1 h preincubation with 20 μM ryanodine) abolished both LTP induction and the enhanced expression of these channels; it also promoted an increase in the surface expression of the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor subunits GluR1 and GluR2 and caused a moderate but significant reduction of dendritic spine density. In addition, training rats in the Morris water maze induced memory consolidation, which lasted for several days after the end of the training period, accompanied by an increase in the mRNA levels and the protein content of the RyR2 channel isoform. Discussion: We confirm in this work that LTP induction by TBS protocols requires functional RyR channels. We propose that the increments in the protein content of RyR2 Ca2+ release channels, induced by LTP or spatial memory training, play a significant role in hippocampal synaptic plasticity and spatial memory consolidation.

ANTIOXIDANTS (BASEL). 2023 NOV 6;12(11):1972. DOI: 10.3390/ANTIOX12111972.

AMYLOID β-OLIGOMERS INHIBIT THE NUCLEAR CA2+ SIGNALS AND THE NEUROPROTECTIVE GENE EXPRESSION INDUCED BY GABAZINE IN HIPPOCAMPAL NEURONS

Pedro Lobos, Ignacio Vega-Vásquez, Barbara Bruna, Silvia Gleitze, Jorge Toledo, Steffen Härtel, Cecilia Hidalgo, Andrea Paula-Lima

Hippocampal neuronal activity generates dendritic and somatic Ca2+ signals, which, depending on stimulus intensity, rapidly propagate to the nucleus and induce the expression of transcription factors and genes with crucial roles in cognitive functions. Soluble amyloid-beta oligomers (AβOs), the main synaptotoxins engaged in the pathogenesis of Alzheimer's disease, generate aberrant Ca2+ signals in

primary hippocampal neurons, increase their oxidative tone and disrupt structural plasticity. Here, we explored the effects of sub-lethal AβOs concentrations on activity-generated nuclear Ca2+ signals and on the Ca2+-dependent expression of neuroprotective genes. To induce neuronal activity, neuron-enriched primary hippocampal cultures were treated with the GABAA receptor blocker gabazine (GBZ), and nuclear Ca2+ signals were measured in AβOs-treated or control neurons transfected with a genetically encoded nuclear Ca2+ sensor. Incubation (6 h) with AβOs significantly reduced the nuclear Ca2+ signals and the enhanced phosphorylation of cyclic AMP response element-binding protein (CREB) induced by GBZ. Likewise, incubation (6 h) with AβOs significantly reduced the GBZ-induced increases in the mRNA levels of neuronal Per-Arnt-Sim domain protein 4 (Npas4), brain-derived neurotrophic factor (BDNF), ryanodine receptor type-2 (RyR2), and the antioxidant enzyme NADPH-quinone oxidoreductase (Nqo1). Based on these findings we propose that AβOs, by inhibiting the generation of activity-induced nuclear Ca2+ signals, disrupt key neuroprotective gene expression pathways required for hippocampal-dependent learning and memory processes.

CENTRO DE IMAGENOLOGÍA

J NEUROIMMUNOL. 2023 MAY 5:378:578085. DOI:10.1016/J.JNEUROIM.2023.578085.

NEURO-SJÖGREN: A CLINICAL-RADIOLOGICAL PARADOX AFFECTING THE CENTRAL NERVOUS SYSTEM

Eduardo Villa, Alejandra Torres, Patricia Orellana, José de Grazia, María Elena Villanueva, Carlos Guevara

Neurological manifestations can occur in up to 67% of patients with primary Sjögren's Syndrome, also known as Neuro-Sjogren's syndrome (NSS), and a 5% can present central nervous system involvement, with severe and possibly lethal consequences. We present the radiological follow-up of a patient with NSS who consulted for limb weakness and visual loss, and fourteen years later developed sicca symptoms. She was diagnosed with a saliva gland biopsy, and started treatment with steroids, cyclophosphamide, and then rituximab, achieving a favourable clinical response and stabilization of lesions. We discuss key aspects regarding the clinical presentation, diagnosis, imaging, and treatment of this elusive disease.

DIAGNOSTICS (BASEL). 2023 OCT 17;13(20):3230. DOI: 10.3390/DIAGNOSTICS13203230.

HYALINE AND CYSTIC DEGENERATION OF UTERINE LEIOMYOMAS: CT AND MR IMAGING WITH HISTOPATHOLOGICAL SAMPLE ANALYSES

Camilo G Sotomayor, Carla Parra, Maximiliano Miranda, Juan Salvador Casas, Gonzalo Cárdenas, Álvaro Sanhueza, Francisca Araya, Iván Gallegos, Sebastián Yévenes

Leiomyomas are the most common solid benign uterine neoplasms; they are usually asymptomatic and are identified incidentally. Yet, responsive to stimulation by estrogens, leiomyomas may expand, potentially outgrowing their blood supply to undergo hemorrhage, fibrosis, calcification, and atrophy. These pathologic mechanisms commonly lead to leiomyomas degeneration, i.e., red, hyaline, cystic, or myxoid. Magnetic resonance (MR) imaging is the most accurate imaging technique for the characterization of leiomyomas. In cases of degeneration, variable features on T2-weighted and contrast-enhanced images can be found. With no recent radiologic pathologic correlation literature available on this matter, herewith, we provide computed tomography (CT)/MR imaging along with histopathological specimens of two young women who were diagnosed with hyaline or hyaline and cyst degeneration of uterine leiomyomas at our university hospital. We report on the imaging features of uterine leiomyomas using CT and MR imaging and discuss the available literature on imaging signs that may be suggestive of hyaline or cyst degeneration using either of the imaging examination methods.

IEEE ACCESS, VOL. 11, PP. 103177-103188, 2023, DOI: 10.1109/ACCESS.2023.3313980

EFFICIENT AND MOTION CORRECTION-FREE MYOCARDIAL PERFUSION SEGMENTATION IN SMALL MRI DATA USING DEEP TRANSFER LEARNING FROM CINE IMAGES: A PROMISING FRAMEWORK FOR CLINICAL IMPLEMENTATION

García-Jara, Germán and Jimenez-Molina, Angel and Reyes, Esteban and Tapia-Rivas, Nicolás and Ramos-Gómez, Cristóbal and De Grazia, José and Sepúlveda, Matías

Perfusion cardiovascular magnetic resonance imaging is used to quantify the heart's blood flow, which requires the segmentation of the myocardium, a laborious task. Deep learning-based methods, the most accurate to accomplish this task, still rely on expensive motion correction steps and require large labeled datasets. This paper presents an innovative, efficient approach to myocardial perfusion segmentation, utilizing deep learning techniques without motion correction and with minimal data requirements. Through transfer learning, this methodology leverages the wealth of information available from large, publicly accessible cine magnetic resonance datasets, which provide anatomically analogous images to perfusion ones. This methodology includes normalization and cropping of cine images using a Region-of-Interest detector based on a Markovian, graph-based visual saliency algorithm improved by a sequence of morphological operations. After pretraining a U-net convolutional neural network, a special fine-tuning scheme optimizes its performance. The parameters learned are the starting point for training on a smaller perfusion dataset from the Clinical Hospital of the University of Chile. After an ablation study, the best model is obtained when using both cropping and fine-tuning from the cine dataset, segmenting the left ventricle endocardium with Dice, IoU, and Hausdorff distance of 92.2%, 85.9%, and 5.1 mm respectively, and 95.6%, 91.7%, and 4.6 mm for the left ventricle epicardium. Notably, fine-tuning achieves a Dice of 91.8% for endocardium and 95.2% for epicardium when only 289 perfusion training images are available. These are promising results for developing targeted implementations in real healthcare settings when only small datasets are available.

DEPARTAMENTO DE ANESTESIOLOGÍA Y MEDINA PERIOPERATORIA

REV ESP ANESTESIOL 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

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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.

REG ANESTH PAIN MED. 2023 OCT;48(10):489-494. DOI: 10.1136/RAPM-2023-104332.

RANDOMIZED CLINICAL TRIAL COMPARING PERICAPSULAR NERVE GROUP (PENG) BLOCK AND PERIARTICULAR LOCAL ANESTHETIC INFILTRATION FOR TOTAL HIP ARTHROPLASTY

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Background: This randomized trial compared pericapsular nerve group block and periarticular local anesthetic infiltration in patients undergoing primary total hip arthroplasty. We hypothesized that, compared with pericapsular nerve group block, periarticular local anesthetic infiltration would decrease the postoperative incidence of quadriceps weakness at 3 hours fivefold (ie, from 45% to 9%). Methods: Sixty patients undergoing primary total hip arthroplasty under spinal anesthesia were randomly allocated to receive a pericapsular nerve group block (n=30) using 20 mL of adrenalized bupivacaine 0.50%, or periarticular local anesthetic infiltration (n=30) using 60 mL of adrenalized bupivacaine 0.25%. Both groups also received 30 mg of ketorolac, either intravenously (pericapsular nerve group block) or periarticularly (periarticular local anesthetic infiltration), as well as 4 mg of intravenous dexamethasone. Postoperatively, a blinded evaluator carried out sensory assessment and motor assessment (knee extension and hip adduction) at 3, 6 and 24 hours. Furthermore, the blinded observer also recorded static and dynamic pain scores at 3, 6, 12, 18, 24, 36 and 48 hours; time to first opioid request; cumulative breakthrough morphine consumption at 24 hours and 48 hours; opioid-related side effects; ability to perform physiotherapy at 6, 24 and 48 hours; as well as length of stay. Results: There were no differences in quadriceps weakness at 3 hours between pericapsular nerve group block and periarticular local anesthetic infiltration (20% vs 33%; p=0.469). Furthermore, no intergroup differences were found in terms of sensory block or motor block at other time intervals; time to first opioid request; cumulative breakthrough morphine consumption; opioid-related side effects; ability to perform physiotherapy; and length of stay. Compared with pericapsular nerve group block, periarticular local anesthetic infiltration resulted in lower static pain scores (at all measurement intervals) and dynamic pain scores (at 3 and 6 hours). Conclusion: For primary total hip arthroplasty, pericapsular nerve group block and periarticular local anesthetic infiltration result in comparable rates of quadriceps weakness. However, periarticular local anesthetic infiltration is associated with lower static pain scores (especially during the first 24 hours) and dynamic pain scores (first 6 hours). Further investigation is required to determine the optimal technique and local anesthetic admixture for periarticular local anesthetic infiltration.

DEPARTAMENTO CARDIOVASCULAR

REV MED CHIL. 2023 JUN;151(6):792-796. DOI: 10.4067/S0034-98872023000600792.

ESTENOSIS TRICUSPÍDEA DE BIOPRÓTESIS TRATADA MEDIANTE IMPLANTE VALVULAR PERCUTÁNEO: UNA SOLUCIÓN SEGURA PARA UN PACIENTE INUSUAL.

Alberto Barria, Ernesto Chaigneau, Jaime Zamorano

Se comunica el caso de una mujer de 31 años quien había sido previamente sometida a reemplazo valvular aórtico, mitral y tricuspídeo en tres episodios quirúrgicos. Fue ingresada a nuestra sección de cardiología con síntomas compatibles con insuficiencia cardiaca derecha. Se efectuó evaluación mediante ecocardiograma, sondeo cardíaco derecho/izquierdo, angioTAC cardíaco y cardio resonancia. Se diagnosticó una estenosis tricuspídea severa secundaria a disfunción de prótesis biológica. Debido a alto riesgo operatorio y riesgo de falla ventricular derecha post-operatorio, la paciente fue rechazada para reemplazo valvular quirúrgico. Se decidió efectuar reemplazo tricuspídeo procedimiento "valve in valve". Se logró efectuar de manera exitosa por abordeje venoso femoral, prótesis balón expansible. Se demostró corrección de la estenosis tricuspídea y la paciente evolucionó con remisión de los síntomas de falla cardíaca.

FREE RADICAL BIOLOGY AND MEDICINE VOLUME 208, SUPPLEMENT 1, 1 NOVEMBER 2023, PAGES S88-S89

EFFECT OF AGEING ON OXIDATIVE STRESS AND INFLAMMATORY RESPONSE BY ON-PUMP CARDIAC SURGERY IN PATIENTS TREATED WITH ANTIOXIDANTS: A RANDOMIZED CONTROLLED TRIAL

José Lillo-Moya, Abraham Isaac Jacob Gajardo Cortez, Juan Carlos Prieto, Ruben Aguayo, Angel Alberto Puentes Rico, Solange Silva, Cristobal Ramos, Karla Ramos, Ramón Rodrigo

Introduction: Cardiac surgery with extracorporeal circulation (CSEC) induces oxidative stress (OS) and inflammatory damage by ischemia reperfusion (IR). OS has been postulated as an important factor in this process and also in human ageing but there are lack evidence about the effect of ageing on IR. Aim: To evaluate whether there is an age-related response on OS and inflammation in patients undergoing CSEC treated with antioxidants. Methods: Randomized controlled trial with 203 patients scheduled for CSEC who were allocated to placebo or antioxidants before CSEC. Patients were divided by age in young patients (44-59 years) and older patients (>60 years). Blood samples were withdrawn before and after CSEC to measure malondialdehyde (MDA), ferric reducing ability of plasma (FRAP), leukocytes and hsCRP. For each parameter a ratio (before/after CSEC) was calculated to assess the OS and inflammatory response induced by CSEC. Linear regression analyses was performed to test the effect of ageing and antioxidants on IR response. Results: Antioxidant supplementation reduced the OS and inflammatory response induced by CSEC in both young and older patients. In placebo group, elderly patients shown a higher MDA and leukocytes ratio but lower FRAP ratio than youngers. On the other hand, antioxidant therapy annulled MDA, FRAP and leukocytes differences between older and young patients, and also induced a lower hsCRP ratio in elderlies. Conclusion: Antioxidant supplementation reduces OS and inflammation by ischemia-reperfusion in CSEC. Although there is an age-related response on OS and inflammation by CSEC, the antioxidant supplementation annuls this effect.

FREE RADICAL BIOLOGY AND MEDICINE. VOLUME 208, SUPPLEMENT 1, 1 NOVEMBER 2023, PAGES S127-S128

PROPOSAL OF A NEW FLUORIMETRIC ASSAY TO MEASURE THE ANTIOXIDANT DRUG VITAMIN C IN HUMAN PLASMA

José Lillo-Moya, Abraham Isaac Jacob Gajardo Cortez, Catalina Rojas-Solé, Daniel San-Martín-Martínez, Juan Carlos Prieto, Ruben Aguayo, Angel Alberto Puentes Rico, Cristobal Ramos, Ramón Rodrigo

Introduction: Vitamin C (VC) is a recognized antioxidant drug that is used in many clinical trials in a variety of human pathologies related to oxidative stress. However, in high doses VC could act as a pro-oxidant agent, a reason to monitor its concentrations in clinical trials. Current methods to measure plasma drug concentrations (such as HPLC) are expensive and not broadly available. On the other hand, fluorometric methods (cheaper and faster) have been developed mainly in aqueous solutions. In this study, we developed a new assay to measure VC in human plasma based on fluorometry. Methods: Blood samples from healthy humans were withdrawn, the plasma fraction obtained by centrifugation, and metaphosphoric acid 5% added to stabilize VC. The method was based on the oxidation of VC with a iodine solution 0.1N and the reaction with o-phenylenediamine (among other agents) in sequential steps. Samples were measured in a fluorometer (Allsheng Fluo100A, 348 nm excitation/423 nm emission). A calibration curve with 10 values (10-800 uM of VC) was constructed to relate optical densities with concentrations. In a validation phase, other 32 plasma samples with known VC concentrations were assessed with the method. Difference between observed (estimated) and known VC concentrations were calculated, together with the R2, and the Linn coefficient. Results: The calibration curve showed a R2 = 0.99 (p-value < 0.001). In the validation phase, the R2 was 0.998 (p-value <0.0001). The observed performance was better in values >100 uM of VC, with the differences between the observed and known values of ±10% µM. The mean difference was 1.93 ± 19.85 and the 95% limits of agreement were (-35.73 to +39.63). The Linn coefficient was 0.993 (0.988-0.996; CI 95%). Conclusion: The developed fluorometric method has a good performance in plasma samples from humans, could be used in clinical trials with VC. Further validation against a gold standard (as HPLC) is needed.

FREE RADICAL BIOLOGY AND MEDICINE. VOLUME 208, SUPPLEMENT 1, 1 NOVEMBER 2023, PAGES S86-S87

COMBINED ANTIOXIDANT THERAPY AGAINST REPERFUSION INJURY IN ACUTE MYOCARDIAL INFARCTION: PRECLINICAL DRUG DEVELOPMENT AND PHASE I CLINICAL TRIAL IN HUMANS

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Introduction: Myocardial reperfusion injury (MRI) accounts about 50% of final infarct size (IS) in acute myocardial infarction (AMI). Oxidative stress has a key role in MRI, however, no effective therapy exists in humans. Herein, we aimed to develop a cardioprotective combined antioxidant therapy (CAT) in rats, to then test it for the first time in humans. Methods: Increasing doses of ascorbic acid (AA), n-acetylcysteine (NAC), and deferoxamine (DFO) were infused during reperfusion in isolated rat hearts subjected to ischemia-reperfusion. The lowest cardioprotective doses of each drug (according to IS) were assessing in combinations, selecting the best to test in humans (namely CAT). Subsequently, CAT was i.v infused for 90-min at two different rates (CAT1 and CAT2) in a phase 1 double-blind trial. Healthy subjects (n=18) were randomized 2:1 to CAT or placebo (NaCl 0.9%). Blood samples were collected to measure plasma drug concentrations and oxidative stress parameters. Adverse events (AE) were registered up to 30 days after. Results: AA, NAC and DFO decreased IS in rats (p<0.005). Compared to placebo (IS 39.4±8.1%) the lowest cardioprotective concentrations were: 10µM DFO, 100µM NAC, and 100µM AA (p<0.05). AA-DFO-NAC had the greatest cardioprotection (IS 7.3±4.4) compared to the other groups (p<0.01). In humans, CAT1 and CAT2 increased drug concentrations compared to placebo (p<0.001); maximum drug concentrations (µmol/L) for CAT1, CAT2 and placebo were, respectively: 826.2±284.2, 742.5±174.1 and 49.9 (AA), 577.3±130.4, 77.2±65.7, and undetectable (NAC), 7.6±2.6, 4.6±2.5, and undetectable (DFO). Pharmacokinetic parameters were similar between CAT1 and CAT2. Meanwhile FRAP levels were increased in CAT1 and CAT2 vs placebo (p-value<0.001), plasma F2-isoprostanes were similar. Severe AE were not found in any patient. Conclusion: Designed CAT is suitable to prevent MRI and safe for humans.

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POLYCYSTIN-1 IS A CRUCIAL REGULATOR OF BIN1 EXPRESSION AND T-TUBULE REMODELING ASSOCIATED WITH THE DEVELOPMENT OF DILATED CARDIOMYOPATHY

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Cardiomyopathy is commonly observed in patients with autosomal dominant polycystic kidney disease (ADPKD), even when they have normal renal function and arterial pressure. The role of cardiomyocyte polycystin-1 (PC1) in cardiovascular pathophysiology remains unknown. PC1 is a potential regulator of BIN1 that maintains T-tubule structure, and alterations in BIN1 expression induce cardiac pathologies. We used a cardiomyocyte-specific PC1-silenced (PC1-KO) mouse model to explore the relevance of cardiomyocyte PC1 in the development of heart failure (HF), considering reduced BIN1 expression induced T-tubule remodeling as a potential mechanism. PC1-KO mice exhibited an impairment of cardiac function, as measured by echocardiography, but no signs of HF until 7-9 months of age. Of the PC1-KO mice, 43% died suddenly at 7 months of age, and 100% died after 9 months with dilated cardiomyopathy. Total BIN1 mRNA, protein levels, and its localization in plasma membrane-enriched fractions decreased in PC1-KO mice. Moreover, the BIN1 + 13 isoform decreased while the BIN1 + 13 + 17 isoform was overexpressed in mice without signs of HF. However, BIN1 + 13 + 17 overexpression was not observed in mice with HF. T-tubule remodeling and BIN1 score measured in plasma samples were associated with decreased PC1-BIN1 expression and HF development. Our results show that decreased PC1 expression in cardiomyocytes induces dilated cardiomyopathy associated with diminished BIN1 expression and T-tubule remodeling. In conclusion, positive modulation of BIN1 expression by PC1 suggests a novel pathway that may be relevant to understanding the pathophysiological mechanisms leading to cardiomyopathy in ADPKD patients.

DEPARTAMENTO DE CIRUGÍA

AESTHETIC PLAST SURG. 2023 OCT;47(5):1896-1904. DOI: 10.1007/S00266-022-03222-W.

WHAT MAKES A BEAUTIFUL BUTTOCK BEAUTIFUL? A CASE-CONTROL STUDY COMPARING BUTTOCKS MODELS VERSUS NORMAL WOMEN BY MAGNETIC RESONANCE IMAGING, PHOTOGRAPHY AND ANTHROPOMETRY

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Objectives: To describe characteristics of women with aesthetically ideal buttocks and differentiate them from women with normal buttocks. Methods: Case-control study comparing anatomy of women with ideal buttocks (buttocks models) to women with normal buttocks using magnetic resonance images, anthropometric measurements and photography. Results: Comparing to normal women, buttocks models have a narrower waist, narrower iliac crest, wider C point, wider hips and bigger and thicker gluteus maximus muscle (GMM). A bigger GMM adds more projection to the C point, point of maximum projection in the lateral view is 2.7 cm higher than the pubic bone. The amount of subcutaneous fat was equal in models and controls. Conclusions: Our study provides new knowledge regarding the tridimensional aspects of the beauty of the buttocks area. A beautiful buttock is a conjunction of adequate bony shape, muscle development, subcutaneous fat layer, and tight skin. Comparing to normal women, buttocks models have a narrower waist, narrower iliac crest, wider C point, wider hips and bigger and thicker Gluteus Maximus Muscle. Accurate understanding of the aesthetic goals in a given patient can guide surgical technique. Level of evidence iii: This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

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

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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.

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LONG-TERM (18 YEARS) RESULTS OF PATIENTS WITH LONG-SEGMENT BARRETT ESOPHAGUS SUBMITTED TO ACID SUPPRESSION-DUODENAL DIVERSION OPERATION: BETTER THAN NISSEN FUNDOPLICATION?

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Objective: To determine late results of AS-DD procedure in long-segment (LSBE) and extralong-segment BE (ELSBE) using subjective and objective measurements to ascertain the histological impact over intestinal metaplasia (IM) and progression to EAC. Summary of background data: Barrett esophagus (BE) is a known precursor of esophageal adenocarcinoma (EAC), and Nissen fundoplication has proven to be unable

to stop mixed reflux among them. Our group proposed a surgical procedure that handles pathophysiological changes responsible for BE. Methods: This prospective study included 127 LSBE and ELSBE subjects submitted to clinical and functional analyses. They were presented to selective vagotomy, fundoplication, partial gastrectomy with Roux-en-Y reconstruction. The changes in IM were determined in both groups. Results: Follow-up was completed at a mean of 18 years in 81% of the cases. Visick I-II scores were seen in 88% of LSBE and 65% in ELSBE ($P < 0.01$). There was significant healing of erosive esophagitis and esophageal peptic ulcers, and strictures were resolved in 71%. There was 38% of IM regression in LSBE. Two cases in each group progressed to EAC at a mean of 15 years. Pathologic acid reflux was abolished in 91% and duodenal in 100%. There was a regression of low-grade dysplasia to IM in 80%. Conclusions: AS-DD permanently eliminates pathologic refluxate to the esophagus. The progression to HGD/EAC is lower compared to medical treatment, with an 8-fold reduction in LSBE and 2.2-fold in ELSBE. AS-DD seems to influence IM behaviors, and it is a tool that could reduce and delay progression to EAC.

ARQ BRAS CIR DIG. 2023 APR 14:36:E1723. DOI: 10.1590/0102-672020230002E1723. ECOLLECTION 2023.

TOMOGRAPHIC SARCOPENIA PREDICTS ANASTOMOTIC LEAKS AND LONG-TERM SURVIVAL IN GASTRIC CANCER PATIENTS OPERATED WITH CURATIVE INTENT

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Background: The preoperative nutritional state has prognostic postoperative value. Tomographic density and area of psoas muscle are validated tools for assessing nutritional status. There are few reports assessing the utility of staging tomography in gastric cancer patients in this field. Aims: This study aimed to determine the influence of sarcopenia, measured by a preoperative staging computed tomography scan, on postoperative morbimortality and long-term survival in patients operated on for gastric cancer with curative intent. Methods: This retrospective study was conducted from 2007 to 2013. The definition of radiological sarcopenia was by measurement of cross-sectional area and density of psoas muscle at the L3 (third lumbar vertebra) level in an axial cut of an abdominopelvic computed tomography scan (in the selection without intravascular contrast media). The software used was OsirixX version 10.0.2, with the tool "propagate segmentation", and all muscle seen in the image was manually adjusted. Results: We included 70 patients, 77% men, with a mean cross-sectional in L3 of 16.6 cm2 (standard deviation+6.1) and mean density of psoas muscle in L3 of 36.1 mean muscle density (standard deviation+7.1). Advanced cancers were 86, 28.6% had signet-ring cells, 78.6% required a total gastrectomy, postoperative surgical morbidity and mortality were 22.8 and 2.8%, respectively, and overall 5-year long-term survival was 57.1%. In the multivariate analysis, cross-sectional area failed to predict surgical morbidity (p=0.4) and 5-year long-term survival (p=0.34), while density of psoas muscle was able to predict anastomotic fistulas (p=0.009; OR 0.86; 95%CI 0.76-0.96) and 5-year long-term survival (p=0.04; OR 2.9; 95%CI 1.04-8.15). Conclusions: Tomographic diagnosis of sarcopenia from density of psoas muscle can predict anastomotic fistulas and long-term survival in gastric cancer patients treated with curative intent.

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INCIDENCIA DE HIPOCALCEMIA POST TIROIDECTOMÍA. FACTORES PREDICTORES (PTH, FÓSFORO, MAGNESIO) Y PROTOCOLO DE MANEJO CON ALTA PRECOZ.

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Se ha propuesto la medición de PTH como predictor de hipocalcemia postoperatoria transitoria y permanente. No hay un estándar de punto de corte o tiempo de toma de muestra. El objetivo es reportar la incidencia de hipocalcemia post tiroidectomía en un grupo quirúrgico de alto volumen y proponer un protocolo de manejo ambulatorio (esquemas de I a V) según niveles postoperatorios (PO) de calcemia, PTHi (normal, baja o indetectable) y síntomas. Y determinar valores de PTH postoperatoria como predictores de hipocalcemia. En 106 pacientes con tiroidectomía total entre 2019 y 2021 se realiza medición de niveles pre y postoperatorios de calcio, magnesio, fosforo y PTHi. Se observó 29% y 1% de hipocalcemia transitoria (< 12 meses) y permanente (> 12 meses). Los puntos de corte para predecir hipocalcemia fueron PTH < 8,8 pg/ml y < 80% de descenso de % de PTH (d % PTH) al día siguiente. Con el manejo propuesto se indica el alta precoz (promedio 1.05 días) y el costo de la prescripción es acotado. No hay asociación significativa de hipomagnesemia e hiperfosfemia PO con la hipocalcemia PO. El tratamiento más utilizado es de carbonato de calcio exclusivo (esquemas I y II). Los pacientes se mantienen con síntomas leves a las 2 semanas PO en 5% y logran suspender el tratamiento vía oral en 93% en este mismo período. Los protocolos de medición de PTH como predictor de hipocalcemia son muy variados. Cada centro debe conocer y establecer sus propios protocolos de manejo. Con esta experiencia demostramos la utilidad y seguridad de un esquema de manejo basado en calcemia, PTH (normal, baja o indetectable) y síntomas, con indicación de tratamiento profiláctico para todos los pacientes y ajuste ambulatorio seguro y de menor costo que una hospitalización prolongada.

DEPARTAMENTO DE MEDICINA

LABORATORIO DE TERAPIA CELULAR

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NON-CANONICAL WNT/WNT5A PATHWAY ACTIVITY IN CIRCULATING MONOCYTES OF UNTREATED PSORIATIC PATIENTS: AN EXPLORATORY STUDY OF ITS ASSOCIATION WITH INFLAMMATORY CYTOKINES AND CARDIOVASCULAR RISK MARKER-ADAMTS7

Claudio Karsulovic, Khanty Loyola, Raul Cabrera, Claudio Perez, Lia Hojman

The leading cause of death in psoriasis is cardiovascular disease. The determinants that induce the increase in this risk are not known. The systemic inflammatory process is dependent on lymphocytes and monocytes, as has been proposed. However, adaptation modules

such as mTOR have recently been mentioned as having a role. Other factors, such as WNT and its non-canonical WNT5a-inducing pathway, are relevant in inflammation, cell migration, and neoangiogenesis. Thus, we studied circulating monocytes from untreated severe psoriatic patients and characterized inflammatory cytokines, chemokines, mTOR activity, and the cardiovascular risk marker ADAMTS7. Peripheral blood from ten severely psoriatic patients (Psoriasis severity index greater than 10) was extracted and age- and sex-matched with healthy subjects. Surface and intracellular flow cytometry were performed for cytokine, chemokine receptors, and mTOR activity. ADAMTS7 was measured using ELISA. Psoriatic patients had a higher frequency of WNT5a+ cells in monocytes, which also had higher levels of IL-1β, IL-6, CXCR3, CCR2, and phosphorylated S6R protein. We found that M1 monocytes are dominant in the WNT5a+ cell group, and intracellular levels of WNT5a were also augmented. Levels of WNT5a were correlated with ADAMTS7, a blood marker related to the pathogenesis of atheromatosis. WNT5a could be relevant to the cardiovascular risk of psoriatic patients considering its association with higher levels of inflammatory cytokines, chemokine receptors and the pro-atherogenic profile of circulating monocytes.

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NEW MARKERS FOR CARDIOVASCULAR DISEASE IN PSORIATIC PATIENTS: PRELIMINARY STUDY ON MONOCYTE PHENOTYPE, ADAMTS7, AND MTOR ACTIVITY

Khanty Loyola, Claudio Karsulovic, Raúl Cabrera, Claudio Perez, Lía Hojman

Psoriasis is a skin disease with occasional involvement of non-cutaneous territories. Beyond the usual, cardiovascular events are more frequent in these patients and correlate only partially with disease activity, suggesting the presence of other unknown factors. We selected ten psoriatic patients without treatment in the last year and matched them for age and gender with eleven healthy subjects. Ficoll-extracted mononuclear cells were analyzed with flow cytometry for monocyte surface phenotype markers, intracellular NFκB/inflammasome-dependent interleukins, and chemotaxis receptor CXCR3. Using ELISA, patient serum was evaluated for ADAMTS7 and CXCL10. Inflammatory M1 monocytes showed higher levels of IL-1β and IL-6 in psoriatic patients. M2 monocytes also showed higher levels of intracellular inflammatory cytokines. Nevertheless, IL-6 values were higher compared to other monocytes and IL-1β. The mTORC activation markers ADAMTS7 and S6Rp were higher in psoriatic patients than in healthy controls. In psoriatic patients, serum levels of ADAMTS7 were elevated, and M2 monocytes showed a distinct inflammatory response with higher relative levels of NFκB-dependent IL-6 and less activity of the CXCR3-CXCL10 chemotactic pathway. These data suggest pathways with potential markers for prediction and early detection of cardiovascular risk in psoriatic patients.

COMITÉ DE INFECCIONES ASOCIADAS A LA ATENCIÓN DE SALUD

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TRENDS AND SOCIOECONOMIC, DEMOGRAPHIC, AND ENVIRONMENTAL FACTORS ASSOCIATED WITH ANTIMICROBIAL RESISTANCE: A LONGITUDINAL ANALYSIS IN 39 HOSPITALS IN CHILE 2008-2017

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Background: Antimicrobial resistance (AMR) is among the most critical global health threats of the 21st century. AMR is primarily driven by the use and misuse of antibiotics but can be affected by socioeconomic and environmental factors. Reliable and comparable estimates of AMR over time are essential to making public health decisions, defining research priorities, and evaluating interventions. However, estimates for developing regions are scant. We describe the evolution of AMR for critical priority antibiotic-bacterium pairs in Chile and examine their association with hospital and community-level characteristics using multivariate rate-adjusted regressions. Methods: Drawing on multiple data sources, we assembled a longitudinal national dataset to analyse AMR levels for critical priority antibiotic-bacterium combinations in 39 private and public hospitals (2008-2017) throughout the country and characterize the population at the municipality level. We first described trends of AMR in Chile. Second, we used multivariate regressions to examine the association of AMR with hospital characteristics and community-level socioeconomic, demographic, and environmental factors. Last, we estimated the expected distribution of AMR by region in Chile. Findings: Our results show that AMR for priority antibiotic-bacterium pairs steadily increased between 2008 and 2017 in Chile, driven primarily by Klebsiella pneumoniae resistant to third-generation cephalosporins and carbapenems, and vancomycin-resistant Enterococcus faecium. Higher hospital complexity, a proxy for antibiotic use, and poorer local community infrastructure were significantly associated with greater AMR. Interpretation: Consistent with research in other countries in the region, our results show a worrisome increase in clinically relevant AMR in Chile and suggest that hospital complexity and living conditions in the community may affect the emergence and spread of AMR. Our results highlight the importance of understanding AMR in hospitals and their interaction with the community and the environment to curtail this ongoing public health crisis. Funding: This research was supported by the Agencia Nacional de Investigación y Desarrollo (ANID), Fondo Nacional de Desarrollo Científico y Tecnológico FONDECYT, The Canadian Institute for Advanced Research (CIFAR), and Centro UC de Políticas Públicas, Pontificia Universidad Católica de Chile.

SERVICIO DE ENDOCRINOLOGÍA

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CLINICAL AND HISTOPATHOLOGICAL FEATURES OF FOLLICULAR THYROID CANCER IN CHILE

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Objective: Follicular thyroid carcinoma (FTC) is less frequent but has a worse prognosis than papillary carcinoma. The available evidence on pre-operative characteristics of FTC is controversial. Our objective was to characterize the clinical, ultrasound and histopathological

presentation of FTC patients treated Chile. Subjects and methods: Retrospective analysis of 97 patients treated for FTC in 6 large centers in Chile. We analyzed their ultrasonographic features and classified the nodules according to ATA risk of malignancy and TI-RADS score, as well as the cytological findings according to the Bethesda system. We described their clinical and histopathological findings at diagnosis and classified their risk of recurrence and mortality according to ATA 2015 recurrence risk category and the eighth edition of the AJCC/UICC staging system, respectively. Results: Median age was 48 years and 73.2% were females. The median diameter was 38.8 mm; only 9.5% of them were microtumors. According to ATA risk of malignancy, 86% of the nodules were low or intermediate suspicious, while 78% were category 3 or 4A nodules according to the TI-RADS. Regarding the Bethesda system, 65.9% had indeterminate cytology (20.6% category III and 45.3% category IV). At histological examination, most were minimally-invasive and angio-invasive tumors with less than 4 foci (54.7% and 28.4% respectively). More than 90% of FTC were unifocal and there was no lymphovascular or extrathyroidal invasion or lymph node involvement. Four patients (4.1%) had distant metastases at diagnosis. Most patients (95%) had stage I or II disease according to the AJCC/UICC staging system, while the risk of recurrence was low at 51.5% when using the ATA risk of recurrence scale. Conclusion: At diagnosis, most FTCs were nodules of low or intermediate suspicion at ultrasound, nearly two thirds had indeterminate cytology according to the Bethesda system, and nearly 50% of them were of low risk of recurrence.

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DETERMINACIÓN DE RANGOS DE BCTX Y N-MID OSTEOCALCINA Y ASOCIACIÓN CON OSTEOPOROSIS EN MUJERES CHILENAS POSMENOPÁUSICAS

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Introducción: La densitometría ósea (DO) tiene alta especificidad para el diagnóstico de osteoporosis, pero sensibilidad bajo lo óptimo para estimar el riesgo de fracturas. Éste, se puede calcular por algoritmos de predictores, y se ha propuesto incluir los marcadores óseos (MO), pero la magnitud de su asociación es incierta. El MO recomendado para medir resorción ósea es Beta-Cross Laps (B-CTx), y uno de formación ósea es la osteocalcina. Objetivos: 1) Establecer rangos de B-CTx y N-MID osteocalcina (N-MID) en mujeres posmenopáusicas (MPM), y comparar los niveles entre grupos: 1) Control sano y 2) Con DO alterada. Material y Métodos: Se reclutaron MPM, con DO del último año. Se realizó encuesta de factores de riesgo de fracturas y medición de MO. Se excluyeron MPM con causa secundaria para compromiso del recambio óseo. Resultados: 117 MPM (57 control, 60 DO alterada), 18 % osteoporosis, comparables. Los rangos de B-CTx y N-MID fueron 0,41 ± 0,18 [IC95% 0,37- 0,45] y 22,76 ± 7,73 [IC95% 21,29-24,24] ng/mL. Los niveles promedios de B-CTx y N-MID fueron más altos en grupo con DO alterada (0,46 ± 0,19 y 24,29 ± 8,04 ng/mL). Se encontró correlación moderada entre ambos MO, pero débil con DO alterada. Conclusiones: Se determinaron por primera vez rangos de B-CTx y N-MID en MPM chilenas, corroborando la similitud a otros países. Se encontraron valores discretamente más elevados de MO en grupo DO alterada, probablemente atribuible a causas secundarias no reportadas. Estos MO podrían constituir una herramienta complementaria a la DO y FRAX en la evaluación ósea.

SERVICIO DE GASTROENTEROLOGÍA

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MELD 3.0 ADEQUATELY PREDICTS MORTALITY AND RENAL REPLACEMENT THERAPY REQUIREMENTS IN PATIENTS WITH ALCOHOL-ASSOCIATED HEPATITIS

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Background & aims: Model for End-Stage Liver Disease (MELD) score better predicts mortality in alcohol-associated hepatitis (AH) but could underestimate severity in women and malnourished patients. Using a global cohort, we assessed the ability of the MELD 3.0 score to predict short-term mortality in AH. Methods: This was a retrospective cohort study of patients admitted to hospital with AH from 2009 to 2019. The main outcome was all-cause 30-day mortality. We compared the AUC using DeLong's method and also performed a time-dependent AUC with competing risks analysis. Results: A total of 2,124 patients were included from 28 centres from 10 countries on three continents (median age 47.2 ± 11.2 years, 29.9% women, 71.3% with underlying cirrhosis). The median MELD 3.0 score at admission was 25 (20-33), with an estimated survival of 73.7% at 30 days. The MELD 3.0 score had a better performance in predicting 30-day mortality (AUC:0.761, 95%CI:0.732-0.791) compared with MELD sodium (MELD-Na; AUC: 0.744, 95% CI: 0.713-0.775; p = 0.042) and Maddrey's discriminant function (mDF) (AUC: 0.724, 95% CI: 0.691-0.757; p = 0.013). However, MELD 3.0 did not perform better than traditional MELD (AUC: 0.753, 95% CI: 0.723-0.783; p = 0.300) and Age-Bilirubin-International Normalised Ratio-Creatinine (ABIC) (AUC:0.757, 95% CI: 0.727-0.788; p = 0.765). These results were consistent in competing-risk analysis, where MELD 3.0 (AUC: 0.757, 95% CI: 0.724-0.790) predicted better 30-day mortality compared with MELD-Na (AUC: 0.739, 95% CI: 0.708-0.770; p = 0.028) and mDF (AUC:0.717, 95% CI: 0.687-0.748; p = 0.042). The MELD 3.0 score was significantly better in predicting renal replacement therapy requirements during admission compared with the other scores (AUC: 0.844, 95% CI: 0.805-0.883). Conclusions: MELD 3.0 demonstrated better performance compared with MELD-Na and mDF in predicting 30-day and 90-day mortality, and was the best predictor of renal replacement therapy requirements during admission for AH. However, further prospective studies are needed to validate its extensive use in AH. Impact and implications: Severe AH has high short-term mortality. The establishment of treatments and liver transplantation depends on mortality prediction. We evaluated the performance of the new MELD 3.0 score to predict short-term mortality in AH in a large global cohort. MELD 3.0 performed better in predicting 30- and 90-day mortality compared with MELD-Na and mDF, but was similar to MELD and ABIC scores. MELD 3.0 was the best predictor of renal replacement therapy requirements. Thus, further prospective studies are needed to support the wide use of MELD 3.0 in AH.

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

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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.

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PANCREATIC STEATOSIS: A FREQUENT FINDING IN A CHILEAN POPULATION

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Introduction and aims: Pancreatic steatosis is an incidental radiologic finding in asymptomatic patients, and its clinical importance is unclear. Primary aim: to study the prevalence of pancreatic steatosis (PS) in consecutive patients registered at our hospital, that underwent computed axial tomography (CAT) scanning of the abdomen and pelvis, excluding known pancreatic diseases. Secondary aim: to review the association of PS with the demographic and clinical data of the patients, as well as with hepatic steatosis (HS). Materials and methods: An observational study was conducted on adult patients that had CAT scans of the abdomen and pelvis. Definitions: a) tissue density was measured in Hounsfield units (HU) in five 1 cm2 areas of the pancreas, three areas of the spleen, and in segments VI and VII of the liver; b) fatty pancreas: a difference < -10 HU between the mean pancreas and mean spleen densities; and c) fatty liver: density < 40 HU. We registered the epidemiologic and laboratory data of the patients. The association of those factors with the presence of PS was analyzed using SPSS version 24.0 software, and statistical significance was set at a p < 0.05. Results: Of the 203 patients, PS was found in 61 (30%). The patients with PS were significantly older and had a higher body mass index. We found no significant association with the rest of the parameters studied, nor with HS (55 patients). None of the patients had symptoms attributable to a disease of the exocrine pancreas. Conclusions: Fatty infiltration of the pancreas is a frequent finding in CAT scans, and its clinical importance is unclear. Aging of the population and the increase in obesity underline the need for future studies on PS.

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EFFECT OF ACUTE ON CHRONIC LIVER FAILURE OVER POST-TRANSPLANT SURVIVAL

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Introduction and objectives: Acute-on-chronic liver failure (ACLF) is associated with reduced short-term survival, and liver transplantation is frequently the only therapeutic option. Nonetheless, the post-transplantation prognosis seems to be worse in ACLF patients. Materials and methods: The databases of two university centers were retrospectively evaluated, and adult patients with cirrhosis who underwent transplantation between 2013 and 2020 were included. One-year survival of patients with ACLF was compared to that of patients without ACLF. Variables associated with mortality were identified. Results: A total of 428 patients were evaluated, and 303 met the inclusion criteria; 57.1% were male, the mean age was 57.1 ± 10.2 years, 75 patients had ACLF, and 228 did not. The main etiologies of ACLF were NASH (36.6%), alcoholic liver disease (13.9%), primary biliary cholangitis (8.6%) and autoimmune hepatitis (7.9%). Mechanical ventilation, renal replacement therapy, the use of vasopressors and the requirement of blood product transfusion during liver transplantation were significantly more frequent in ACLF patients. Among those recipients without and with ACLF, survival at 1, 3 and 5 years was 91.2% vs. 74.7%, 89.1% vs. 72.6% and 88.3% vs. 72.6%, respectively (p=0.001). Among pre-transplantation variables, only the presence of ACLF

was independently associated with survival (HR 3.2, 95% CI: 1.46-7.11). Post-transplantation variables independently associated with survival were renal replacement therapy (HR 2.8, 95% CI: 1.1-6.8) and fungal infections (HR 3.26, 95% CI: 1.07-9.9). Conclusions: ACLF is an independent predictor of one-year post-transplantation survival. Importantly, transplant recipients with ACLF require the use of more resources than patients without ACLF.

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GENETIC ANCESTRY, RACE, AND SEVERITY OF ACUTELY DECOMPENSATED CIRRHOSIS IN LATIN AMERICA

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Background & Aims Genetic ancestry or racial differences in health outcomes exist in diseases associated with systemic inflammation (eg, COVID-19). This study aimed to investigate the association of genetic ancestry and race with acute-on-chronic liver failure (ACLF), which is characterized by acute systemic inflammation, multi-organ failure, and high risk of short-term death. Methods This prospective cohort study analyzed a comprehensive set of data, including genetic ancestry and race among several others, in 1274 patients with acutely decompensated cirrhosis who were nonelectively admitted to 44 hospitals from 7 Latin American countries. Results Three hundred ninety-five patients (31.0%) had ACLF of any grade at enrollment. Patients with ACLF had a higher median percentage of Native American genetic ancestry and lower median percentage of European ancestry than patients without ACLF (22.6% vs 12.9% and 53.4% vs 59.6%, respectively). The median percentage of African genetic ancestry was low among patients with ACLF and among those without ACLF. In terms of race, a higher percentage of patients with ACLF than patients without ACLF were Native American and a lower percentage of patients with ACLF than patients without ACLF were European American or African American. In multivariable analyses that adjusted for differences in sociodemographic and clinical characteristics, the odds ratio for ACLF at enrollment was 1.08 (95% CI, 1.03–1.13) with Native American genetic ancestry and 2.57 (95% CI, 1.84–3.58) for Native American race vs European American race. Conclusions In a large cohort of Latin American patients with acutely decompensated cirrhosis, increasing percentages of Native American ancestry and Native American race were factors independently associated with ACLF at enrollment.

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ACTIVE ALCOHOL CONSUMPTION IS ASSOCIATED WITH ACUTE-ON-CHRONIC LIVER FAILURE IN HISPANIC PATIENTS

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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.

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THE C.415C>T POLYMORPHISM IN NUDT15 IS MORE FREQUENT THAN THE POLYMORPHISMS IN TPMT IN CHILEAN PATIENTS WHO USE THIOPURINE DRUGS

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Azathioprine (AZA) and 6-mercaptopurine (6-MP) are drugs widely used in the treatment of autoimmune diseases. Among the enzymes involved in the metabolism of AZA and 6-MP are thiopurine methyltransferase (TPMT) and nudix hydrolase 15 (NUDT15). The existence of single nucleotide polymorphisms in the genes that code for these enzymes could decreased enzymatic activity AND lead to severe myelosuppression. The most relevant polymorphism is NUDT15*3 (rs116855232), where the replacement of cytosine for thymine at position 415, which in turn leads to a loss of enzymatic activity. In a previous study, it was identified that together the polymorphisms in the TPMT gene reach an allelic frequency of 3.81%. There is no information regarding the rs116855232 polymorphism in the NUDT15 gene, so this corresponds to the objective of this report. Blood samples from Chilean adult patients with indications for the use of AZA or 6-MP for different pathologies and who had undergone a TPMT gene polymorphism study were retrospectively analyzed. A total of 253 blood samples were analyzed. Of the 253 patients, 47 presented the c.415C>T polymorphism in the NUDT15 gene, 3 being homozygous and 44 heterozygous. Four of the heterozygous patients for NUDT15 also had the *3A variant in the TPMT gene, also heterozygous. The allelic frequency of the minor T allele found (9.88%) was very similar to that found in patients of Asian origin, and much higher than that reported for the European Caucasian or Latin American population.

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CELIAC DISEASE IN CHILEAN ADULTS

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Introduction and aim: To characterize a university hospital population of Chilean adult patients with celiac disease. Patients and method: We retrospectively reviewed the records of patients under control that were diagnosed with celiac disease through clinical characteristics, serology, and histology. Results: A total of 149 patients were included, 119 (79.9%) of whom were women. Mean patient age was 42 years at diagnosis and 13.4% of patients had a family history of celiac disease. Mean body mass index was 24.3kg/m2, 55.3% presented with normal weight, 37.9% with overweight and obesity, and 6.8% with underweight. The main reasons for consultation were diarrhea (47%), weight loss (31%), dyspepsia (43%), and fatigue (26.1%). Anemia (26.1%), elevated transaminases (17.4%), low ferritin (11.4%), and hypovitaminosis D (9.3%) stood out, among others, in the initial laboratory work-up. The more frequent associated diseases were hypothyroidism (15.4%) and depressive disorder (11.4%). Small intestinal bacterial overgrowth was found in 10.1% and lactose malabsorption in 15.4%. The primary histologic diagnosis was celiac disease, with Marsh stage 3a villous atrophy (34.9%). Conclusion: Our results were similar to those of other case series on adults, finding that celiac disease was more frequent in women, disease began in the fourth decade of life, extraintestinal symptoms predominated, and there was an association with other autoimmune diseases. An important percentage of patients were also overweight and obese.

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AFP SCORE AND METROTICKET 2.0 PERFORM SIMILARLY AND COULD BE USED IN A "WITHIN-ALL" CLINICAL DECISION TOOL

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Background & aims: Two recently developed composite models, the alpha-fetoprotein (AFP) score and Metroticket 2.0, could be used to select patients with hepatocellular carcinoma (HCC) who are candidates for liver transplantation (LT). The aim of this study was to compare the predictive performance of both models and to evaluate the net risk reclassification of post-LT recurrence between them using each model's original thresholds. Methods: This multicenter cohort study included 2,444 adult patients who underwent LT for HCC in 47 centers from Europe and Latin America. A competing risk regression analysis estimating sub-distribution hazard ratios (SHRs) and 95% CIs for recurrence was used (Fine and Gray method). Harrell's adapted c-statistics were estimated. The net reclassification index for recurrence was compared based on each model's original thresholds. Results: During a median follow-up of 3.8 years, there were 310 recurrences and 496 competing events (20.3%). Both models predicted recurrence, HCC survival and survival better than Milan criteria ($p < 0.0001$). At last tumor reassessment before LT, c-statistics did not significantly differ between the two composite models, either as original or threshold versions, for recurrence (0.72 vs. 0.68; $p = 0.06$), HCC survival, and overall survival after LT. We observed predictive gaps and overlaps between the model's thresholds, and no significant gain on reclassification. Patients meeting both models ("within-ALL") at last tumor reassessment presented the lowest 5-year cumulative incidence of HCC recurrence (7.7%; 95% CI 5.1-11.5) and higher 5-year post-LT survival (70.0%; 95% CI 64.9-74.6). Conclusions: In this multicenter cohort, Metroticket 2.0 and the AFP score demonstrated a similar ability to predict HCC recurrence post-LT. The combination of these composite models might be a promising clinical approach. Impact and implications: Composite models were recently proposed for the selection of liver transplant (LT) candidates among individuals with hepatocellular carcinoma (HCC). We found that both the AFP score and Metroticket 2.0 predicted post-LT HCC recurrence and survival better than Milan criteria; the Metroticket 2.0 did not result in better reclassification for transplant selection compared to the AFP score, with predictive gaps and overlaps between the two models; patients who met low-risk thresholds for both models had the lowest 5-year recurrence rate. We propose prospectively testing the combination of both models, to further optimize the LT selection process for candidates with HCC.

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IMPLEMENTATION OF A RE-LINKAGE TO CARE STRATEGY IN PATIENTS WITH CHRONIC HEPATITIS C WHO WERE LOST TO FOLLOW-UP IN LATIN AMERICA

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To achieve WHO's goal of eliminating hepatitis C virus (HCV), innovative strategies must be designed to diagnose and treat more patients. Therefore, we aimed to describe an implementation strategy to identify patients with HCV who were lost to follow-up (LTFU) and offer them re-linkage to HCV care. We conducted an implementation study utilizing a strategy to contact patients with HCV who were not under regular follow-up in 13 countries from Latin America. Patients with HCV were identified by the international classification of diseases (ICD-9/10) or equivalent. Medical records were then reviewed to confirm the diagnosis of chronic HCV infection defined by anti-HCV+ and detectable HCV-RNA. Identified patients who were not under follow-up by a liver specialist were contacted by telephone or email, and offered a medical reevaluation. A total of 10,364 patients were classified to have HCV. After reviewing their medical charts, 1349 (13%) had undetectable HCV-RNA or were wrongly coded. Overall, 9015 (86.9%) individuals were identified with chronic HCV infection. A total of 5096 (56.5%) patients were under routine HCV care and 3919 (43.5%) had been LTFU. We were able to contact 1617 (41.3%) of the 3919 patients who were LTFU at the primary medical institution, of which 427 (26.4%) were cured at a different institutions or were dead. Of the remaining patients, 906 (76.1%) were candidates for retrieval. In our cohort, about one out of four patients with chronic HCV who were LTFU were candidates to receive treatment. This strategy has the potential to be effective, accessible and significantly impacts on the HCV care cascade.

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GASTROINTESTINAL SYMPTOMS AND COMPLICATIONS IN PATIENTS HOSPITALIZED DUE TO COVID-19, AN INTERNATIONAL MULTICENTRE PROSPECTIVE COHORT STUDY (TIVURON PROJECT)

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Background: Retrospective studies suggest that coronavirus disease (COVID-19) commonly involves gastrointestinal (GI) symptoms and complications. Our aim was to prospectively evaluate GI manifestations in patients hospitalized for COVID-19. Methods: This international multicentre prospective cohort study recruited COVID-19 patients hospitalized at 31 centres in Spain, Mexico, Chile, and Poland, between May and September 2020. Patients were followed-up until 15 days post-discharge and completed comprehensive questionnaires assessing GI symptoms and complications. A descriptive analysis as well as a bivariate and multivariate analysis were performer using binary logistic regression. p<0.05 was considered significant. Results: Eight hundred twenty-nine patients were enrolled; 129 (15.6%) had severe COVID-19, 113 (13.7%) required ICU admission, and 43 (5.2%) died. Upon admission, the most prevalent GI symptoms were anorexia (n=413; 49.8%), diarrhoea (n=327; 39.4%), nausea/vomiting (n=227; 27.4%), and abdominal pain (n=172; 20.7%), which were mild/moderate throughout the disease and resolved during follow-up. One-third of patients exhibited liver injury. Non-severe COVID-19 was associated with ≥2 GI symptoms upon admission (OR 0.679; 95% CI 0.464-0.995; p=0.046) or diarrhoea during hospitalization (OR 0.531; 95% CI 0.328-0.860; p=0.009). Multivariate analysis revealed that worse hospital outcomes were not independently associated with liver injury or GI symptoms. Conclusion: GI symptoms were more common than previously documented, and were mild, rapidly resolved, and not independently associated with COVID-19 severity. Liver injury was a frequent complication in hospitalized patients not independently associated with COVID-19 severity.

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SURVEY ON INITIAL MANAGEMENT OF ACUTE PANCREATITIS IN LATIN AMERICA

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Objective: The population of Latin America harbors the highest incidence of gallstones and acute biliary pancreatitis, yet little is known about the initial management of acute pancreatitis in this large geographic region. Participants and methods: We performed a post hoc analysis of responses from physicians based in Latin America to the international multidisciplinary survey on the initial management of acute pancreatitis. The questionnaire asked about management of patients during the first 72h after admission, related to fluid therapy, prescription of prophylactic antibiotics, feeding and nutrition, and timing of cholecystectomy. Adherence to clinical guidelines in this region was compared with the rest of the world. Results: The survey was completed by 358 participants from 19 Latin American countries (median age, 39 years [33-47]; women, 27.1%). The proportion of participants in Latin America vs. the rest of the world who chose non-compliant options with clinical guidelines were: prescription of fluid therapy rate other than moderate (42.2% vs 34.3%, P=.02); prescription of prophylactic antibiotics for severe (10.6% vs 18.0%, P=.002), necrotizing (28.5% vs 36.9%, P=.008), or systemic inflammatory response syndrome-associated (21.2% vs 30.6%, P=.002) acute pancreatitis; not starting an oral diet to patients with oral tolerance (77.9% vs 71.1%, P=.02); and delayed cholecystectomy (16.2% vs 33.8%, P<.001). Conclusions: Surveyed physicians in Latin America are less likely to prescribe antibiotics and to delay cholecystectomy when managing patients in the initial phase of acute pancreatitis compared to physicians in the rest of the world. Feeding and nutrition appear to require the greatest improvement.

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INTERNATIONAL MULTIDISCIPLINARY SURVEY ON THE INITIAL MANAGEMENT OF ACUTE PANCREATITIS: PERSPECTIVE OF POINT-OF-CARE SPECIALISTS FOCUSED ON DAILY PRACTICE

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Background: The initial management of patients with acute pancreatitis impacts both morbidity and mortality. Point-of-care decisions have been reported to differ from clinical guideline recommendations. Methods: An online anonymous questionnaire was distributed through scientific associations and social media using REDCap. Multivariable logistic regression was used to identify the characteristics of participants associated with compliance with the recommendations. Results: A total of 1054 participants from 94 countries completed the questionnaire; median age (IQR) was 39 (32-47) years; 30.7% were women. Among the participants, 37% opted for nonmoderate flow of i.v. fluid, 31% for fluid type other than Ringer's lactate; 73.4% were in favor of nil per os to patients who could eat, 75.5% for other than enteral feeding to patients with oral intolerance; 15.5% used prophylactic antibiotic in patients with severe acute pancreatitis, 34.1% in necrotizing acute pancreatitis, and 27.4% in patients with systemic inflammatory response syndrome; 27.8% delayed cholecystectomy after biliary acute pancreatitis. Participants with publications in PubMed on acute pancreatitis showed better compliance (OR, 1.62; 95% CI: 1.15-2.32; P = .007) with recommendations of the clinical guidelines.

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

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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.

LABORATORIO INMUNOGASTROENTEROLOGÍA

J NEUROGASTROENTEROL MOTIL. 2023 JAN 30;29(1):72-84. DOI: 10.5056/JNM22009.

THE STRESSED GUT: REGION-SPECIFIC IMMUNE AND NEUROPLASTICITY CHANGES IN RESPONSE TO CHRONIC PSYCHOSOCIAL STRESS

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Background/aims: Chronic psychological stress affects gastrointestinal physiology which may underpin alterations in the immune response and epithelial transport, both functions are partly regulated by enteric nervous system. However, its effects on enteric neuroplasticity are still unclear. This study aims to investigate the effects of chronic unpredictable psychological stress on intestinal motility and prominent markers of enteric function. Methods: Adult male C57BL/6J mice were exposed to 19 day of unpredictable stress protocol schedule of social defeat and overcrowding. We investigated the effects on plasma corticosterone, food intake, and body weight. In vivo gastrointestinal motility was assessed by fecal pellet output and by whole-gastrointestinal transit (using the carmine red method). Tissue monoamine level, neural and glial markers, neurotrophic factors, monoamine signaling, and Toll-like receptor expression in the proximal and distal colon, and terminal ileum were also assessed. Results: Following chronic unpredictable psychological stress, stressed mice showed increased food intake and body weight gain ($P < 0.001$), and reduced corticosterone levels ($P < 0.05$) compared to control mice. Stressed mice had reduced stool output without differences in water content, and showed a delayed gastrointestinal transit compared to control mice ($P < 0.05$). Stressed mice exhibited decreased mRNA expression of tyrosine hydroxylase (Th), brain-derived neurotrophic factor (Bdnf) and glial cell-derived neurotrophic factor (Gdnf), as well as Toll-like receptor 2 (Tlr2) compared to control ($P < 0.05$), only proximal colon. These molecular changes in proximal colon were associated with higher levels of monoamines in tissue. Conclusion: Unpredictable psychological chronic stress induces region-specific impairment in monoamine levels and neuroplasticity markers that may relate to delayed intestinal transit.

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RHINITIS ASSOCIATED WITH ASTHMA IS DISTINCT FROM RHINITIS ALONE: THE ARIA-MEDALL HYPOTHESIS

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Asthma, rhinitis, and atopic dermatitis (AD) are interrelated clinical phenotypes that partly overlap in the human interactome. The concept of "one-airway-one-disease," coined over 20 years ago, is a simplistic approach of the links between upper- and lower-airway allergic diseases. With new data, it is time to reassess the concept. This article reviews (i) the clinical observations that led to Allergic Rhinitis and its Impact on Asthma (ARIA), (ii) new insights into polysensitization and multimorbidity, (iii) advances in mHealth for novel phenotype definitions, (iv) confirmation in canonical epidemiologic studies, (v) genomic findings, (vi) treatment approaches, and (vii) novel concepts on the onset of rhinitis and multimorbidity. One recent concept, bringing together upper- and lower-airway allergic diseases with skin, gut, and neuropsychiatric multimorbidities, is the "Epithelial Barrier Hypothesis." This review determined that the "one-airway-one-disease" concept does not always hold true and that several phenotypes of disease can be defined. These phenotypes include an extreme "allergic" (asthma) phenotype combining asthma, rhinitis, and conjunctivitis. Rhinitis alone and rhinitis and asthma multimorbidity represent two distinct diseases with the following differences: (i) genomic and transcriptomic background (Toll-Like Receptors and IL-17 for rhinitis alone as a local disease; IL-33 and IL-5 for allergic and non-allergic multimorbidity as a systemic disease), (ii) allergen sensitization patterns (mono- or pauci-sensitization versus polysensitization), (iii) severity of symptoms, and (iv) treatment response. In conclusion, rhinitis alone (local disease) and rhinitis with asthma multimorbidity (systemic disease) should be considered as two distinct diseases, possibly modulated by the microbiome, and may be a model for understanding the epidemics of chronic and autoimmune diseases.

SERVICIO DE GERIATRÍA

FRONT AGING. 2023 MAR 23:4:1141792. DOI: 10.3389/FRAGI.2023.1141792. ECOLLECTION 2023.

CONSIDERATIONS AND ANALYSIS OF THE IMPLEMENTATION OF ONCOGERIATRICS IN CHILE AND ITS IMPORTANCE: REVIEW OF CURRENT LITERATURE

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The Chilean census of 2017 reported that 11.4% of the local population are 65 years or older, and according to the National Institute of Statistics (INE) the current expectancy of life in Chile is 76 years for men and 81 years for women respectively. Cancer in Chile is a major public health problem. Aging is a significant risk factor for cancer development which added to the improved life expectancy, it increases the incidence of cancer. In 2040, new cancer cases will increase from 19.3 to 30.2 million worldwide. Older people are a heterogeneous group requiring specialized and individualized management. Chronological age does not necessarily correlate with physiological age. More than half of the geriatric patients with cancer have at least one comorbidity which is relevant when defining a cancer treatment. Likewise, polypharmacy is frequent and is an important issue to consider in people with cancer due to the risk associated with drug interactions. Oncogeriatric assessment consists of a comprehensive multidimensional evaluation, including functional and biopsychosocial issues, addressing aspects of the neoplastic disease such as the risk of toxicities due to systemic therapy and life expectancy. This tool has proven to be helpful in the diagnosis of conditions that are not evident in a routine oncological evaluation, such as geriatric syndromes, frailty, functional dependence, and cognitive impairment among others, which have an impact when deciding on therapy, predicting risks of treatment toxicity and mortality. In this article we aim to describe the current situation of Oncogeriatrics and to provide epidemiological information about cancer in the elderly population in Chile attempting to highlight the importance of the Oncogeriatrics units, within cancer departments, for a better decision taking in the elderly cancer patient.

ACTA PSYCHIATR SCAND. 2023 MAY;147(5):420-429. DOI: 10.1111/ACPS.13468.

EPIDEMIOLOGY OF DELIRIUM IN HOSPITALIZED PATIENTS IN LATIN AMERICA: A SYSTEMATIC REVIEW

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Background: Accurate epidemiological data are essential for the planning of policies aimed at the identification, prevention, and management of delirium. The reported occurrence of delirium in hospitalized patients varies widely among studies, ranging between 5% to more than 80% in the international literature. The exact occurrence in Latin America is not well described. Objective: The aim of this study is to conduct a systematic analysis of the published data on the epidemiology of delirium in hospitalized patients in Latin America. Methods: We conducted a systematic review following PRISMA guidelines. Both MEDLINE and LILACS databases were searched for original research articles reporting the occurrence of delirium among adult hospitalized patients in Latin American countries. Studies including pediatric populations were excluded from this analysis. Two authors independently applied eligibility criteria, assessed quality, and extracted data. The corresponding authors of the original articles were contacted to obtain relevant information about the study when this was not present in the published manuscripts. Results: Seven hundred and eighteen original articles were identified. After screening titles and abstracts, 149 studies were included in the final analysis. The occurrence of delirium varied depending on the clinical scenario: (1) in the general medico-surgical wards, it ranged from 2.1% to 60.4%, (2) in the Intensive Care Units (ICUs), from 9.6% to 94.8%, (3) in the post-operatory population, from 5.45% and 52.3%, and (4) it was found to be between 10.7% and 62% in the emergency department setting. The most used delirium assessment tools were the "Confusion Assessment Method" (CAM; in the general population), and the "Confusion Assessment Method for the ICU" (CAM-ICU). Fourteen out of 149 studies were conducted in clinical settings who actively implemented some form of non-pharmacological delirium prevention bundles, most of them as part of ICU sedation-analgesia protocols. Conclusion: Delirium occurs frequently in hospitalized patients in Latin America throughout a variety of clinical scenarios, including ICU, general wards, post-operatory populations, and among the emergency department setting. The CAM and the CAM-ICU are the most used delirium assessment tools. Bundles of non-pharmacological interventions to prevent delirium are not universally implemented.

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.

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

COMBINED VERTEBRAL AUGMENTATION

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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 $\varepsilon 4$ 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.

SERVICIO DE HEMATOLOGÍA

BLOOD (2023) 142 (SUPPLEMENT 1): 5921. HTTPS://DOI.ORG/10.1182/BLOOD-2023-185288

SECONDARY ACUTE MYELOID LEUKEMIA FROM A PREVIOUS CHRONIC MYELOPROLIFERATIVE NEOPLASM: A STUDY OF GRELAM-CHILE CONCERNING CHILEAN PATIENTS ON BEHALF OF AML PETHEMA REGISTRY

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Secondary Acute Myeloid Leukemia (sAML) from Chronic Myeloproliferative Neoplasm (chMPN) is associated with an unfavorable prognosis and is characterized by a unique set of cytogenetic and molecular features distinct from de novo AML. The only cure for these patients is allogeneic Stem Cell Transplantation (SCT), which usually is not possible given the advanced age and comorbidities from this patient population. Methods: We present a retrospective analysis of sAML Chilean patients due to chMPN from the multicentric epidemiological registry of AML of the PETHEMA Spanish Group. Results: There are 802 AML Chilean patients incorporated in the online PETHEMA platform. 158 are sAMLand 26 are secondary to chMPN. Compared with the sAML group, patients with previous chMPN were mainly male (56% vs. 76%, respectively), had a larger white blood cell count (32,720 mm3 vs. 61,130 mm3), and had splenomegaly (P <0.05). There was no difference in age (median 62,35 years old), peripheral blood blasts (media 28,8%), brinogen (287 mg/dl), or other laboratory tests (p>0.05). Regardless of the type of chMPN: Chronic Myeloid Leukemia: 8 patients: Chronic myelomonocytic leukemia: 5, Primary Myelobrosis: 5, Chronic Myeloproliferative Syndrome not specied subtype: 6, Polycythemia Vera/essential Thrombocytosis 2. 50% received previously chemotherapy, mainly Tyrosine Kinase Inhibitors (7) and hydroxycarbamide (7). Regardless sAML % had an abnormal karyotype. Treatment used, it was Anthracycline/Daunorubicin (38%), azacytidine with or without Venetoclax (19%), and palliative care (23%). In the rst induction, the rate of Complete response (CR), or complete response with incomplete hematological response (iCR), was reached in only 3 patients, and these had negative MRD. From the patients with partial responses, 9 patients received a second line of treatment, mainly azacytidine. After that, three more patients reached CR. Only one patient received allogeneic SCT. The average stay in the hospital was 41,4 days, and Overall survival (OS) was 12,2 months (OS in all sAML was 14,2 months, N.S. p>0.05). The mortality rate was 84%, and the main cause was progressive disease in 60% of those cases. Conclusion: We present our local experience with this type of sAML. The outcome remains poor; it seems that allogeneic SCT is the only cure, but most patients cannot reach it. More research is needed to improve the high rates of mortality for this patient population.

SERVICIO DE INFECTOLOGÍA

REV. CHIL. INFECTOL. [INTERNET]. 2023 DEC; 40(6): 599-608

PERFIL DE USO DE TIGECICLINA EN UN HOSPITAL UNIVERSITARIO EN CHILE

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Introducción: El uso de tigeciclina ha ido en aumento en los últimos años, debido al incremento de la resistencia bacteriana y la escasez de alternativas terapéuticas. Objetivo: Caracterizar y evaluar las prescripciones de tigeciclina en pacientes internados en un hospital universitario, durante los años 2017 y 2018. Metodología: Estudio observacional retrospectivo, donde se caracterizaron los pacientes, las terapias, la microbiología asociada, los desenlaces clínicos y las reacciones adversas asociadas a los tratamientos con tigeciclina. Se determinó la proporción de prescripciones apropiadas por un comité de expertos y el consumo de tigeciclina medido en DDD/100 camas-día. Resultados: Se caracterizaron 89 pacientes, de los cuales 67 (75,3%) cumplieron los criterios de selección. El 53,7% de los pacientes eran hombres, con una edad promedio de 60 ± 15 años. El principal motivo de hospitalización fue quirúrgico (65,7%). El 67,1% de los tratamientos con tigeciclina se inició en una Unidad de Paciente Critico y el foco de infección predominante fue abdominal (64,3%).

El 50% de las terapias con tigeciclina fueron dirigidas según la microbiología identificada. En 65,7% de los casos se usó tigeciclina como monoterapia en la dosis habitual (62,9%). Náuseas (8,6%), diarrea (7,1%) y vómitos (4,3%) fueron los efectos adversos más reportados. El 84,3% de los tratamientos se consideraron apropiados. El año 2017 se consumió 0,4 DDD/100 camas-día y 0,6 DDD/100 camas/día el 2018, siendo la UCI el servicio que presentó el mayor uso en ambos años. Discusión: Tigeciclina fue utilizada principalmente en monoterapia para el tratamiento de infecciones intraabdominales en pacientes hospitalizados, por motivos quirúrgicos, en una unidad de paciente crítico, en las dosis habituales recomendadas de 100 mg como dosis de carga seguida de 50 mg cada 12 hs IV. En 50% de los casos, la terapia fue dirigida según microbiología. Los eventos adversos más habituales fueron los gastrointestinales. Conclusión: La mayoría de las terapias prescritas fueron consideradas apropiadas por el comité de expertos.

REV. CHIL. INFECTOL. VOL.40 NO.3 SANTIAGO JUN. 2023HTTP://DX.DOI.ORG/10.4067/S0716-10182023000300203

CARACTERIZACIÓN DE LA UTILIZACIÓN DE COLISTÍN EN UN HOSPITAL DE ALTA COMPLEJIDAD

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El aumento de la resistencia y la escasez de nuevos antibacterianos ha requerido la reintroducción de antiguos antimicrobianos entre ellos colistín. Objetivo: Caracterizar la utilización de colistín durante el año 2017 en un hospital universitario, mediante la descripción de los pacientes, los tratamientos, la microbiología asociada y efectos adversos. Pacientes y Métodos: Trabajo observacional retrospectivo. Se revisaron los datos de todos los pacientes que recibieron colistín intravenoso (IV) por al menos 48 horas, durante el año 2017. Resultados: Se incluyeron 53 pacientes, equivalentes a 91 tratamientos. El foco respiratorio fue el principal (46,2%). El 68,1% de los tratamientos fue iniciado en la UCI. La mayoría de los pacientes tenía una hospitalización reciente (83,5%), y presentaban uso previo de antibacterianos (89%). Los dos patógenos mayoritariamente identificados fueron Pseudomonas aeruginosa y Klebsiella spp. El consumo promedio de colistín fue de 2,4 DDD/100 camas/día. El servicio que más consumió colistín fue la UCI, con 45,5 DDD/100 camas/día, usando generalmente la dosis de 3 MUI cada 8 horas IV y con una baja utilización de dosis de carga. Conclusión: Colistín corresponde a un antimicrobiano de uso restringido a infecciones sospechadas o confirmadas por agentes bacterianos multi resistentes. En esta serie, su uso inicial fue principalmente empírico, en pacientes con factores de riesgo para resistencia antibacteriana; se usó en forma asociada a otros antimicrobianos, siendo el foco principal el respiratorio.

SERVICIO DE INMUNOLOGÍA

WORLD ALLERGY ORGAN J. 2023 MAR 2;16(3):100753. DOI: 10.1016/J.WAOJOU.2023.100753. ECOLLECTION 2023 MAR.

WAO CONSENSUS ON DEFINITION OF FOOD ALLERGY SEVERITY (DEFASE)

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Background: While several scoring systems for the severity of anaphylactic reactions have been developed, there is a lack of consensus on definition and categorisation of severity of food allergy disease as a whole. Aim: To develop an international consensus on the severity of food allergy (DEfinition of Food Allergy Severity, DEFASE) scoring system, to be used globally. Methods phase 1: We conducted a mixed-method systematic review (SR) of 11 databases for published and unpublished literature on severity of food allergy management and set up a panel of international experts. Phase 2: Based on our findings in Phase 1, we drafted statements for a two-round modified electronic Delphi (e-Delphi) survey. A purposefully selected multidisciplinary international expert panel on food allergy (n = 60) was identified and sent a structured questionnaire, including a set of statements on different domains of food allergy severity related to symptoms, health-related quality of life, and economic impact. Participants were asked to score their agreement on each statement on a 5-point Likert scale ranging from “strongly agree” to “strongly disagree”. Median scores and percentage agreements were calculated. Consensus was defined a priori as being achieved if 70% or more of panel members rated a statement as “strongly agree” to “agree” after the second round. Based on feedback, 2 additional online voting rounds were conducted. Results: We received responses from 92% of Delphi panel members in round 1 and 85% in round 2. Consensus was achieved on the overall score and in all of the 5 specific key domains as essential components of the DEFASE score. Conclusions: The DEFASE score is the first comprehensive grading of food allergy severity that considers not only the severity of a single reaction, but the whole disease spectrum. An international consensus has been achieved regarding a scoring system for food allergy disease. It offers an evaluation grid, which may help to rate the severity of food allergy. Phase 3 will involve validating the scoring system in research settings, and implementing it in clinical practice.

LABORATORIO MEDICINA MOLECULAR

DIAGN MICROBIOL INFECT DIS. 2023 DEC;107(4):116083. DOI: 10.1016/J.DIAGMICROBIO.2023.116083.

PRELIMINARY REPORT OF TRANSMITTED DRUG RESISTANCE TO INTEGRASE STRAND CHAIN TRANSFER INHIBITORS IN TREATMENT-NAÏVE HIV INFECTED PATIENTS

Pablo Ferrer, Verónica Ramos, Maria Ignacia Puente, Alejandro Afani

Transmitted Resistance exists in a newly diagnosed person who has not yet started their treatment. Our objective was to obtain a profile of HIV-1 resistance to integrase inhibitors in newly diagnosed treatment-naïve patients. Fifty people newly diagnosed with HIV-1 infection who had never received antiretroviral treatment were recruited. The complete integrase gene was amplified by nested RTPCR and the sequences obtained were analyzed with the ReCall and HIVdb v9.0. The overall prevalence transmitted due to mutations with some impact on integrase

strand transfer inhibitors (INSTI) activity during the study period was 8%. The major E138K mutation was detected in only 1 patient and the secondary G163R mutation was detected in the other 3. The transmitted resistance for the first generation INSTI was 8% and for the second generation it was 0%. In Chile the resistance transmitted to INSTI is low and it is in according values detect in other part of the world.

SERVICIO DE MEDICINA FÍSICA Y REHABILITACIÓN

BRAIN STIMUL. 2023 JAN-FEB;16(1):40-47. DOI: 10.1016/J.BRS.2022.12.008.

EARLY TRANSCRANIAL DIRECT CURRENT STIMULATION WITH MODIFIED CONSTRAINT-INDUCED MOVEMENT THERAPY FOR MOTOR AND FUNCTIONAL UPPER LIMB RECOVERY IN HOSPITALIZED PATIENTS WITH STROKE: A RANDOMIZED, MULTICENTRE, DOUBLE-BLIND, CLINICAL TRIAL

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Background: Constraint-induced movement therapy (CIMT) and transcranial direct current stimulation (tDCS) are used to reduce interhemispheric imbalance after stroke, which is why the combination of these therapies has been used for neurological recovery, but not in the acute phase. Objectives: To evaluate the effectiveness of combining active or sham bihemispheric tDCS with modified CIMT (mCIMT) for the recovery of the Upper Limb (UL) in hospitalized patients with acute and subacute stroke. Methods: This randomized controlled, double-blind, placebo-controlled, parallel group clinical trial was executed between September 2018 to March 2021 recruited 70 patients. The patients were randomized to one of two groups to receive treatment for 7 consecutive days, which included 20 min of active or sham bihemispheric tDCS daily (anodal ipsilesional and cathodal contralesional), with an mCIMT protocol. The primary outcome was the difference in the evolution of motor and functional upper limb recovery with assessment on days 0, 5, 7, 10 and 90. The secondary outcomes were independence in activities of daily living (ADL) and quality of life. Results: The active group presented a statistically significant gap compared to the simulated group throughout the trend in the scores of the FMA (motor function and joint pain) and WMFT (functional ability and weight to box) ($p < 0.05$) and showed a minimal clinically important difference (FMA: difference between groups of 4.9 points [CI: 0.007- 9.799]; WMFT: difference between groups of 6.54 points [CI: 1.10-14.15]). In the secondary outcomes, there was a significant difference between the groups in ADL independence (Functional Independence Measure: difference of 8.63 [CI: 1.37-18.64]) and perceived recovery of quality of life evaluated at 90 days ($p = 0.0176$). Conclusions: Combining mCIMT with bihemispheric tDCS in patients hospitalized with acute-subacute stroke allows us to maximize the motor and functional recovery of the paretic upper limb in the early stages and independence in ADL, maintaining the effects over time.

J HAND THER. 2023 SEP 29:S0894-1130(23)00123-0. 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.

BMC GERIATR. 2023 AUG 5;23(1):472. DOI: 10.1186/S12877-023-04189-2.

SOFTWARE-GUIDED (PREVEDEL) COGNITIVE STIMULATION TO PREVENT DELIRIUM IN HOSPITALISED OLDER ADULTS: STUDY PROTOCOL

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Background: Delirium is a clinical condition characterised by acute and fluctuating deterioration of the cognitive state, generally secondary to an acute pathology. Delirium is associated with negative outcomes in older adults, such as longer hospitalisations, higher mortality, and short and medium-term institutionalisation. Randomised clinical trials have shown that delirium is preventable through non-pharmacological prevention measures, decreasing its incidence by 30-50%. These interventions include promoting physical activity, facilitating the use of glasses and hearing aids, cognitive stimulation, and providing frequent reorientation of time and space, among others. These measures are currently seldom applied in hospitals in Chile and around the world for reasons including the heavy workload of clinical staff, the lack of trained personnel, and in general the absence of a systematic implementation processes. We developed a software called PREVEDEL,

which includes non-pharmacological strategies such as cognitive stimulation, early mobilisation, orientation, and pain assessment. We propose a randomised clinical trial to evaluate whether cognitive stimulation guided by PREVEDEL software prevents delirium status (full/subsyndromal delirium) in hospitalised older adults. Method: A randomised controlled trial, with parallel, multicentre groups. We will recruite patients 65 years or older who have been hospitalised for less than 48 h in the general ward or the intermediate care units of four hospitals in Santiago, Chile. The participants in the intervention group will use a tablet with cognitive stimulation software for delirium prevention for five continuous days versus the control group who will use the tablet without the software. We will evaluate the incidence, duration, density of delirium, subsyndromal delirium with the Confusion Assessment Method, cognitive with the Montreal Cognitive Assessment, and functional status with the Functional Independence Measure at discharge. Moreover, we will evaluate the adherence to prevention measures, as well as demographic variables of interest. Discussion: The use of cognitive PREVEDEL software could increase and improve the implementation of non-pharmacological prevention measures for delirium in hospitalised older adults, thus reducing its incidence and contributing to patients and health professionals.

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A LATIN AMERICAN CONSENSUS MEETING ON THE ESSENTIALS OF MIXED PAIN

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Objectives: The term “mixed pain” has been established when a mixture of different pain components (e.g. nociceptive, neuropathic, and nociplastic) are present. It has gained more and more acceptance amongst pain experts worldwide, but many questions around the concept of mixed pain are still unsolved. The sensation of pain is very personal. Cultural, social, personal experiences, idiomatic, and taxonomic differences should be taken into account during pain assessment. Therefore, a Latin American consensus committee was formed to further elaborate the essentials of mixed pain, focusing on the specific characteristics of the Latin American population. Methods: The current approach was based on a systematic literature search and review carried out in Medline. Eight topics about the definition, diagnosis, and treatment of mixed pain were discussed and voted for by a Latin American consensus committee and recommendations were expressed. Results: At the end of the meeting a total of 14 voting sheets were collected. The full consensus was obtained for 21 of 25 recommendations (15 strong agreement and 6 unanimous agreement) formulated for the above described 8 topics (7 of the 8 topics had for all questions at least a strong agreement - 1 topic had no agreement for all 4 questions). Conclusion: In a subject as complex as mixed pain, a consensus has been reached among Latin American specialists on points related to the definition and essence of this pain, its diagnosis and treatment. Recommendations for diagnosis and treatment of mixed pain in Latin America were raised.

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EARLY OCCUPATIONAL THERAPY IN MECHANICALLY VENTILATED PATIENTS IMPROVES FUNCTIONAL STATUS: STUDY PROTOCOL

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Background: Experts suggest implementing measures that include analgesia, sedation, delirium prevention and early mobilization (ASDM) in patients undergoing mechanical ventilation (MV) to reduce complications. However, there is limited evidence of occupational therapy in these patients. The aim of the research is to compare functional independence in patients undergoing MV of an intensive and early occupational therapy protocol versus to standard ASDM strategy. Method/Design: A prospective, multicenter, randomized clinical trial, with parallel groups (control and intervention groups). Participants will be hospitalized patients, over 18 years of age, admitted to the intensive care unit (ICU) and with the need of invasive MV. The intervention group will receive two daily 30-minute sessions of occupational therapy for 10 days. This study will research the effect of occupational therapy on functional independence, motor and cognitive status, evaluating at days 28 and 90. Discussion: This work contributes to the theoretical and practical work of occupational therapists who work in the ICU. The implementation of protocols of occupational therapy in mechanically ventilated patients can contribute to the independence and functionality of patients. Conclusion: Our research aims to contribute to the generation of systematized, organized, and feasible protocols that can be implemented in ICU.

SERVICIO DE MEDICINA INTERNA

REV MED CHIL. 2023 APR;151(4):461-468. DOI: 10.4067/S0034-98872023000400461.

EVALUACIÓN DEL PANEL DE ENFERMEDADES HEPÁTICAS AUTOINMUNES (INMUNOBLOT) EN EL DIAGNÓSTICO DE ENFERMEDADES HEPÁTICAS

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Introduction: For the diagnosis of liver diseases, clinical criteria, biochemical, immunological and histological parameters are included. The autoimmune panel is an immunoblot that contemplates the detection of antibodies against 9 different hepatic antigens, which could guide the diagnosis of these pathologies. Objective: To describe the usefulness of the autoimmune panel in the diagnosis of liver diseases. Methods: Observational, descriptive study. All autoimmune panels performed between January 2020 and August 2021 (n = 279) were reviewed, and the ones with positive result selected (n = 101). Clinical records were reviewed, including: clinical, biochemical, immunological and histological characteristics. Diagnosis was determined by clinical suspicion (clinical, biochemical and immunological parameters), only through autoimmune panel, and according to liver biopsy in available cases. Results: 45 patients with complete clinical history were included in the analysis; 82% women, median age 58 years (16-79). Clinical suspicions included autoimmune hepatitis (AIH) in 12 patients (27%),

primary biliary cholangitis (PBC) in 10 patients (22%), overlap syndrome (AIH/PBC) in 17 (38%), and others in 6 (13%). The diagnosis of PBC was confirmed by autoimmune panel in 9/10 and 11/17 patients with clinical suspicion of PBC and HAI/PBC, respectively. Of the 27 patients with initial clinical suspicion of PBC, 14 had negative AMA and AMA-M2 (6 had Sp100 and 5 gp210 as the only markers and 3 had positive Sp100 and PML). In 10/14 patients, the diagnosis was confirmed by panel and/or compatible liver biopsy. Conclusion: The autoimmune panel turns out to be a useful diagnostic tool for liver diseases, especially PBC in isolation or in overlap syndrome.

SERVICIO DE NEFROLOGÍA

BIOMOLECULES. 2023 OCT 3;13(10):1481. DOI: 10.3390/BIOM13101481.

A COMBINED BIOMARKER THAT INCLUDES PLASMA FIBROBLAST GROWTH FACTOR 23, ERYTHROPOIETIN, AND KLOTHO PREDICTS SHORT- AND LONG-TERM MORBIMORTALITY AND DEVELOPMENT OF CHRONIC KIDNEY DISEASE IN CRITICAL CARE PATIENTS WITH SEPSIS: A PROSPECTIVE COHORT

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Acute Kidney Injury (AKI) is a frequent complication in intensive care unit (ICU) patients that increases mortality and chronic kidney disease (CKD) development. AKI is associated with elevated plasma fibroblast growth factor 23 (FGF23), which can be modulated by erythropoietin (EPO) and Klotho. We aimed to evaluate whether a combined biomarker that includes these molecules predicted short-/long-term outcomes. We performed a prospective cohort of ICU patients with sepsis and previously normal renal function. They were followed during their inpatient stay and for one year after admission. We measured plasma FGF23, EPO, and Klotho levels at admission and calculated a combined biomarker (FEK). A total of 164 patients were recruited. Of these, 50 (30.5%) had AKI at admission, and 55 (33.5%) developed AKI within 48 h. Patients with AKI at admission and those who developed AKI within 48 h had 12- and 5-fold higher FEK values than non-AKI patients, respectively. Additionally, patients with higher FEK values had increased 1-year mortality (41.9% vs. 18.6%, p = 0.003) and CKD progression (26.2% vs. 8.3%, p = 0.023). Our data suggest that the FEK indicator predicts the risk of AKI, short-/long-term mortality, and CKD progression in ICU patients with sepsis. This new indicator can improve clinical outcome prediction and guide early therapeutic strategies.

TOXINS (BASEL). 2023 JAN 19;15(2):97. DOI: 10.3390/TOXINS15020097.

HIGH PLASMA LEVELS OF FIBROBLAST GROWTH FACTOR 23 ARE ASSOCIATED WITH INCREASED RISK OF COVID-19 IN END-STAGE RENAL DISEASE PATIENTS ON HEMODIALYSIS: RESULTS OF A PROSPECTIVE COHORT

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End-stage renal disease (ESRD) patients are a population with high rates of COVID-19 and mortality. These patients present a low response to anti-SARS-CoV-2 immunization, which is associated with immune dysfunction. ESRD patients also present high plasma titers of Fibroblast Growth Factor 23 (FGF23), a protein hormone that reduces immune response in vivo and in vitro. Increased FGF23 levels associate with higher infection-related hospitalizations and adverse infectious outcomes. Thus, we evaluated whether ESRD patients with high FGF23 titers have an increased rate of SARS-CoV-2 infection. Methods: We performed a prospective cohort of ESRD patients in hemodialysis who had measurements of plasma intact FGF23 in 2019. We determined COVID-19 infections, hospitalizations, and mortality between January 2020 and December 2021. Results: We evaluated 243 patients. Age: 60.4 ± 10.8 years. Female: 120 (49.3%), diabetes: 110 (45.2%). During follow-up, 45 patients developed COVID-19 (18.5%), 35 patients were hospitalized, and 12 patients died (mortality rate: 26.6%). We found that patients with higher FGF23 levels (defined as equal or above median) had a higher rate of SARS-CoV-2 infection versus those with lower levels (18.8% versus 9.9%; Hazard ratio: 1.92 [1.03-3.56], p = 0.039). Multivariate analysis showed that increased plasma FGF23 was independently associated with SARS-CoV-2 infection and severe COVID-19. Discussion: Our results suggest that high plasma FGF23 levels are a risk factor for developing COVID-19 in ESRD patients. These data support the potential immunosuppressive effects of high circulating FGF23 as a factor implicated in the association with worse clinical outcomes. Further data are needed to confirm this hypothesis.

AM J NEPHROL. 2023;54(9-10):425-433. DOI: 10.1159/000531147.

URINARY COPPER EXCRETION IS ASSOCIATED WITH LONG-TERM GRAFT FAILURE IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: In chronic kidney disease, proteinuria increases urinary copper excretion, inducing oxidative tubular damage and worsening kidney function. We investigated whether this phenomenon occurred in kidney transplant recipients (KTRs). In addition, we studied the associations of urinary copper excretion with the biomarker of oxidative tubular damage urinary liver-type fatty-acid binding protein (u-LFABP) and death-censored graft failure. Methods: This prospective cohort study was performed in the Netherlands between 2008 and 2017, including outpatient KTR with a functioning graft for longer than 1 year, who were extensively phenotyped at baseline. Twenty-four-hour urinary copper excretion was measured by inductively coupled plasma mass spectrometry. Multivariable linear and Cox regression analyses were performed. Results: In 693 KTR (57% men, 53 ± 13 years, estimated glomerular filtration rate [eGFR] 52 ± 20 mL/min/1.73 m2), baseline median urinary copper excretion was 23.6 (interquartile range 11.3-15.9) µg/24 h. Urinary protein excretion was positively associated with urinary copper excretion (standardized β = 0.39, p < 0.001), and urinary copper excretion was positively associated with u-LFABP (standardized β = 0.29, p < 0.001). During a median follow-up of 8 years, 109 (16%) KTR developed graft failure. KTR with relatively high copper excretion were at higher risk of long-term graft failure (hazard ratio [HR]: 1.57, 95% confidence interval [CI]: 1.32-1.86

per log2, p < 0.001), independent of multiple potential confounders like eGFR, urinary protein excretion, and time after transplantation. A dose-response relationship was observed over increasing tertiles of copper excretion (HR: 5.03, 95% CI: 2.75-9.19, tertile 3 vs. 1, p < 0.001). u-LFABP was a significant mediator of this association (74% of indirect effect, p < 0.001). Conclusion: In KTR, urinary protein excretion is positively correlated with urinary copper excretion. In turn, higher urinary copper excretion is associated with an independent increased risk of kidney graft failure, with a substantial mediating effect through oxidative tubular damage. Further studies are warranted to investigate whether copper excretion-targeted interventions could improve kidney graft survival

ANTIOXIDANTS (BASEL). 2023 FEB 10;12(2):454. DOI: 10.3390/ANTIOX12020454.

PLASMA COPPER CONCENTRATION IS ASSOCIATED WITH CARDIOVASCULAR MORTALITY IN MALE KIDNEY TRANSPLANT RECIPIENTS

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Kidney transplant recipients (KTR) are at increased risk of cardiovascular mortality. We investigated whether, in KTR, post-transplantation copper status is associated with the risk of cardiovascular mortality and potential effect modification by sex. In this cohort study, plasma copper was measured using mass spectrometry in extensively-phenotyped KTR with a functioning allograft >1-year. Cox regression analyses with the inclusion of multiplicative interaction terms were performed. In 660 KTR (53 ± 13 years old, 56% male), the median baseline plasma copper was 15.42 (IQR 13.53-17.63) µmol/L. During a median follow-up of 5 years, 141 KTR died, 53 (38%) due to cardiovascular causes. Higher plasma copper was associated with an increased risk of cardiovascular mortality in the overall KTR population (HR 1.37; 95% CI, 1.07-1.77 per 1-SD, p = 0.01). Sex was a significant effect modifier of this association (Pinteraction = 0.01). Among male KTR, higher plasma copper concentration was independently associated with a two-fold higher risk of cardiovascular mortality (HR 2.09; 95% CI, 1.42-3.07 per 1-SD, p < 0.001). Among female KTR, this association was absent. This evidence offers a rationale for considering a sex-specific assessment of copper's role in cardiovascular risk evaluation. Further studies are warranted to elucidate whether copper-targeted interventions may decrease cardiovascular mortality in male KTR.

BLOOD PURIF. 2023;52(7-8):668-675. DOI: 10.1159/000530464.

A NEW CYCLER FOR AUTOMATED PERITONEAL DIALYSIS TO PROVIDE EFFICIENT DIALYSIS AND IMPROVED SLEEP QUALITY

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Introduction: Automated peritoneal dialysis (APD) employs cyclers to control inflow and outflow of the dialysis fluid to the patient's abdomen. To allow more patients to use this modality, cyclers should support the achievement of an adequate dialysis dose and be easy to use, cost-effective, and silent. The new SILENCIA cycler (Fresenius Medical Care, Bad Homburg, Germany), designed to improve these characteristics in comparison to its predecessor device, was evaluated in this respect in a prospective study. Methods: This cross-over study comprised two 2-week study periods, separated by a 3-week training phase. First, patients underwent APD with their current cycler (PD-NIGHT [Fresenius Medical Care, Bad Homburg, Germany] or HomeChoice Pro [Baxter, Deerfield, IL, USA] as control), followed by training on the SILENCIA cycler. Then, patients were switched to the SILENCIA cycler. During each treatment period, we collected data on total Kt/Vurea, ultrafiltration (UF) volume, patient-reported outcomes (sleep quality, among others), and device handling. Results: Sixteen patients were enrolled; 2 patients terminated the study prematurely before study intervention, 1 patient due to a protocol violation. In 13 patients, total Kt/Vurea and UF could be evaluated. Neither Kt/Vurea nor UF differed significantly between control and SILENCIA cyclers. Out of 10 patients answering the questionnaire on sleep quality after the 2-week phase with the SILENCIA cycler, sleep quality improved in 5 patients; in the other patients, sleep quality was rated unchanged compared to the previously used cycler. The average reported sleep time was 5.9 ± 1.8 h with the PD-NIGHT, 7.2 ± 2.1 h with HomeChoice Pro, and 8.0 ± 1.6 h with the SILENCIA cycler. All patients were much or very much satisfied with the new cycler. Conclusion: The SILENCIA cycler delivers adequate urea clearance and UF. Importantly, sleep quality improved, possibly related to less caution messages and alarms.

NEPHROL DIAL TRANSPLANT. 2023 SEP 29;38(10):2321-2329. DOI: 10.1093/NDT/GFAD046.

LOW SELENIUM INTAKE IS ASSOCIATED WITH RISK OF ALL-CAUSE MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Deficiency of the essential trace element selenium is common in kidney transplant recipients (KTR), potentially hampering antioxidant and anti-inflammatory defence. Whether this impacts the long-term outcomes of KTR remains unknown. We investigated the association of urinary selenium excretion, a biomarker of selenium intake, with all-cause mortality; and its dietary determinants. Methods: In this cohort study, outpatient KTR with a functioning graft for longer than 1 year were recruited (2008-11). Baseline 24-h urinary selenium excretion was measured by mass spectrometry. Diet was assessed by a 177-item food frequency questionnaire, and protein intake was calculated by the Maroni equation. Multivariable linear and Cox regression analyses were performed. Results: In 693 KTR (43% men, 52 ± 12 years), baseline urinary selenium excretion was 18.8 (interquartile range 15.1-23.4) µg/24-h. During a median follow-up of 8 years, 229 (33%) KTR died. KTR in the first tertile of urinary selenium excretion, compared with those in the third, had over a 2-fold risk of all-cause mortality [hazard ratio 2.36 (95% confidence interval 1.70-3.28); P < .001], independent of multiple potential confounders including time since transplantation and plasma albumin concentration. The most important dietary determinant of urinary selenium excretion was protein intake (Standardized β 0.49, P < .001). Conclusions: Relatively low selenium intake is associated with a higher risk of all-cause mortality in KTR. Dietary protein intake is its most important determinant. Further research is required to evaluate the potential benefit of accounting for selenium intake in the care of KTR, particularly among those with low protein intake.

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NEPHROLOGISTS' PERSPECTIVES ON THE IMPACT OF COVID-19 ON CARING FOR PATIENTS UNDERGOING DIALYSIS IN LATIN AMERICA: A QUALITATIVE STUDY

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Objective To describe the experiences of nephrologists on caring for patients undergoing in-centre haemodialysis during the COVID-19 pandemic in Latin America. Design Twenty-five semistructured interviews were conducted by Zoom videoconference in English and Spanish languages during 2020 until data saturation. Using thematic analysis, we conducted line-by-line coding to inductively identify themes. Setting 25 centres across nine countries in Latin America. Participants Nephrologists (17 male and 8 female) were purposively sampled to include diverse demographic characteristics and clinical experience. Results We identified five themes: shock and immediate mobilisation for preparedness (overwhelmed and distressed, expanding responsibilities to manage COVID-19 infection and united for workforce resilience); personal vulnerability (being infected with COVID-19 and fear of transmitting COVID-19 to family); infrastructural susceptibility of dialysis units (lacking resources and facilities for quarantine, struggling to prevent cross-contamination, and depletion of personal protective equipment and cleaning supplies); helplessness and moral distress (being forced to ration life-sustaining equipment and care, being concerned about delayed and shortened dialysis sessions, patient hesitancy to attend to dialysis sessions, being grieved by socioeconomic disparities, deterioration of patients with COVID-19, harms of isolation and inability to provide kidney replacement therapy); and fostering innovative delivery of care (expanding use of telehealth, increasing uptake of PD and shifting focus on preventing syndemics). Conclusion Nephrologists felt personally and professionally vulnerable and reported feeling helpless and morally distressed because they doubted their capacity to provide safe care for patients undergoing dialysis. Better availability and mobilisation of resources and capacities to adapt models of care, including telehealth and home-based dialysis, are urgently needed.

HUM VACCIN IMMUNOTHER. 2023 DEC 31;19(1):2173904. DOI: 10.1080/21645515.2023.2173904.

EFFICACY OF VACCINATION AGAINST THE SARS-COV-2 VIRUS IN PATIENTS WITH CHRONIC KIDNEY DISEASE ON HEMODIALYSIS

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SARS-CoV-2 has had a great impact on world health, patients on hemodialysis have a higher rate of infection and death due to COVID-19. Vaccination is important to control infection and improve the prognosis of infected patients. To describe the efficacy of vaccination against SARS-CoV-2 in Chilean patients on hemodialysis during the year 2021. Retrospective observational study. A total of 9,712 clinical records were reviewed. Data were presented as summary measures. Fisher's exact test, Mann-Whitney U test, and multivariate logistic regression were used for the analysis. Risk and survival analysis were calculated, considering a statistical significance of less than 0.05. The average age of the patients attended was 61.5 ± 14.6 years. Average time on dialysis 67.6 months and 35.0% diabetic. 93.2% of patients were vaccinated against SARS-CoV-2, 70.7% of them received booster doses. The risk of infection was higher for those who received one or no dose, compared to those who received booster doses against SARS-CoV-2: OR = 252.46 [165.13; 401.57]. Of the infected patients, 15.7% died from COVID-19. The risk of death was higher in unvaccinated or single-dose patients compared to those vaccinated with two doses: OR = 2.64 [2.23; 3.12]. Patients with two doses and a booster had a longer survival compared to those who received one or no dose of vaccination against SARS-CoV-2 ($p < .05$). The vaccination in Chile, which started in February 2021, has demonstrated that booster doses against SARS-CoV-2 significantly reduced the risk of infection, hospitalization, and death due to COVID-19 in patients on hemodialysis.

SERVICIO DE NEUMOLOGÍA

SENSORS (BASEL). 2023 SEP 1;23(17):7590. DOI: 10.3390/S23177590.

AUTOMATIC DETECTION OF DYSPNEA IN REAL HUMAN-ROBOT INTERACTION SCENARIOS

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A respiratory distress estimation technique for telephony previously proposed by the authors is adapted and evaluated in real static and dynamic HRI scenarios. The system is evaluated with a telephone dataset re-recorded using the robotic platform designed and implemented for this study. In addition, the original telephone training data are modified using an environmental model that incorporates natural robot-generated and external noise sources and reverberant effects using room impulse responses (RIRs). The results indicate that the average accuracy and AUC are just 0.4% less than those obtained with matched training/testing conditions with simulated data. Quite surprisingly, there is not much difference in accuracy and AUC between static and dynamic HRI conditions. Moreover, the beamforming methods delay-and-sum and MVDR lead to average improvement in accuracy and AUC equal to 8% and 2%, respectively, when applied to training and testing data. Regarding the complementarity of time-dependent and time-independent features, the combination of both types of classifiers provides the best joint accuracy and AUC score.

SENSORS (BASEL). 2023 FEB 22;23(5):2441. DOI: 10.3390/S23052441.

DYSPNEA SEVERITY ASSESSMENT BASED ON VOCALIZATION BEHAVIOR WITH DEEP LEARNING ON THE TELEPHONE

Eduardo Alvarado, Nicolás Grágeda, Alejandro Luzanto, Rodrigo Mahu, Jorge Wuth, Laura Mendoza, Néstor Becerra Yoma

In this paper, a system to assess dyspnea with the mMRC scale, on the phone, via deep learning, is proposed. The method is based on modeling the spontaneous behavior of subjects while pronouncing controlled phonetization. These vocalizations were designed, or chosen, to deal with the stationary noise suppression of cellular handsets, to provoke different rates of exhaled air, and to stimulate different levels of

fluency. Time-independent and time-dependent engineered features were proposed and selected, and a k-fold scheme with double validation was adopted to select the models with the greatest potential for generalization. Moreover, score fusion methods were also investigated to optimize the complementarity of the controlled phonetizations and features that were engineered and selected. The results reported here were obtained from 104 participants, where 34 corresponded to healthy individuals and 70 were patients with respiratory conditions. The subjects' vocalizations were recorded with a telephone call (i.e., with an IVR server). The system provided an accuracy of 59% (i.e., estimating the correct mMRC), a root mean square error equal to 0.98, false positive rate of 6%, false negative rate of 11%, and an area under the ROC curve equal to 0.97. Finally, a prototype was developed and implemented, with an ASR-based automatic segmentation scheme, to estimate dyspnea on line.

SERVICIO DE ONCOLOGÍA

INT J CANCER. 2023 SEP 15;153(6):1151-1161. DOI: 10.1002/IJC.34607.

DEVELOPMENT AND INTERNAL VALIDATION OF A MULTIFACTORIAL RISK PREDICTION MODEL FOR GALLBLADDER CANCER IN A HIGH-INCIDENCE COUNTRY

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Since 2006, Chile has been implementing a gallbladder cancer (GBC) prevention program based on prophylactic cholecystectomy for gallstone patients aged 35 to 49 years. The effectiveness of this prevention program has not yet been comprehensively evaluated. We conducted a retrospective study of 473 Chilean GBC patients and 2137 population-based controls to develop and internally validate three GBC risk prediction models. The Baseline Model accounted for gallstones while adjusting for sex and birth year. Enhanced Model I also included the non-genetic risk factors: body mass index, educational level, Mapuche surnames, number of children and family history of GBC. Enhanced Model II further included Mapuche ancestry and the genotype for rs17209837. Multiple Cox regression was applied to assess the predictive performance, quantified by the area under the precision-recall curve (AUC-PRC) and the number of cholecystectomies needed (NCN) to prevent one case of GBC at age 70 years. The AUC-PRC for the Baseline Model (0.44%, 95%CI 0.42-0.46) increased by 0.22 (95%CI 0.15-0.29) when non-genetic factors were included, and by 0.25 (95%CI 0.20-0.30) when incorporating non-genetic and genetic factors. The overall NCN for Chileans with gallstones (115, 95%CI 104-131) decreased to 92 (95%CI 60-128) for Chileans with a higher risk than the median according to Enhanced Model I, and to 80 (95%CI 59-110) according to Enhanced Model II. In conclusion, age, sex and gallstones are strong risk factors for GBC, but consideration of other non-genetic factors and individual genotype data improves risk prediction and may optimize allocation of financial resources and surgical capacity.

FRONT MED (LAUSANNE). 2023 NOV 27:10:1284689. DOI: 10.3389/FMED.2023.1284689. ECOLLECTION 2023.

INSPIRATORY MUSCLE TRAINING IN PATIENTS WITH OBESITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Obesity is a chronic medical condition that affects, among others, the cardiovascular and respiratory systems. Interventions for its treatment focus on sustained weight reduction and general health improvement, leaving respiratory management aside. Our objective was to determine the effects of inspiratory muscle training (IMT) in patients with obesity. Methods: A systematic review was performed in Embase, Cochrane Library (CENTRAL), CINAHL, Web of Science, and PubMed/MEDLINE on June 26, 2023. Randomized clinical trials (RCTs), and quasi-randomized clinical trials investigating the effects of IMT in people with obesity were included. Selected studies were screened by two independent reviewers who extracted data and assessed the quality of the evidence. Results: The initial search returned 705 potential studies were included. Ultimately, eight studies met the criteria for eligibility and were included in the review. IMT improves physical capacity [6-minute walk test (6MWT): 44.5 m, 95% CI: 30.5 to 58.5; $p < 0.0001$] and the strength of the inspiratory muscles [maximal inspiratory pressure (MIP): -28.4 cm H2O, 95% CI: -41.9 to -14.8; $p < 0.0001$] compared to the controls, without differences in the pulmonary function, body mass index (BMI) and metabolic parameters. Conclusion: Inspiratory muscle training improves physical capacity and inspiratory muscle strength without significant changes in lung function, BMI, and metabolic parameters.

CANCERS (BASEL). 2023 AUG 9;15(16):4033. DOI: 10.3390/CANCERS15164033.

GALLBLADDER CANCER RISK AND INDIGENOUS SOUTH AMERICAN MAPUCHE ANCESTRY: INSTRUMENTAL VARIABLE ANALYSIS USING ANCESTRY-INFORMATIVE MARKERS

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A strong association between the proportion of indigenous South American Mapuche ancestry and the risk of gallbladder cancer (GBC) has been reported in observational studies. Chileans show the highest incidence of GBC worldwide, and the Mapuche are the largest indigenous people in Chile. We set out to assess the confounding-free effect of the individual proportion of Mapuche ancestry on GBC risk and to investigate the mediating effects of gallstone disease and body mass index (BMI) on this association. Genetic markers of Mapuche ancestry were selected based on the informativeness for assignment measure, and then used as instrumental variables in two-sample Mendelian randomization analyses and complementary sensitivity analyses. Results suggested a putatively causal effect of Mapuche ancestry on GBC risk (inverse variance-weighted (IVW) risk increase of 0.8% per 1% increase in Mapuche ancestry proportion, 95% CI 0.4% to 1.2%, $p = 6.7 \times 10\text{-}5$) and also on gallstone disease (3.6% IVW risk increase, 95% CI 3.1% to 4.0%), pointing to a mediating effect of gallstones on the association between Mapuche ancestry and GBC. In contrast, the proportion of Mapuche ancestry showed a negative

effect on BMI (IVW estimate -0.006 kg/m2, 95% CI -0.009 to -0.003). The results presented here may have significant implications for GBC prevention and are important for future admixture mapping studies. Given that the association between the individual proportion of Mapuche ancestry and GBC risk previously noted in observational studies appears to be free of confounding, primary and secondary prevention strategies that consider genetic ancestry could be particularly efficient.

WORLD J CLIN ONCOL. 2023 OCT 24;14(10):409-419. DOI: 10.5306/WJCO.V14.I10.409.

CLASSIFICATION OF PATIENTS WITH METASTATIC COLORECTAL CANCER INTO CONSENSUS MOLECULAR SUBTYPES INTO REAL-WORLD: A PILOT STUDY

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Background: Colorectal cancer is a complex disease with high mortality rates. Over time, the treatment of metastatic colorectal cancer (mCRC) has gradually improved due to the development of modern chemotherapy and targeted therapy regimens. However, due to the inherent heterogeneity of this condition, identifying reliable predictive biomarkers for targeted therapies remains challenging. A recent promising classification system-the consensus molecular subtype (CMS) system-offers the potential to categorize mCRC patients based on their unique biological and molecular characteristics. Four distinct CMS categories have been defined: immune (CMS1), canonical (CMS2), metabolic (CMS3), and mesenchymal (CMS4). Nevertheless, there is currently no standardized protocol for accurately classifying patients into CMS categories. To address this challenge, reverse transcription polymerase chain reaction (RT-qPCR) and next-generation genomic sequencing (NGS) techniques may hold promise for precisely classifying mCRC patients into their CMSs. Aim: To investigate if mCRC patients can be classified into CMS categories using a standardized molecular biology workflow. Methods: This observational study was conducted at the University of Chile Clinical Hospital and included patients with unresectable mCRC who were undergoing systemic treatment with chemotherapy and/or targeted therapy. Molecular biology techniques were employed to analyse primary tumour samples from these patients. RT-qPCR was utilized to assess the expression of genes associated with fibrosis (TGF-β and β-catenin) and cell growth pathways (c-MYC). NGS using a 25-gene panel (TumorSec) was performed to identify specific genomic mutations. The patients were then classified into one of the four CMS categories according to the clinical consensus of a Tumour Board. Informed consent was obtained from all the patients prior to their participation in this study. All techniques were conducted at University of Chile. Results: Twenty-six patients were studied with the techniques and then evaluated by the Tumour Board to determine the specific CMS. Among them, 23% (n = 6), 19% (n = 5), 31% (n = 8), and 19% (n = 5) were classified as CMS1, CMS2, CMS3, and CMS4, respectively. Additionally, 8% of patients (n = 2) could not be classified into any of the four CMS categories. The median overall survival of the total sample was 28 mo, and for CMS1, CMS2, CMS3 and CMS4 it was 11, 20, 30 and 45 mo respectively, with no statistically significant differences between groups. Conclusion: A molecular biology workflow and clinical consensus analysis can be used to accurately classify mCRC patients. This classification process, which divides patients into the four CMS categories, holds significant potential for improving research strategies and targeted therapies tailored to the specific characteristics of mCRC.

UNIDAD PACIENTES CRÍTICOS

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DYNAMIC RELATIVE REGIONAL LUNG STRAIN ESTIMATED BY COMPUTED TOMOGRAPHY AND ELECTRICAL IMPEDANCE TOMOGRAPHY IN ARDS PATIENTS

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Background: In the acute distress respiratory syndrome (ARDS), specific lung regions can be exposed to excessive strain due to heterogeneous disease, gravity-dependent lung collapse and injurious mechanical ventilation. Computed tomography (CT) is the gold standard for regional strain assessment. An alternative tool could be the electrical impedance tomography (EIT). We aimed to determine whether EIT-based methods can predict the dynamic relative regional strain (DRRS) between two levels of end-expiratory pressure (PEEP) in gravity-non-dependent and dependent lung regions. Methods: Fourteen ARDS patients underwent CT and EIT acquisitions (at end-inspiratory and end-expiratory) at two levels of PEEP: a low-PEEP based on ARDS-net strategy and a high-PEEP titrated according to EIT. Three EIT-based methods for DRRS were compared to relative CT-based strain: (1) the change of the ratio between EIT ventilation and end-expiratory lung impedance in arbitrary units ([ΔZAU low-PEEP/EELIAU low-PEEP]/[ΔZAU high-PEEP/EELIAU high-PEEP]), (2) the change of ΔZ/EELI ratio calibrated to mL ([ΔZml low-PEEP/EELIml low-PEEP]/[ΔZml high-PEEP/EELIml high-PEEP]) using CT data, and (3) the relative change of ΔZAU (ΔZAU low-PEEP/ΔZAU high-PEEP). We performed linear regressions analysis and calculated bias and limits of agreement to assess the performance of DRRS by EIT in comparison with CT. Results: The DRRS assessed by (ΔZml low-PEEP/EELIml low-PEEP)/(ΔZml high-PEEP/EELIml high-PEEP) and ΔZAU low-PEEP/ΔZAU high-PEEP showed good relationship and agreement with the CT method (R2 of 0.9050 and 0.8679, respectively, in non-dependent region; R2 of 0.8373 and 0.6588, respectively, in dependent region; biases ranging from - 0.11 to 0.51 and limits of agreement ranging from - 0.73 to 1.16 for both methods and lung regions). Conversely, DRRS based on EELIAU ([ΔZAU low-PEEP/EELIAU low-PEEP]/[ΔZAU high-PEEP/EELIAU high-PEEP]) exhibited a weak negative relationship and poor agreement with the CT method for both non-dependent and dependent regions (R2 ~ 0.3; bias of 3.11 and 2.08, and limits of agreement of - 2.13 to 8.34 and from - 1.49 to 5.64, respectively). Conclusion: Changes in DRRS during a PEEP trial in ARDS patients could be monitored using EIT, based on changes in ΔZmL/EELIml and ΔZAU. The relative change ΔZAU offers the advantage of not requiring CT data for calibration

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MORTALIDAD EN PACIENTES CON COVID-19 GRAVE SOMETIDOS A TRAQUEOSTOMÍA POR VENTILACIÓN MECÁNICA PROLONGADA

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Antecedentes: La utilidad de la traqueostomía en pacientes COVID-19 sometidos a ventilación mecánica invasiva (VMI) prolongada ha sido cuestionada. Objetivo: Comparar la mortalidad a 90 días en estos pacientes, con y sin traqueostomía. Material y Métodos: Estudiamos una cohorte histórica de 92 pacientes COVID-19 con VMI prolongada (>10 días). El desenlace prima-rio fue mortalidad a 90 días. Se consideraron desenlaces secundarios los días en VMI, estadía hospitalaria/UCI, frecuencia de infecciones nosocomiales, y eventos trombóticos. Mediante regresión logística se ajustó el efecto de la traqueostomía en la mortalidad, por SOFA y días de VMI. Resultados: Cuarenta y seis pacientes de 54 a 66 años (72% hombres) fueron traqueostomizados. Ellos tenían una mediana de dos comorbilidades, y recibieron el procedimiento luego de una mediana de 20,5 días en VMI (rango intercuartílico: 17-26). En el análisis crudo, la mortalidad a 90 días fue menor en los pacientes con traqueostomía que en el grupo control (6,5% vs. 32,6%; p < 0,001). No obstante, luego de controlar por factores de confusión, no se encontraron diferencias en mortalidad (riesgo relativo 0,303; p = 0,233). Las infecciones asociadas a la atención de salud y la estadía en hospital/UCI fueron mayores en los pacientes traqueostomizados que en los controles. Los eventos trombóticos ocurrieron en el 42,4% de los pacientes, sin diferencias entre grupos. No hubo casos de COVID-19 en el personal de salud que realizó las traqueostomías. Conclusiones: En pacientes con COVID-19 sometidos a VMI prolongada, la realización de una traqueostomía no se asocia a un exceso de mortalidad, y es un procedimiento seguro para el personal sanitario.

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TIC-TAC: A TRANSLATIONAL APPROACH IN MECHANISMS ASSOCIATED WITH IRREGULAR HEARTBEAT AND SINUS RHYTHM RESTORATION IN ATRIAL FIBRILLATION PATIENTS

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Atrial fibrillation (AF) is a prevalent cardiac condition predominantly affecting older adults, characterized by irregular heartbeat rhythm. The condition often leads to significant disability and increased mortality rates. Traditionally, two therapeutic strategies have been employed for its treatment: heart rate control and rhythm control. Recent clinical studies have emphasized the critical role of early restoration of sinus rhythm in improving patient outcomes. The persistence of the irregular rhythm allows for the progression and structural remodeling of the atria, eventually leading to irreversible stages, as observed clinically when AF becomes permanent. Cardioversion to sinus rhythm alters this progression pattern through mechanisms that are still being studied. In this review, we provide an in-depth analysis of the pathophysiological mechanisms responsible for maintaining AF and how they are modified during sinus rhythm restoration using existing therapeutic strategies at different stages of clinical investigation. Moreover, we explore potential future therapeutic approaches, including the promising prospect of gene therapy.

ANN INTENSIVE CARE. 2023 OCT 18;13(1):104. DOI: 10.1186/S13613-023-01203-Z.

PHYSIOLOGICAL EFFECTS OF HIGH-FLOW NASAL CANNULA OXYGEN THERAPY AFTER EXTUBATION: A RANDOMIZED CROSSOVER STUDY

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Background: Prophylactic high-flow nasal cannula (HFNC) oxygen therapy can decrease the risk of extubation failure. It is frequently used in the postextubation phase alone or in combination with noninvasive ventilation. However, its physiological effects in this setting have not been thoroughly investigated. The aim of this study was to determine comprehensively the effects of HFNC applied after extubation on respiratory effort, diaphragm activity, gas exchange, ventilation distribution, and cardiovascular biomarkers. Methods: This was a prospective randomized crossover physiological study in critically ill patients comparing 1 h of HFNC versus 1 h of standard oxygen after extubation. The main inclusion criteria were mechanical ventilation for at least 48 h due to acute respiratory failure, and extubation after a successful spontaneous breathing trial (SBT). We measured respiratory effort through esophageal/transdiaphragmatic pressures, and diaphragm electrical activity (ΔEAdi). Lung volumes and ventilation distribution were estimated by electrical impedance tomography. Arterial and central venous blood gases were analyzed, as well as cardiac stress biomarkers. Results: We enrolled 22 patients (age 59 ± 17 years; 9 women) who had been intubated for 8 ± 6 days before extubation. Respiratory effort was significantly lower with HFNC than with standard oxygen therapy, as evidenced by esophageal pressure swings (5.3 [4.2-7.1] vs. 7.2 [5.6-10.3] cmH2O; p < 0.001), pressure-time product (85 [67-140] vs. 156 [114-238] cmH2O*s/min; p < 0.001) and ΔEAdi (10 [7-13] vs. 14 [9-16] μV; p = 0.022). In addition, HFNC induced increases in end-expiratory lung volume and PaO2/FiO2 ratio, decreases in respiratory rate and ventilatory ratio, while no changes were observed in systemic hemodynamics, Troponin T, or in amino-terminal pro-B-type natriuretic peptide. Conclusions: Prophylactic application of HFNC after extubation provides substantial respiratory support and unloads respiratory muscles. Trial registration January 15, 2021. NCT04711759.

ANN INTENSIVE CARE. 2023 DEC 20;13(1):131. DOI: 10.1186/S13613-023-01230-W.

PENDELLUFT IN HYPOXEMIC PATIENTS RESUMING SPONTANEOUS BREATHING: PROPORTIONAL MODES VERSUS PRESSURE SUPPORT VENTILATION

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Background: Internal redistribution of gas, referred to as pendelluft, is a new potential mechanism of effort-dependent lung injury. Neurally-adjusted ventilatory assist (NAVA) and proportional assist ventilation (PAV +) follow the patient's respiratory effort and improve synchrony compared with pressure support ventilation (PSV). Whether these modes could prevent the development of pendelluft compared with PSV is unknown. We aimed to compare pendelluft magnitude during PAV + and NAVA versus PSV in patients with resolving acute respiratory distress syndrome (ARDS). Methods: Patients received either NAVA, PAV +, or PSV in a crossover trial for 20-min using comparable assistance levels after controlled ventilation (> 72 h). We assessed pendelluft (the percentage of lost volume from the non-dependent

lung region displaced to the dependent region during inspiration), drive (as the delta esophageal swing of the first 100 ms [ΔPes 100 ms]) and inspiratory effort (as the esophageal pressure-time product per minute [PTPmin]). We performed repeated measures analysis with post-hoc tests and mixed-effects models. Results: Twenty patients mechanically ventilated for 9 [5-14] days were monitored. Despite matching for a similar tidal volume, respiratory drive and inspiratory effort were slightly higher with NAVA and PAV + compared with PSV (ΔPes 100 ms of -2.8 [-3.8--1.9] cm H2O, -3.6 [-3.9--2.4] cm H2O and -2.1 [-2.5--1.1] cm H2O, respectively, $p < 0.001$ for both comparisons; PTPmin of 155 [118-209] cm H2O s/min, 197 [145-269] cm H2O s/min, and 134 [93-169] cm H2O s/min, respectively, $p < 0.001$ for both comparisons). Pendelluft magnitude was higher in NAVA (12 ± 7%) and PAV + (13 ± 7%) compared with PSV (8 ± 6%), $p < 0.001$. Pendelluft magnitude was strongly associated with respiratory drive ($\beta = -2.771$, p-value < 0.001) and inspiratory effort ($\beta = 0.026$, $p < 0.001$), independent of the ventilatory mode. A higher magnitude of pendelluft in proportional modes compared with PSV existed after adjusting for PTPmin ($\beta = 2.606$, $p = 0.010$ for NAVA, and $\beta = 3.360$, $p = 0.004$ for PAV +), and only for PAV + when adjusted for respiratory drive ($\beta = 2.643$, $p = 0.009$ for PAV +). Conclusions: Pendelluft magnitude is associated with respiratory drive and inspiratory effort. Proportional modes do not prevent its occurrence in resolving ARDS compared with PSV.

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ASSOCIATION OF LUNG RECRUITMENT AND CHANGE IN RECRUITMENT-TO-INFLATION RATIO FROM SUPINE TO PRONE POSITION IN ACUTE RESPIRATORY DISTRESS SYNDROME

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Prone positioning is an evidence-based treatment for patients with moderate-to-severe acute respiratory distress syndrome. Lung recruitment has been proposed as one of the mechanisms by which prone positioning reduces mortality in this group of patients. Recruitment-to-inflation ratio (R/I) is a method to measure potential for lung recruitment induced by a change in positive end-expiratory pressure (PEEP) on the ventilator. The association between R/I and potential for lung recruitment in supine and prone position has not been studied with computed tomography (CT) scan imaging. In this secondary analysis, we sought to investigate the correlation between R/I measured in supine and prone position with CT and the potential for lung recruitment as measured by CT scan. Among 23 patients, the median R/I did not significantly change from supine (1.9 IQR 1.6-2.6) to prone position (1.7 IQR 1.3-2.8) (paired t test $p = 0.051$) but the individual changes correlated with the different response to PEEP. In supine and in prone position, R/I significantly correlated with the proportion of lung tissue recruitment induced by the change of PEEP. Lung tissue recruitment induced by a change of PEEP from 5 to 15 cmH2O was 16% (IQR 11-24%) in supine and 14.3% (IQR 8.4-22.6%) in prone position, as measured by CT scan analysis (paired t test $p = 0.56$). In this analysis, PEEP-induced recruitability as measured by R/I correlated with PEEP-induced lung recruitment as measured by CT scan, and could help to readjust PEEP in prone position.

FRONT MED (LAUSANNE). 2023 FEB 2:10:1099594. DOI: 10.3389/FMED.2023.1099594. ECOLLECTION 2023.

NON-PHARMACOLOGICAL PREVENTION OF POSTOPERATIVE DELIRIUM BY OCCUPATIONAL THERAPY TEAMS: A RANDOMIZED CLINICAL TRIAL

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Background: Patients who develop postoperative delirium (POD) have several clinical complications, such as increased morbidity, increased hospital stays, higher hospital costs, cognitive and functional impairment, and higher mortality. POD is a clinical condition preventable by standard non-pharmacological measures An intensive Occupational Therapy (OT) intervention has been shown to be highly effective in preventing delirium in critically ill medical patients, but it is unknown the effect in surgical patients. Thus, we designed a prospective clinical study with the aim to determine whether patients undergoing intervention by the OT team have a lower incidence of POD compared to the group treated only with standard measures. Methods: A multicenter, single-blind, randomized clinical trial was conducted between October 2018 and April 2021, in Santiago of Chile, at a university hospital and at a public hospital. Patients older than 75 years undergoing elective major surgery were eligible for the trial inclusion. Patients with cognitive impairment, severe communication disorder and cultural language limitation, delirium at admission or before surgery, and enrolled in another study were excluded. The intervention consisted of OT therapy twice a day plus standard internationally recommended non-pharmacological prevention intervention during 5 days after surgery. Our primary outcome was development of delirium and postoperative subsyndromal delirium. Results: In total 160 patients were studied. In the interventional group, treated with an intensive prevention by OT, nine patients (12.9%) developed delirium after surgery and in the control group four patients (5.5%) [p = 0.125, RR 2.34 CI 95 (0.75-7.27)]. Whereas subsyndromal POD was present in 38 patients in the control group (52.1%) and in 34 (48.6%) in the intervention group [p = 0.4, RR 0.93 CI95 (0.67-1.29)]. A post hoc analysis determined that the patient's comorbidity and cognitive status prior to hospitalization were the main risk factors to develop delirium after surgery. Discussion: Patients undergoing intervention by the OT team did not have a lower incidence of POD compared to the group treated only with standard non-pharmacological measures in adults older than 75 years who went for major surgery.

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CHANGES IN LUNG VOLUMES DURING BRONCHOALVEOLAR LAVAGE ACCORDING TO BEDSIDE POSITION. CASE SERIES

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Introduction: Bronchoalveolar lavage (BAL) is used in the diagnosis of pneumonia in patients with Mechanical Ventilation. Its performance involves the instillation of saline solution, which is associated with lung collapse and worsening hypoxemia. Positioning the patient's

head at 0° could increase the loss of lung volume and oxygenation. A therapeutic option to mitigate this effect could be to perform this procedure with head elevation at 30°. Aims and Objectives: The study aimed to assess changes in lung volumes in relation to the position of the patient's head. Methods: Case series of 3 patients. End-expiratory Lung Impedance (EELI) measurements were performed (Pulmovista V500) in the following situations: Head at 30° before BAL, 0° before BAL, 0° post-BAL and 30° post-BAL. Results: In patients 1 and 2, the change of headrest from 30° to 0° before BAL resulted in an overall decrease in EELI (83.1% - 20.2%). Performing BAL increased the drop in EELI, with greater expression in the regions where BAL was performed. After BAL was completed, in both patients, the repositioning of the headrest to 30° produced an increase in global EELI without reaching the values obtained with the headrest at 30° before BAL (Patient 1 80.5% - Patiente 2 52.9%). In patient 3, the change of head position from 30° to 0° after BAL showed a 12.5% decrease in EELI. Performing BAL deepened the drop in overall EELI (-44.4%), as did repositioning the headrest to 30° (-70%) post-BAL. Conclusion: Changes in bedside positioning before BAL resulted in a reduction in EELI in all 3 patients. The repositioning of the head after BAL had a heterogeneous behavior increasing the EELI in patients 1 and 2, and decreasing it in patient 3.

SERVICIO DE REUMATOLOGÍA

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PAN AMERICAN LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY RECOMMENDATIONS FOR THE MANAGEMENT OF AXIAL SPONDYLOARTHRITIS

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Axial spondyloarthritis (axSpA) comprises a spectrum of chronic inflammatory manifestations affecting the axial skeleton and represents a challenge for diagnosis and treatment. Our objective was to generate a set of evidence-based recommendations for the management of axSpA for physicians, health professionals, rheumatologists and policy decision makers in Pan American League of Associations for Rheumatology (PANLAR) countries. Grading of Recommendations, Assessment, Development and Evaluation-ADOLOPMENT methodology was used to adapt existing recommendations after performing an independent systematic search and synthesis of the literature to update the evidence. A working group consisting of rheumatologists, epidemiologists and patient representatives from countries within the Americas prioritized 13 topics relevant to the context of these countries for the management of axSpA. This Evidence-Based Guideline article reports 13 recommendations addressing therapeutic targets, the use of NSAIDs and glucocorticoids, treatment with DMARDs (including conventional synthetic, biologic and targeted synthetic DMARDs), therapeutic failure, optimization of the use of biologic DMARDs, the use of drugs for extra-musculoskeletal manifestations of axSpA, non-pharmacological interventions and the follow-up of patients with axSpA.

ANNALS OF THE RHEUMATIC DISEASES 2023;82:2004-2005.

POSITIVE MRI OF THE SPINE AS IMAGING CRITERION FOR DIAGNOSIS OF AXIAL PSORIATIC ARTHRITIS

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Background MRI is essential for axial spondyloarthritis (axSpA) diagnosis. A positive MRI in the ASAS classification criteria of axSpA is based on inflammatory lesions in the sacroiliac joints. These lesions are defined as one bone marrow edema (BME) highly suggestive of axSpA present on ≥ 2 consecutive slices or ≥ 2 BME A on a single slice. The addition of MRI of the spine as an imaging criterion to the ASAS axSpA criteria had a low yield of newly classified patients and is therefore not recommended. Axial psoriatic arthritis (axPsA) remains poorly defined despite its high prevalence among patients with PsA. Studies comparing axPsA with other axSpA, such as Anquilosing Spondylitis (AS), have found differences in the former, including more frequent asymmetric spine and SIJ involvement, cervical involvement, and isolated spondylitis. Objectives Describe the presence of inflammatory and structural lesions on MRI-spine and SIJ in patients with psoriasis. Evaluate the added value of spinal inflammatory lesions on MRI-spine and structural lesions on MRI-SIJ as imaging criterion for axPsA diagnosis. Methods We performed a retrospective study of patients with psoriasis with at least a whole spine and sacroiliac joints (SIJ) MRI performed at Universidad de Chile Clinical Hospital between January 2015 and December 2021. MRI were performed in a 1.5 T machine, following a non-contrast protocol. Sagittal T1-weighted (T1w) and T2-weighted fat-suppressed fast spin echo sequences were available for the spine, while semi-coronal T1w and short inversion recovery sequences for the SIJ. Structural and inflammatory lesions were defined according to the ASAS/OMERACT definitions. Results are presented as mean and SD or numbers and percentages. Results 34 patients with psoriasis were analyzed, 17 (50%) were male, and the mean age at the time the MRI was performed was 43.7 ± 10.6 years. The most common type of psoriasis was vulgaris (85%) and time from diagnosis was greater than ten years at least in 65% of patients. The majority of patients experienced chronic back pain (82%), and 15 (44%) patients had IBP according to ASAS criteria. MRI-SIJ showed structural and/or inflammatory changes in 16 patients. In 15 of them, BME was present. Of these 16 patients, 8 (50%) had no lesions in MRI-spine. In MRI-spine, 11 patients showed structural and/or inflammatory changes, and 5 of these 11 patients (55%) had BME suggestive of axSpA according to ASAS/OMERACT criteria. When we analyzed patients with an MRI negative for sacroiliitis (19 patients), 3 had BME on MRI-spine, with only two patients with three or more BME lesions according to ASAS/OMERACT criteria. Finally, when a chronic lesion on MRI-SIJ was considered as a possible criterion for classification, among patients without sacroiliitis, one patient could be deemed to have axSpA. The findings in this image of SIJ were erosions and fatty deposition (Romanus sign). Conclusion A positive MRI-spine in patients with suspected axPsA was more frequent than previously described for axSpA. Furthermore, spinal inflammation in the absence of sacroiliitis was present in 2 of the 19 patients in this cohort. Therefore, MRI-spine could be considered in the classification criterion for patients suspected of axPsA.

ANNALS OF THE RHEUMATIC DISEASES 2023;82:1671.

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

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Background Systemic sclerosis (SSc) is an autoimmune disorder characterized by vasculopathy and fibrosis of skin and internal organs. Gastrointestinal (GI) system is affected in up to 90% of patients and dysmotility is the primary abnormality [1]. Gastric dismotility contributes to esophageal symptoms and causes nausea, vomiting, abdominal bloating, and early satiety. It also impacts quality of life and when severe is associated with increased mortality [2]. GI dysmotility can be evaluated with Electrogastrography (EGG), a non-invasive and safe test. It measures gastric myoelectrical activity, and when impaired it predicts delayed gastric emptying with an accuracy of 85% [3]. To the date gastric involvement in patients with early SSc has not been directly studied. Objectives Describe the prevalence of gastric dysrhythmias in early SSc and the association between GI symptoms and GI dysmotility. Methods SSc patients fulfilling the 2013 ACR/EULAR classification criteria with early disease (≤ 3 years from the first non-Raynaud symptom) were included and cross-sectionally assessed. Pregnancy and Diabetes Mellitus were exclusion criteria. All patients signed informed consent. GI symptoms were assessed using the UCLA GIT 2.0 questionnaire [4]. Gastric myoelectrical activity was measured using surface EGG and informed as preprandial, postprandial or continuous brady or tachygastria. Continuous bradygastria was considered a severe abnormality. It was informed by an expert gastroenterologist blinded to patient characteristics. Statistical analyses: Categorical variables were described as frequencies and percentages, and quantitative variables as mean, SD and IQR. The associations between variables were analyzed using the Fisher exact test. Statistical significancy was defined as $p < 0,05$. Results 30 patients were included, 96,6 % were female, with a mean age of 48.7 years (25–72 years). SSc was limited in 76.6%. 14/28 patients had an anticentromere antinuclear antibody pattern and 6 had anti Scl 70. Organ involvement was interstitial lung disease in 7/29, altered echocardiogram in 10/25 and erosive esophagitis in 11/15. Half of the patients were under immunosuppressive treatment, 43% on methotrexate and 50% mycophenolate. EGG was abnormal in 28/29 patients, 71.4% had bradygastria, 10.7% tachygastria an 17.8% mixed. Bradygastria was mostly preprandial (45%) and continuous (50%). According to the UCLA GIT 2.0 questionnaire, two thirds of the patients had a moderate to severe GI involvement. Other score items are described in Table 1. There was no correlation between symptoms and severity of the gastric motility disorder, but the presence of bradygastria was associated to a worse social functioning score (p 0, 018). Conclusion Gastric dysrhythmias, especially bradygastria occurs early in systemic sclerosis. Bradygastria was associated with a worse social functioning score.

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AN INTERNATIONAL SURVEY OF CURRENT MANAGEMENT PRACTICES FOR POLYMYALGIA RHEUMATICA BY GENERAL PRACTITIONERS AND RHEUMATOLOGISTS

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Objectives To explore current management practices for PMR by general practitioners (GPs) and rheumatologists including implications for clinical trial recruitment. Methods In English language questionnaire was constructed by a working group of rheumatologists and GPs from six countries. The questionnaire focused on: 1: Respondent characteristics; 2: Referral practices; 3: Treatment with glucocorticoids; 4: Diagnostics; 5: Comorbidities; and 6: Barriers to research. The questionnaire was distributed to rheumatologists and GPs worldwide via members of the International PMR/Giant Cell Arteritis Study Group. Results In total, 394 GPs and 937 rheumatologists responded to the survey. GPs referred a median of 25% of their suspected PMR patients for diagnosis and 50% of these were returned to their GP for management. In general, 39% of rheumatologists evaluated patients with suspected PMR >2 weeks after referral, and a median of 50% of patients had started prednisolone before rheumatologist evaluation. Direct comparison of initial treatment showed that the percentage prescribing >25 mg prednisolone daily for patients was 30% for GPs and 12% for rheumatologists. Diagnostic imaging was rarely used. More than half (56%) of rheumatologists experienced difficulties recruiting people with PMR to clinical trials. Conclusion This large international survey indicates that a large proportion of people with PMR are not referred for diagnosis, and that the proportion of treatment-naive patients declined with increasing time from referral to assessment. Strategies are needed to change referral and management of people with PMR, to improve clinical practice and facilitate recruitment to clinical trials.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

ALZHEIMERS DEMENT. 2023 SEP;19(9):4046-4060. DOI: 10.1002/ALZ.13101.

LATIN AMERICAN INITIATIVE FOR LIFESTYLE INTERVENTION TO PREVENT COGNITIVE DECLINE (LATAM-FINGERS): STUDY DESIGN AND HARMONIZATION

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Introduction: Latin American Initiative for Lifestyle Intervention to Prevent Cognitive Decline (LatAm-FINGERS) is the first non-pharmacological multicenter randomized clinical trial (RCT) to prevent cognitive impairment in Latin America (LA). Our aim is to present the study design and discuss the strategies used for multicultural harmonization. Methods: This 1-year RCT (working on a 1-year extension) investigates the feasibility of a multi-domain lifestyle intervention in LA and the efficacy of the intervention, primarily on cognitive function. An external harmonization process was carried out to follow the FINGER model, and an internal harmonization was performed to ensure this study was feasible and comparable across the 12 participating LA countries. Results: Currently, 1549 participants have been screened, and 815 randomized. Participants are ethnically diverse (56% are Nestizo) and have high cardiovascular risk (39% have metabolic syndrome). Discussion: LatAm-FINGERS overcame a significant challenge to combine the region's diversity into a multi-domain risk reduction intervention feasible across LA while preserving the original FINGER design.

BIOMEDICINES. 2023 MAY 25;11(6):1525. DOI: 10.3390/BIOMEDICINES11061525.

SPATIAL AND ECOLOGICAL FACTORS MODULATE THE INCIDENCE OF ANTI-NMDAR ENCEPHALITIS-A SYSTEMATIC REVIEW

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Anti-NMDAR encephalitis has been associated with multiple antigenic triggers (i.e., ovarian teratomas, prodromal viral infections) but whether geographic, climatic, and environmental factors might influence disease risk has not been explored yet. We performed a systematic review and a meta-analysis of all published papers reporting the incidence of anti-NMDAR encephalitis in a definite country or region. We performed several multivariate spatial autocorrelation analyses to analyze the spatial variations in the incidence of anti-NMDA encephalitis depending on its geographical localization and temperature. Finally, we performed seasonal analyses in two original datasets from France and Greece and assessed the impact of temperature using an exposure-lag-response model in the French dataset. The reported incidence of anti-NMDAR encephalitis varied considerably among studies and countries, being higher in Oceania and South America (0.2 and 0.16 per 100,000 persons-year, respectively) compared to Europe and North America (0.06 per 100,000 persons-year) ($p < 0.01$). Different regression models confirmed a strong negative correlation with latitude (Pearson's $R = -0.88$, $p < 0.00001$), with higher incidence in southern hemisphere countries far from the equator. Seasonal analyses showed a peak of cases during warm months. Exposure-lag-response models confirmed a positive correlation between extreme hot temperatures and the incidence of anti-NMDAR encephalitis in France ($p = 0.03$). Temperature analyses showed a significant association with higher mean temperatures and positive correlation with higher ultraviolet exposure worldwide. This study provides the first evidence that geographic and climatic factors including latitude, mean annual temperature, and ultraviolet exposure, might modify disease risk.

NEUROPATHOL APPL NEUROBIOL. 2023 AUG;49(4):E12918. DOI: 10.1111/NAN.12918.

A CENTRONUCLEAR MYOPATHY-CAUSING MUTATION IN DYNAMIN-2 DISRUPTS NEURONAL MORPHOLOGY AND EXCITATORY SYNAPTIC TRANSMISSION IN A MURINE MODEL OF THE DISEASE

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Aims: Dynamin-2 is a large GTPase, a member of the dynamin superfamily that regulates membrane remodelling and cytoskeleton dynamics. Mutations in the dynamin-2 gene (DNM2) cause autosomal dominant centronuclear myopathy (CNM), a congenital neuromuscular disorder characterised by progressive weakness and atrophy of the skeletal muscles. Cognitive defects have been reported in some DNM2-linked CNM patients suggesting that these mutations can also affect the central nervous system (CNS). Here we studied how a dynamin-2 CNM-causing mutation influences the CNS function. Methods: Heterozygous mice harbouring the p.R465W mutation in the dynamin-2 gene (HTZ), the most common causing autosomal dominant CNM, were used as disease model. We evaluated dendritic arborisation and spine density in hippocampal cultured neurons, analysed excitatory synaptic transmission by electrophysiological field recordings in hippocampal slices, and evaluated cognitive function by performing behavioural tests. Results: HTZ hippocampal neurons exhibited reduced dendritic arborisation and lower spine density than WT neurons, which was reversed by transfecting an interference RNA against the dynamin-2 mutant allele. Additionally, HTZ mice showed defective hippocampal excitatory synaptic transmission and reduced recognition memory compared to the WT condition. Conclusion: Our findings suggest that the dynamin-2 p.R465W mutation perturbs the synaptic and cognitive function in a CNM mouse model and support the idea that this GTPase plays a key role in regulating neuronal morphology and excitatory synaptic transmission in the hippocampus.

ALZHEIMERS DEMENT. 2023 JUL;19(7):3210-3221. DOI: 10.1002/ALZ.12995.

A CALL FOR CLINICAL TRIAL GLOBALIZATION IN ALZHEIMER'S DISEASE AND RELATED DEMENTIA

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Background: The burden of Alzheimer's disease and related dementia (ADRD) is projected to disproportionally impact low-middle-income countries (LMICs). However, there is a systematic under-representation of LMICs in ADRD clinical trial platforms. Methods: We aimed to determine the global distribution of ADRD clinical trials and identify existing barriers for conducting clinical trials in LMICs. Primary data sources to identify trial distribution in LMICs included ClinicalTrials.gov and the International Trials Registry Platform. An additional systematic review and expert consensus interviews were conducted to identify barriers for conducting clinical trials in LMICs. Findings: Among 1237 disease-modifying therapies tested in ADRD clinical trials, only 11.6% have been or are conducted in emerging economies (upper-middle income [9.6%] and low-middle income [2.0%]). We identified several limitations for trial implementation including a lack of financial resources, low industry presence, regulatory obstacles, and operational barriers INTERPRETATION: Although LMICs bear the greatest burden of ADRD globally, substantial development of clinical trial platforms to address this inequity and health disparity is lacking.

AM J AUDIOL. 2023 MAR;32(1):150-159. DOI: 10.1044/2022_AJA-22-00042.

PREVALENCE OF COGNITIVE IMPAIRMENT AND ITS ASSOCIATION WITH HEARING LOSS AMONG ADULTS OVER 50 YEARS OF AGE: RESULTS FROM A POPULATION-BASED SURVEY IN SANTIAGO, CHILE

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Purpose: The purpose of this study was to estimate the prevalence of cognitive impairment and explore its association with hearing loss and other sociodemographic and clinical risk factors, using an objective measurement of hearing levels, in adults over 50 years of age. Method: A population-based survey was completed in Santiago, Chile between December 2019 and March 2020. Participants were screened for cognitive impairment using the Short Chilean Mini-Mental State Examination and hearing levels were assessed with tonal

audiometry (hearTest). Data on demographic, socioeconomic, and clinical characteristics were collected. Results: A total of 538 persons completed the assessment. The prevalence of cognitive impairment in the 50+ population was 9.3% (95% confidence interval [CI] [5.8, 14.7]). Cognitive impairment was significantly higher in individuals with any level of hearing loss (odds ratio [OR] = 2.19, 95% CI [1.00, 4.80], adjusted for age, sex, education, socioeconomic position [SEP], and head trauma). Subjects with hearing loss and who reported any use of hearing aids (16% of the sample) had a lower risk of cognitive impairment (OR of nonusers 3.64, 95% CI [1.00, 13.28], adjusted for age, sex, education, SEP, and head trauma). Conclusion: Strategies for addressing cognitive impairment should further explore the integration of early diagnosis of hearing loss and the regular use of hearing aids.

CUREUS. 2023 AUG 17;15(8):E43645. DOI: 10.7759/CUREUS.43645. ECOLLECTION 2023 AUG.

PERCUTANEOUS BALLOON COMPRESSION FOR THE TREATMENT OF TRIGEMINAL NEURALGIA: A REVIEW OF 10 YEARS OF CLINICAL EXPERIENCE

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Background: Trigeminal neuralgia (TN) is defined as a spontaneous painful sensation in the trigeminal nerve territory. The pain intensity of TN is classified into different grades of suffering that affect a patient's quality of life. Percutaneous balloon compression of the ganglion is a neurosurgical option that is easy, reproducible, and can reduce the morbidity of TN. Methods: We retrospectively analyzed all patients treated with trigeminal nerve percutaneous balloon compression at the Clinical Hospital of the University of Chile between January 2012 and May 2022. Data collected from electronic records included demographic information, medical and surgical history, type of anesthesia and drugs used during surgery, balloon inflation time, surgery time, operative room time, intraoperative events, postoperative complications, duration of hospitalization, and duration of follow-up. Results: We identified 63 patients who met our inclusion criteria. The median patient age was 62 years (interquartile range [IQR] 57-69 years). Sixty-five percent of the patients were female. The simultaneous involvement of the second and third branches of the trigeminal nerve was the most frequent symptom. Before surgery, the patients experienced an average of 6.6 years of pain (IQR 2-10 years). Right neuralgia was the most frequent laterality type (69%). Forty percent of the patients had a previous surgical procedure for neuralgia, with treatment failure being the most frequent surgical indication (63%). According to the procedure, the mean balloon insufflation volume was 0.89±0.12 mL with a median compression time of 2.5 min (IQR 2.1-4.0 min). No hemorrhagic complications were observed. Furthermore, during follow-up, there were no surgical complications among any of the patients; however, 6.4% of patients required a second intervention. The pain-free period was two years in 60% of patients and five years in 23% of patients. Conclusions: TN is a painful condition. Although there are multiple surgical approaches, we believe that percutaneous balloon compression is an excellent alternative treatment option that offers high effectiveness, low morbidity, and low hospital stay.

CUREUS. 2023 NOV 8;15(11):E48517. DOI: 10.7759/CUREUS.48517. ECOLLECTION 2023 NOV.

COMBINED VERTEBRAL AUGMENTATION FOR VERTEBRAL BODY FRACTURE WITH CONTRAINDICATIONS FOR TRADITIONAL TECHNIQUES

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Introduction and objective: A vertebral compression fracture (VCF) can be found in trauma, osteoporosis, and tumor pathology. The most frequent is the pathological fracture in osteoporotic vertebrae in the elderly. Percutaneous techniques of vertebral cementation allow treatment of A1-A2 AO spine fractures, improving pain control and spine stabilization and decreasing mobility and mortality. Traditionally, the selection of patients is fundamental for spine surgery success, with an absolute contraindication being posterior wall involvement (A3-A4 AO spine fractures) or VCF with a loss of height greater than 50%. In this report, we present a variant surgical technique combining percutaneous spine surgery with cementoplasty for patients with classical spine surgery contraindications. Methods: Five patients with complex symptomatic VCF or A3-A4 AO spine fractures in pathologic bone with MRI short tau inversion recovery (STIR) sequence (+) were operated on with a combined technique (percutaneous kyphoplasty (KP) and vesselplasty). The visual analog scale (VAS) was used to measure postoperative pain. Results: The procedure was performed within 60 days of the fracture in all patients. The mean hospital stay was two days. No patient developed major complications. All the patients had a satisfactory clinical (improvement in pain control) and radiological response at the perioperative period and at a 30-day follow-up. Conclusions: The combined percutaneous technique allows surgical resolution of cases previously considered contraindicated, especially in elderly patients and those with comorbidities, without involving higher cost, complications, surgical time, and hospital stay. We suggest a novel, safe, and effective variation of the vertebral cementoplasty technique.

FRONT NEUROL. 2023 SEP 14:14:1251581. DOI: 10.3389/FNEUR.2023.1251581. ECOLLECTION 2023.

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

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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.

FRONT AGING NEUROSCI. 2023 AUG 30:15:1196641. DOI: 10.3389/FNAGI.2023.1196641. ECOLLECTION 2023.

EXPLORING THE RELATIONSHIP BETWEEN FRAILTY AND EXECUTIVE DYSFUNCTION: THE ROLE OF FRONTAL WHITE MATTER HYPERINTENSITIES

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Introduction: Frailty is a geriatric syndrome frequently associated with executive dysfunction and white matter hyperintensities (WMH). But the relation between executive dysfunction and brain changes is poorly understood in frail subjects. Our hypothesis is that frontal-WMH mediates the association between frailty and executive dysfunction. Methods: A convenience sample of 113 subjects older than 65 years without dementia was studied with neuropsychological test, a structured clinical interview, physical examination and brain MRI. They were classified as robust or pre-frail and frail using the frailty phenotype score (0-5). The frontal WMH (F-WMH) were manually graduated (0-6) using the "Age-Related White Matter Changes score" from FLAIR sequences at a 3 Tesla brain MRI. A mediation analysis was done for testing whether F-WMH could act as a link factor between frailty phenotype score and executive dysfunction. Results: The group's mean age was 74 ± 6 years, subjects with higher frailty score had more depressive symptoms and worse performance in executive function tests. A regression analysis that explained 52% of the variability in executive functions, revealed a significant direct effect of frailty score (Standardized βcoeff [95% CI] -0.201, [-0.319, -0.049], and F-WMH (-0.152[-0.269, -0.009]) on executive functions, while the F-WMH showed a small partial mediation effect between frailty and executive functions (-0.0395, [-0.09, -0.004]). Discussion: Frontal matter hyperintensities had a small mediation effect on the association between frailty and executive dysfunction, suggesting that other neuropathological and neurofunctional changes might also be associated with executive dysfunction in frail subjects.

J NEUROL. 2023 DEC;270(12):5849-5865. DOI: 10.1007/S00415-023-11862-4.

ANALYSIS OF MUSCLE MAGNETIC RESONANCE IMAGING OF A LARGE COHORT OF PATIENT WITH VCP-MEDIATED DISEASE REVEALS CHARACTERISTIC FEATURES USEFUL FOR DIAGNOSIS

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Background: The diagnosis of patients with mutations in the VCP gene can be complicated due to their broad phenotypic spectrum including myopathy, motor neuron disease and peripheral neuropathy. Muscle MRI guides the diagnosis in neuromuscular diseases (NMDs); however, comprehensive muscle MRI features for VCP patients have not been reported so far. Methods: We collected muscle MRIs of 80 of the 255 patients who participated in the "VCP International Study" and reviewed the T1-weighted (T1w) and short tau inversion recovery (STIR) sequences. We identified a series of potential diagnostic MRI based characteristics useful for the diagnosis of VCP disease and validated them in 1089 MRIs from patients with other genetically confirmed NMDs. Results: Fat replacement of at least one muscle was identified in all symptomatic patients. The most common finding was the existence of patchy areas of fat replacement. Although there was a wide variability of muscles affected, we observed a common pattern characterized by the involvement of periscapular, paraspinal, gluteal and quadriceps muscles. STIR signal was enhanced in 67% of the patients, either in the muscle itself or in the surrounding fascia. We identified 10 diagnostic characteristics based on the pattern identified that allowed us to distinguish VCP disease from other neuromuscular diseases with high accuracy. Conclusions: Patients with mutations in the VCP gene had common features on muscle MRI that are helpful for diagnosis purposes, including the presence of patchy fat replacement and a prominent involvement of the periscapular, paraspinal, abdominal and thigh muscles.

NEUROL GENET. 2023 AUG 15;9(5):E200093.

CLINICAL CLASSIFICATION OF VARIANTS IN THE VALOSIN-CONTAINING PROTEIN GENE ASSOCIATED WITH MULTISYSTEM PROTEINOPATHY

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Background and objectives: Pathogenic variants in the valosin-containing protein (VCP) gene cause a phenotypically heterogeneous disorder that includes myopathy, motor neuron disease, Paget disease of the bone, frontotemporal dementia, and parkinsonism termed multisystem proteinopathy. This hallmark pleiotropy makes the classification of novel VCP variants challenging. This retrospective study describes and assesses the effect of 19 novel or nonpreviously clinically characterized VCP variants identified in 28 patients (26 unrelated families) in the retrospective VCP International Multicenter Study. Methods: A 6-item clinical score was developed to evaluate the phenotypic level of evidence to support the pathogenicity of the novel variants. Each item is allocated a value, a score ranging from 0.5 to 5.5 points. A receiver-operating characteristic curve was used to identify a cutoff value of 3 to consider a variant as high likelihood disease associated. The scoring system results were confronted with results of in vitro ATPase activity assays and with in silico analysis. Results: All variants were missense, except for one small deletion-insertion, 18 led to amino acid changes within the N and D1 domains, and 13 increased the enzymatic activity. The clinical score coincided with the functional studies in 17 of 19 variants and with the in silico analysis in 12 of 19. For 12 variants, the 3 predictive tools agreed, and for 7 variants, the predictive tools disagreed. The pooled data supported the pathogenicity of 13 of 19 novel VCP variants identified in the study. Discussion: This study provides data to support pathogenicity of 14 of 19 novel VCP variants and provides guidance for clinicians in the evaluation of novel variants in the VCP gene.

REV MED CHIL. 2023 FEB;151(1):61-71. DOI: 10.4067/S0034-98872023000100061.

IMPLEMENTACIÓN DE UNA JORNADA VIRTUAL DE TELESALUD Y CAPACITACIÓN MASIVA PARA PERSONAS MAYORES CHILENAS Y ESTUDIANTES DE LA SALUD. IMPACTO EN LA COBERTURA

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Fondo: El envejecimiento aumenta la vulnerabilidad a enfermedades y cambios ambientales como la pandemia de COVID-19. La telesalud y la teleeducación son vitales para prevenir los efectos nocivos del confinamiento prolongado, y para capacitar a la comunidad y a los estudiantes de medicina y profesionales de la salud en constante rotación. Objetivo: Evaluar la percepción y el impacto de un curso online sobre envejecimiento saludable dirigido a la comunidad y a profesionales de la salud. Material y métodos: Se llevó a cabo un curso abierto en línea de una jornada de duración para promover el envejecimiento saludable. Una encuesta transversal en línea sobre el curso fue respondida por 386 asistentes y se aplicó una prueba de conocimientos a 114 personas. Resultados: El setenta y cinco por ciento de los encuestados asistieron al curso de forma sincrónica. De ellos, el 79% eran mujeres, el 20% eran personas mayores y el 53% eran cuidadores de una persona mayor. Todos los encuestados adquirieron nuevos conocimientos y estaban dispuestos a participar nuevamente. La frecuencia del interés por el cuidado de sí mismo es tres veces mayor que por el cuidado de otra persona. En una persona mayor, el interés es 101 veces mayor por el cuidado de sí mismo que por el cuidado de otra persona. El noventa y cinco por ciento de los encuestados se sintió más activo y el 84% se sintió más acompañado. Conclusiones: El curso facilitó el acceso a información sobre la promoción del envejecimiento activo y saludable en la comunidad con una percepción favorable y un impacto positivo. Se debe mejorar la cobertura para las personas mayores con brecha digital.

NEUROMUSCULAR DISORDERS, VOLUME 33, SUPPLEMENT 1, 2023, PAGE S77, DOI.ORG/10.1016/J.NMD.2023.07.055.

REFINING MRI PATTERN IN SARCOGLYCANOPATHIES: UPPER BODY PATTERN AND NEW APPROACHES TO ASSESS DISEASE PROGRESSION

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Sarcoglycanopathies are autosomal recessive limb-girdle muscular dystrophies caused by mutations in γ, α, β, and δ sarcoglycan genes. The lower limb (LL) MRI pattern has already been reported and gives diagnostic clues. Instead, the MRI pattern of the upper body (UB) has not been described and could be valuable to understand the imaging phenotype and progression of muscle involvement in sarcoglycanopathies. To describe the UB MRI pattern in sarcoglycanopathies and its correlation with pattern of the LL, disease duration and motor status. MRI from UB and LL of 64 patients with LGMDR3-6 were included in an international collaborative study. Muscle fatty replacement (FR) was evaluated semiquantitatively on T1-weighted images according to Lamminen score, and represented in a heatmap. We correlated FR of each muscle with motor status. We assessed variability of the FR score within each muscle using the homogeneity index (HI). We also tested the relationship between ambulatory status and FR along the different body regions with random forests. Partial correlation analysis and proportional odds logistic regressions were used to assess the relationship between FR in each muscle, disease duration and age at onset. The involvement of the UB muscles started early during the ambulant period. Some muscles of the scapular girdle (latissimus dorsi, subscapularis and serratus anterior) are early involved while muscles from head, neck and forearms are mostly spared, even in advanced disease stages. A caudocranial gradient of involvement in axial muscles (mainly, paravertebral muscles and trapezius) was consistently found in most of the patients. FRs of most scapular girdle and LL muscles are correlated with motor status. Ambulant patients show lower HI than non-ambulant patients. Random forests trained with information from different body parts predicts well ambulatory status with small differences in accuracy. Partial correlations of disease duration controlled by age at onset were high or moderate. The effect of disease duration seems higher in patients with earlier onset. UB fingerprint in sarcoglycanopathy exists and it is related with LL involvement and functional status. Disease duration is the main driver of FR in sarcoglycanopathies and early onset seems to accelerate it.

REV. MÉD. CHILE [ONLINE]. 2023, VOL.151, N.4, PP.524-529.

CANVAS: UNA NUEVA ETIOLOGÍA DE LA ATAXIA DEL ADULTO. LA ASOCIACIÓN CON TOS ORIENTA AL DIAGNÓSTICO. COMUNICACIÓN DE 2 PACIENTES.

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Presentamos dos pacientes no relacionados con ataxia cerebelosa de inicio tardío asociada con neuropatía y tos seca de larga data. Un paciente tenía dos hermanos afectados con neuropatía sensorial y tos. Ambos probandos tuvieron investigaciones extensas que incluyó pruebas genéticas negativas para las ataxias más comunes, así como pruebas paraneoplásicas y otras causas inmunológicas. Ambos pacientes mostraron una expansión intrónica anormal en el pentanucleótido AAGGG del gen RFC1.

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

FRONT CARDIOVASC MED. 2023 OCT 25:10:1223928. DOI: 10.3389/FCVM.2023.1223928. ECOLLECTION 2023.

CARDIOMETABOLIC SEX DIFFERENCES IN ADULTS BORN SMALL FOR GESTATIONAL AGE

Mérida Rodríguez-López, Álvaro Sepúlveda-Martínez, Gabriel Bernardino, Francesca Crovetto, Carolina Pajuelo, Marta Sitges, Bart Bijnens, Eduard Gratacós, Fàtima Crispi

Aim: This study aimed to assess the cardiometabolic sex similarities and differences in adults born small for gestational age. Methods: This study was an ambispective cohort study from a birth registry in Barcelona, Spain, including 523 adult participants (20-40 years-old) subdivided as born small for gestational age (SGA, if birth weight <10th centile) or adequate fetal growth for gestational age (AGA).

Cardiometabolic health was assessed by echocardiography, electrocardiogram, blood pressure measurement, vascular ultrasound, anthropometric measurements, and serum glycemia and lipid profile. Stratified analyses by sex were performed by estimation of adjusted absolute difference (AAD) using inverse probability weighting. Results: Compared with AGA, the stratified analyses by sex showed a more pronounced reduction in ejection fraction [AAD: female -1.73 (95% CI -3.2 to -0.28) vs. male -1.33 (-3.19 to 0.52)] and increment in heart rate [female 3.04 (0.29-5.8) vs. male 2.25 (-0.82 to 5.31)] in SGA females compared with SGA males. In contrast, a more pronounced reduction in PR interval [female -1.36 (-6.15 to 3.42) vs. male -6.61 (-11.67 to -1.54)] and an increase in systolic blood pressure [female 0.06 (-2.7 to 2.81) vs. male 2.71 (-0.48 to 5.9)] and central-to-peripheral fat ratio [female 0.05 (-0.03 to 0.12) vs. male 0.40 (0.17-0.62)] were mainly observed in SGA male compared with SGA female. Conclusions: Sex differences were observed in the effect of SGA on cardiometabolic endpoints with female being more prone to cardiac dysfunction and male to electrocardiographic, vascular, and metabolic changes. Future research including sex-stratification data is warranted.

CASE REP WOMENS HEALTH. 2023 MAY 5:38:E00513. DOI: 10.1016/J.CRWH.2023.E00513. ECOLLECTION 2023 JUN.

TUMOR-LIKE PRESENTATION OF HERPETIC CERVICITIS: A CASE REPORT

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The case of a 20-year-old immunocompetent woman with necrotizing cervicitis of the cervix caused by a primary infection with herpes simplex virus type 2 is presented, along with its respective evolution in images. Cervical cancer was included in the differential diagnoses, but biopsies ruled out malignancy and laboratory tests demonstrated the viral etiology of the cervical inflammation. After initiating specific treatment, the cervical lesions completely healed within 3 weeks. This case highlights the need to consider herpes simplex infection in the differential diagnosis of cervical inflammation and tumor formation. Additionally, it provides images that can aid in diagnosis and allow for the observation of its clinical evolution.

BJOG. 2023 OCT;130(11):1346-1354. DOI: 10.1111/1471-0528.17484.

A CORE OUTCOME SET FOR TRIALS IN MISCARRIAGE MANAGEMENT AND PREVENTION: AN INTERNATIONAL CONSENSUS DEVELOPMENT STUDY

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Objective: To develop core outcome sets (COS) for miscarriage management and prevention. Design: Modified Delphi survey combined with a consensus development meeting. Setting: International. Population: Stakeholder groups included healthcare providers, international experts, researchers, charities and couples with lived experience of miscarriage from 15 countries: 129 stakeholders for miscarriage management and 437 for miscarriage prevention. Methods: Modified Delphi method and modified nominal group technique. Results: The final COS for miscarriage management comprises six outcomes: efficacy of treatment, heavy vaginal bleeding, pelvic infection, maternal death, treatment or procedure-related complications, and patient satisfaction. The final COS for miscarriage prevention comprises 12 outcomes: pregnancy loss <24 weeks' gestation, live birth, gestation at birth, pre-term birth, congenital abnormalities, fetal growth restriction, maternal (antenatal) complications, compliance with intervention, patient satisfaction, maternal hospitalisation, neonatal or infant hospitalisation, and neonatal or infant death. Other outcomes identified as important were mental health-related outcomes, future fertility and health economic outcomes. Conclusions: This study has developed two core outcome sets, through robust methodology, that should be implemented across future randomised trials and systematic reviews in miscarriage management and prevention. This work will help to standardise outcome selection, collection and reporting, and improve the quality and safety of future studies in miscarriage.

J CLIN ULTRASOUND. 2023 FEB;51(2):249-264. DOI: 10.1002/JCU.23336.

CARDIAC REMODELING FROM THE FETUS TO ADULTHOOD

Lina Youssef, Roberta Castellani, Brenda Valenzuela-Alcaraz, Álvaro Sepulveda-Martinez, Francesca Crovetto, Fàtima Crispi

Prenatal cardiac remodeling refers to in utero changes in the fetal heart that occur as a response to an adverse intrauterine environment. In this article, we will review the main mechanisms leading to cardiac remodeling and dysfunction, summarizing and describing the major pathological conditions that have been reported to be related to this in utero plastic adaptive process. We will also recap the current evidence regarding the persistence of fetal cardiac remodeling and dysfunction, both in infancy and later in adult life. Moreover, we will discuss primary, secondary, and tertiary preventive measures and future clinical and research aspects.

PEDIATR CARDIOL. 2023 AUG 19. 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 ≥ 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.

EUR HEART J CARDIOVASC IMAGING. 2023 JUN 21;24(7):930-937. DOI: 10.1093/EHJCI/JEAC262.

ASSOCIATION OF CENTRAL OBESITY WITH UNIQUE CARDIAC REMODELLING IN YOUNG ADULTS BORN SMALL FOR GESTATIONAL AGE

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Aims: Being born small for gestational age (SGA, 10% of all births) is associated with increased risk of cardiovascular mortality in adulthood together with lower exercise tolerance, but mechanistic pathways are unclear. Central obesity is known to worsen cardiovascular outcomes, but it is uncertain how it affects the heart in adults born SGA. We aimed to assess whether central obesity makes young adults born SGA more susceptible to cardiac remodelling and dysfunction. Methods and results: A perinatal cohort from a tertiary university hospital in Spain of young adults (30-40 years) randomly selected, 80 born SGA (birth weight below 10th centile) and 75 with normal birth weight (controls) was recruited. We studied the associations between SGA and central obesity (measured via the hip-to-waist ratio and used as a continuous variable) and cardiac regional structure and function, assessed by cardiac magnetic resonance using statistical shape analysis. Both SGA and waist-to-hip were highly associated to cardiac shape ($F = 3.94$, $P < 0.001$; $F = 5.18$, $P < 0.001$ respectively) with a statistically significant interaction ($F = 2.29$, $P = 0.02$). While controls tend to increase left ventricular end-diastolic volumes, mass and stroke volume with increasing waist-to-hip ratio, young adults born SGA showed a unique response with inability to increase cardiac dimensions or mass resulting in reduced stroke volume and exercise capacity. Conclusion: SGA young adults show a unique cardiac adaptation to central obesity. These results support considering SGA as a risk factor that may benefit from preventive strategies to reduce cardiometabolic risk.

INT J GYNAECOL OBSTET. 2023 JUN;161(3):1083-1091. DOI: 10.1002/IJGO.14657.

INTERGROWTH-21ST AND WORLD HEALTH ORGANIZATION FETAL GROWTH CHARTS FOR THE DETECTION OF SMALL-FOR-GESTATIONAL AGE NEONATES IN LATIN AMERICA

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Objective: To evaluate the performance of INTERGROWTH-21st (IG-21st) and World Health Organization (WHO) fetal growth charts to identify small-for-gestational-age (SGA) and fetal growth restriction (FGR) neonates, as well as their specific risks for adverse neonatal outcomes. Methods: Multicenter cross-sectional study including 67 968 live births from 10 maternity units across four Latin American countries. According to each standard, neonates were classified as SGA and FGR (birth weight <10th and less than third centiles, respectively). The relative risk (RR) and diagnostic performance for a low APGAR score and low ponderal index were calculated for each standard. Results: WHO charts identified more neonates as SGA than IG-21st (13.9% vs 7%, respectively). Neonates classified as having FGR by both standards had the highest RR for a low APGAR (RR, 5.57 [95% confidence interval (CI), 3.99-7.78]), followed by those who were SGA by both curves (RR, 3.27 [95% CI, 2.52-4.24]), while neonates with SGA identified by WHO alone did not have an additional risk (RR, 0.87 [95% CI, 0.55-1.39]). Furthermore, the diagnostic odds ratio for a low APGAR was higher when IG-21st was used. Conclusion: In a population from Latin America, the WHO charts seem to identify more SGA neonates, but the diagnostic performance of the IG-21st charts for low APGAR score and low ponderal index is better.

INT UROGYNECOL J. 2023 NOV;34(11):2657-2688. DOI: 10.1007/S00192-023-05629-8.

INTERNATIONAL UROGYNECOLOGY CONSULTATION CHAPTER 2 COMMITTEE 3: THE CLINICAL EVALUATION OF PELVIC ORGAN PROLAPSE INCLUDING INVESTIGATIONS INTO ASSOCIATED MORBIDITY/PELVIC FLOOR DYSFUNCTION

Heather Barbier, Cassandra L Carberry, Päivi K Karjalainen, Charlotte K Mahoney, Valentín Manríquez Galán, Anna Rosamilia, Esther Ruess, David Shaker, Karishma Thariani

Introduction and hypothesis: This manuscript from Chapter 2 of the International Urogynecology Consultation (IUC) on Pelvic Organ Prolapse (POP) reviews the literature involving the clinical evaluation of a patient with POP and associated bladder and bowel dysfunction. Methods: An international group of 11 clinicians performed a search of the literature using pre-specified search MESH terms in PubMed and Embase databases (January 2000 to August 2020). Publications were eliminated if not relevant to the clinical evaluation of patients or did not include clear definitions of POP. The titles and abstracts were reviewed using the Covidence database to determine whether they met the inclusion criteria. The manuscripts were reviewed for suitability using the Specialist Unit for Review Evidence checklists. The data from full-text manuscripts were extracted and then reviewed. Results: The search strategy found 11,242 abstracts, of which 220 articles were used to inform this narrative review. The main themes of this manuscript were the clinical examination, and the evaluation of comorbid conditions including the urinary tract (LUTS), gastrointestinal tract (GIT), pain, and sexual function. The physical examination of patients with pelvic organ prolapse (POP) should include a reproducible method of describing and quantifying the degree of POP and only the Pelvic Organ Quantification (POP-Q) system or the Simplified Pelvic Organ Prolapse Quantification (S-POP) system have enough reproducibility to be recommended. POP examination should be done with an empty bladder and patients can be supine but should be upright if the prolapse cannot be reproduced. No other parameters of the examination aid in describing and quantifying POP. Post-void residual urine volume >100 ml is commonly used to assess for voiding difficulty. Prolapse reduction can be used to predict the possibility of postoperative persistence of voiding difficulty. There is no benefit of urodynamic testing for assessment of detrusor overactivity as it does not change the management. In women with POP and

stress urinary incontinence (SUI), the cough stress test should be performed with a bladder volume of at least 200 ml and with the prolapse reduced either with a speculum or by a pessary. The urodynamic assessment only changes management when SUI and voiding dysfunction co-exist. Demonstration of preoperative occult SUI has a positive predictive value for de novo SUI of 40% but most useful is its absence, which has a negative predictive value of 91%. The routine addition of radiographic or physiological testing of the GIT currently has no additional value for a physical examination. In subjects with GIT symptoms further radiological but not physiological testing appears to aid in diagnosing enteroceles, sigmoidoceles, and intussusception, but there are no data on how this affects outcomes. There were no articles in the search on the evaluation of the co-morbid conditions of pain or sexual dysfunction in women with POP. Conclusions: The clinical pelvic examination remains the central tool for evaluation of POP and a system such as the POP-Q or S-POP should be used to describe and quantify. The value of investigation for urinary tract dysfunction was discussed and findings presented. The routine addition of GI radiographic or physiological testing is currently not recommended. There are no data on the role of the routine assessment of pain or sexual function, and this area needs more study. Imaging studies alone cannot replace clinical examination for the assessment of POP

LABORATORIO DE ENDOCRINOLOGÍA Y BIOLOGÍA DE LA REPRODUCCIÓN

FRONT ENDOCRINOL (LAUSANNE). 2023 MAR 28:14:1143261. DOI: 10.3389/FENDO.2023.1143261. ECOLLECTION 2023.

CONVENTIONAL AND NEW PROPOSALS OF GNRH THERAPY FOR OVARIAN, BREAST, AND PROSTATIC CANCERS

Maritza P Garrido, Andrea Hernandez, Margarita Vega, Eyleen Araya, Carmen Romero

For many years, luteinizing hormone-releasing hormone or gonadotropin-releasing hormone (GnRH) analogs have been used to treat androgen or estrogen-dependent tumors. However, emerging evidence shows that the GnRH receptor (GnRH-R) is overexpressed in several cancer cells, including ovarian, endometrial, and prostate cancer cells, suggesting that GnRH analogs could exert direct antitumoral actions in tumoral tissues that express GnRH-R. Another recent approach based on this knowledge was the use of GnRH peptides for developing specific targeted therapies, improving the delivery and accumulation of drugs in tumoral cells, and decreasing most side effects of current treatments. In this review, we discuss the conventional uses of GnRH analogs, together with the recent advances in GnRH-based drug delivery for ovarian, breast, and prostatic cancer cells.

INT J MOL SCI. 2023 JAN 11;24(2):1439. DOI: 10.3390/IJMS24021439.

ANTITUMORAL ACTIVITY OF LEPTOCARPHA RIVULARIS FLOWER EXTRACTS AGAINST GASTRIC CANCER CELLS

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Leptocarpha rivularis is a native South American plant used ancestrally by Mapuche people to treat gastrointestinal ailments. L. rivularis flower extracts are rich in molecules with therapeutic potential, including the sesquiterpene lactone leptocarpin, which displays cytotoxic effects against various cancer types in vitro. However, the combination of active molecules in these extracts could offer a hitherto unexplored potential for targeting cancer. In this study, we investigated the effect of L. rivularis flower extracts on the proliferation, survival, and spread parameters of gastric cancer cells in vitro. Gastric cancer (AGS and MKN-45) and normal immortalized (GES-1) cell lines were treated with different concentrations of L. rivularis flower extracts (DCM, Hex, EtOAc, and EtOH) and we determined the changes in proliferation (MTS assay, cell cycle analysis), cell viability/cytotoxicity (trypan blue exclusion assay, DEVDase activity, mitochondrial membrane potential MMP, and clonogenic ability), senescence (β-galactosidase activity) and spread potential (invasion and migration assays using the Boyden chamber approach) in all these cells. The results showed that the DCM, EtOAc, and Hex extracts display a selective antitumoral effect in gastric cancer cells by affecting all the cancer parameters tested. These findings reveal an attractive antitumoral potential of L. rivularis flower extracts by targeting several acquired capabilities of cancer cells.

PHARMACEUTICALS (BASEL). 2023 OCT 24;16(11):1515. DOI: 10.3390/PH16111515.

MECHANISMS OF REGULATION OF THE EXPRESSION OF MIRNAS AND LNCRNAS BY METFORMIN IN OVARIAN CANCER

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Ovarian cancer (OC) is one of the most lethal gynecological malignancies. The use of biological compounds such as non-coding RNAs (ncRNAs) is being considered as a therapeutic option to improve or complement current treatments since the deregulation of ncRNAs has been implicated in the pathogenesis and progression of OC. Old drugs with antitumoral properties have also been studied in the context of cancer, although their antitumor mechanisms are not fully clear. For instance, the antidiabetic drug metformin has shown pleiotropic effects in several in vitro models of cancer, including OC. Interestingly, metformin has been reported to regulate ncRNAs, which could explain its diverse effects on tumor cells. In this review, we discuss the mechanism of epigenetic regulation described for metformin, with a focus on the evidence of metformin-dependent microRNA (miRNAs) and long non-coding RNA (lncRNAs) regulation in OC.

DEPARTAMENTO DE OFTALMOLOGÍA

FRONT HUM NEUROSCI. 2023 FEB 3:17:1056432. DOI: 10.3389/FNHUM.2023.1056432. ECOLLECTION 2023.

COMBINED THERAPY OF BILATERAL TRANSCRANIAL DIRECT CURRENT STIMULATION AND OCULAR OCCLUSION IMPROVES VISUAL FUNCTION IN ADULTS WITH AMBLYOPIA, A RANDOMIZED PILOT STUDY

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Background: Amblyopia is the interocular visual acuity difference of two lines or more with the best correction in both eyes. It is treated with ocular occlusion therapy, but its success depends on neuroplasticity, and thus is effective in children but not adults. Transcranial Direct Current Stimulation (tDCS) is suggested to increase neuroplasticity. Objective: To determine if combined intervention of bilateral tDCS and ocular occlusion improves visual function in adults with amblyopia. Methods: A double-blind randomized, controlled pilot trial was conducted in 10 volunteers with amblyopia. While applying ocular occlusion and performing a reading task, participants received bilateral tDCS (n = 5) or sham stimulation (n = 5), with the anodal tDCS electrode in the contralateral visual cortex and the cathodal in the ipsilateral visual cortex in relation to the amblyopic eye. Visual function (through visual acuity, stereopsis, and contrast sensitivity tests) and visual evoked potential (with checkerboard pattern stimuli presentation) were evaluated immediately after. Results: A total of 30 min after treatment with bilateral tDCS, visual acuity improved by 0.16 (± 0.025) LogMAR in the treatment group compared with no improvement (-0.02 ± 0.02) in five controls (p = 0.0079), along with a significant increase in the amplitude of visual evoked potentials of the amblyopic eye response (p = 0.0286). No significant changes were observed in stereopsis and contrast sensitivity. No volunteer reported any harm derived from the intervention. Conclusion: Our study is the first to combine anodal and cathodal tDCS for the treatment of amblyopia, showing transient improved visual acuity in amblyopic adults.

PLOS ONE. 2023 APR 3;18(4):E0283845. DOI: 10.1371/JOURNAL.PONE.0283845. ECOLLECTION 2023.

RISK FACTORS FOR RECURRENCES AND VISUAL IMPAIRMENT IN PATIENTS WITH OCULAR TOXOPLASMOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Ocular toxoplasmosis (OT) is caused by the parasite Toxoplasma gondii. OT is the leading cause of posterior uveitis globally; it is a recurrent disease that may result in visual impairment and blindness. This systematic review and meta-analysis aim to summarize and evaluate the risk factors for recurrences, visual impairment, and blindness described in the literature worldwide. Methods and findings: We performed a systematic literature search in PubMed, Embase, VHL, Cochrane Library, Scopus, and DANS EASY Archive. All studies reporting patients with clinically and serologically confirmed OT presenting any clinical or paraclinical factor influencing recurrences, visual impairment, and blindness were included. Studies presenting secondary data, case reports, and case series were excluded. An initial selection was made by title and abstract, and then the studies were reviewed by full text where the eligible studies were selected. Then, the risk of bias was assessed through validated tools. Data were extracted using a validated extraction format. Qualitative synthesis and quantitative analysis were done. This study was registered on PROSPERO (CRD42022327836). Results: Seventy two studies met the inclusion criteria. Fifty-three were summarized in the qualitative synthesis in three sections: clinical and environmental factors, parasite and host factors, and treatment-related factors. Of the 72 articles, 39 were included in the meta-analysis, of which 14 were conducted in South America, 13 in Europe, four in Asia, three multinational, two in North America and Central America, respectively, and only one in Africa. A total of 4,200 patients with OT were analyzed, mean age ranged from 7.3 to 65.1 year of age, with similar distribution by sex. The frequency of recurrences in patients with OT was 49% (95% CI 40%-58%), being more frequent in the South American population than in Europeans. Additionally, visual impairment was presented in 35% (95% CI 25%-48%) and blindness in 20% (95% CI 13%-30%) of eyes, with a similar predominance in South Americans than in Europeans. On the other hand, having lesions near the macula or adjacent to the optic nerve had an OR of 4.83 (95% CI; 2.72-8.59) for blindness, similar to having more than one recurrence that had an OR of 3.18 (95% CI; 1.59-6.38). Finally, the prophylactic therapy with Trimethoprim/Sulfamethoxazole versus the placebo showed a protective factor of 83% during the first year and 87% in the second year after treatment. Conclusion: Our Systematic Review showed that clinical factors such as being older than 40 years, patients with de novo OT lesions or with less than one year after the first episode, macular area involvement, lesions greater than 1 disc diameter, congenital toxoplasmosis, and bilateral compromise had more risk of recurrences. Also, environmental and parasite factors such as precipitations, geographical region where the infection is acquired, and more virulent strains confer greater risk of recurrences. Therefore, patients with the above mentioned clinical, environmental, and parasite factors could benefit from using prophylactic therapy.

EYE (LOND). 2023 JUN;37(9):1895-1903. DOI: 10.1038/S41433-022-02267-0.

SUCCESSFUL TREATMENT OF CYTOMEGALOVIRUS RETINITIS WITH ORAL/INTRAVITREAL ANTIVIRALS IN HIV-NEGATIVE PATIENTS WITH LYMPHOMA

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Objectives: To report patients with systemic lymphoma and cytomegalovirus (CMV) retinitis, treated with a combination of oral and intravitreal antiviral agents on an outpatient basis. Methods: Retrospective cases series. Information was gathered from the database of the Uveitis clinics at Moorfields Eye Hospital, United Kingdom from December 2014 to December 2018. The inclusion criteria comprised the diagnosis of systemic lymphoma, associated with a diagnosis of CMV retinitis. Exclusion criteria were alternative ocular diagnosis, human immunodeficiency virus (HIV), primary intraocular lymphoma, or other causes of immunosuppression. Results: All seven subjects had been under oncologist care for systemic lymphoma. CMV retinitis presented with a median of 61 months after the systemic lymphoma diagnosis. Five patients underwent a vitreous biopsy, and four of them returned PCR positive for CMV and the fifth patient had PCR positive in a blood sample. All patients were treated with oral Valganciclovir, with an induction dose of 900 mg every 12 h for up to 3 weeks until disease resolution and a maintenance dose thereafter. All but one received additional intravitreal Foscarnet injections, with a dose of 2.4 mg /0.1 ml. Conclusions: The management of patients with systemic lymphoma and CMV retinitis with oral and intravitreal antiviral agents, resulted in effective disease control.

DEPARTAMENTO DE OTORRINOLARINGOLOGÍA

BRAIN SCI. 2023 DEC 23;14(1):16. DOI: 10.3390/BRAINSCI14010016.

FUNCTIONAL DIZZINESS AS A SPATIAL COGNITIVE DYSFUNCTION

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Background: Persistent postural-perceptual dizziness (PPPD) is a common chronic dizziness disorder with an unclear pathophysiology. It is hypothesized that PPPD may involve disrupted spatial cognition processes as a core feature. Methods: A cohort of 19 PPPD patients underwent psycho-cognitive testing, including assessments for anxiety, depression, memory, attention, planning, and executive functions, with an emphasis on spatial navigation via a virtual Morris water maze. These patients were compared with 12 healthy controls and 20 individuals with other vestibular disorders but without PPPD. Vestibular function was evaluated using video head impulse testing and vestibular evoked myogenic potentials, while brain magnetic resonance imaging was used to exclude confounding pathology. Results: PPPD patients demonstrated unique impairments in allocentric spatial navigation (as evidenced by the virtual Morris water maze) and in other high-demand visuospatial cognitive tasks that involve executive functions and planning, such as the Towers of London and Trail Making B tests. A factor analysis highlighted spatial navigation and advanced visuospatial functions as being central to PPPD, with a strong correlation to symptom severity. Conclusions: PPPD may broadly impair higher cognitive functions, especially in spatial cognition. We discuss a disruption in the creation of enriched cognitive spatial maps as a possible pathophysiology for PPPD.

INT J AUDIOL. 2023 JAN;62(1):53-61. DOI: 10.1080/14992027.2021.1998675.

PREVALENCE, RISK FACTORS AND CAUSES OF HEARING LOSS AMONG ADULTS 50 YEARS AND OLDER IN SANTIAGO, CHILE: RESULTS FROM A RAPID ASSESSMENT OF HEARING LOSS SURVEY

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Objective: Among a representative sample of adults aged 50 years and older too (i) determine the prevalence of hearing loss, (ii) evaluate probable causes and risk factors of hearing loss, and (iii) assess the association between hearing loss measured by audiometry and self-report. Design: A population-based survey of adults aged 50 and older in Santiago, Chile using the Rapid Assessment of Hearing Loss (RAHL) survey. Study sample: 538 participants completed a questionnaire, which included questions on socio-demographic and health characteristics and self-reported hearing loss. Hearing and possible cause of hearing loss was assessed using pure tone audiometry (0.5-4.0 kHz), tympanometry, and otoscopy. Results: The prevalence of any level of hearing loss in adults aged 50 years and older was 41% (95% CI 33.2, 49.2). In terms of aetiologies, 89.3% of ears with mild or worse hearing loss were classified as sensorineural. Otoscopy was abnormal in 10.7% of subjects with impacted earwax being the most common finding (4.4%) followed by chronic otitis media (3.5%). Hearing aid usage was 16.6%. Older age, lower socioeconomic position, lack of education, and solvent exposure were significantly associated with hearing loss.

ACTA OTOLARYNGOL 2023 MAR;143(3):242-9.DOI:10.1080/00016489.2023.2184864.

MATE1 EXPRESSION IN THE COCHLEA AND ITS POTENTIAL INVOLVEMENT IN CISPLATIN CELLULAR UPTAKE AND OTOTOXICITY

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Background: Cisplatin appears to enter the cochlear cells through the organic cation transporter 2 (OCT2). There is recent evidence that multidrug and toxin extrusion protein 1 (MATE1) is involved in cisplatin-induced nephrotoxicity. Its presence and role in the ear are unknown. Aims/objectives: Evaluate the presence and localization of MATE1, and determine the localization of OCT2, in the cochlea. Evaluate cisplatin uptake with regard to MATE1 and OCT2 expression. Material and methods: Murine cochlear explants and paraffin-embedded cochleae were evaluated with immunohistochemistry for OCT2 and MATE1. Explant cultures were also treated with Texas Red cisplatin to determine their cellular uptake. Results: MATE1 is present in the cochlea. Most intense labeling of MATE1 and OCT2 was seen in the outer hair cells (OHCs) and pillar cells, respectively. Both transporters were observed in the spiral ganglion neurons and stria vascularis. Expression levels of OCT2 and MATE1 decreased following cisplatin exposure. Texas Red cisplatin staining was strong in OHCs and pillar cells. Conclusions and significance: To the best of our knowledge, this is the first study demonstrating the presence and localization of MATE1 in the cochlea. OCT2 labeling was seen in pillar cells. Consistently, OHCs and pillar cells uptake Texas Red cisplatin.

BRAIN SCI. 2023 MAY 12;13(5):794. DOI: 10.3390/BRAINSCI13050794.

MAINTAINED SPATIAL LEARNING AND MEMORY FUNCTIONS IN MIDDLE-AGED α9 NICOTINIC RECEPTOR SUBUNIT KNOCK-OUT MICE

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Age-related hearing loss is linked to cognitive impairment, but the mechanisms that relate to these conditions remain unclear. Evidence shows that the activation of medial olivocochlear (MOC) neurons delays cochlear aging and hearing loss. Consequently, the loss of MOC function may be related to cognitive impairment. The α9/α10 nicotinic receptor is the main target of cholinergic synapses between the MOC neurons and cochlear outer hair cells. Here, we explored spatial learning and memory performance in middle-aged wild-type (WT) and α9-nAChR subunit knock-out (KO) mice using the Barnes maze and measured auditory brainstem response (ABR) thresholds and the number of cochlear hair cells as a proxy of cochlear aging. Our results show non-significant spatial learning differences between WT and KO mice, but KO mice had a trend of increased latency to enter the escape box and freezing time. To test a possible reactivity to the escape box, we evaluated the novelty-induced behavior using an open field and found a tendency towards more freezing time in KO mice.

There were no differences in memory, ABR threshold, or the number of cochlear hair cells. We suggest that the lack of α9-nAChR subunit alters novelty-induced behavior, but not spatial learning in middle-aged mice, by a non-cochlear mechanism.

FRONT NEURAL CIRCUITS. 2024 JAN 4:17:1301962. DOI: 10.3389/FNCIR.2023.1301962. ECOLLECTION 2023.

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

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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. traumaConclusion: 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.

ACTA OTOLARYNGOL. 2023 JAN;143(1):28-30. DOI: 10.1080/00016489.2022.2162959.

HEARING LOSS IN SCHOOL-AGED CHILDREN

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Background: Hearing loss is a common disability affecting 5% of the world's population. A lack of opportune diagnosis affects both the individual and society. In order to develop public health policies in the field of hearing health, countries must have information about epidemiology. Aims/objectives: In this review, we describe the information available about prevalence and incidence of hearing loss in school-aged children. Material and methods: Review of the literature in PubMed. Results: Reported prevalence of hearing loss in school-aged children varied between 0.2% and 7.8%. Several factors could explain the discrepancy in numbers such as definition of hearing loss, cause, and the inclusion of high-frequency hearing loss. The rate of delayed-onset hearing loss at the age of six years old varied between 0.6 and 0.8 per 1000. derConclusions and significance: The prevalence of hearing loss in school-aged children varied between 0.2% and 7.8%, and the rate of delayed-onset hearing loss at the age of six years old varied between 0.6 and 0.8 per 1000.

SERVICIO ANATOMÍA PATOLÓGICA

ENVIRON RES. 2023 FEB 15:219:115030. DOI: 10.1016/J.ENVRES.2022.115030.

ARSENIC MAY BE A CARCINOGENIC DETERMINANT OF A SUBSET OF GALLBLADDER CANCER: A PILOT STUDY

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Gallbladder cancer (GBC) is one of the deadliest malignancy and treatment options are deplorably limited. Better strategies of prevention are urgently needed but knowledge on risk factors remains scarce. Recent data suggested that arsenic (As) may be involved in GBC carcinogenesis but the question remains debated. To date, there are no data on As measurement in GBC samples. This pilot study aimed to measure As concentrations in tissue samples from patients with GBC compared to non-cancerous gallbladder (NCGB). Included patients underwent cholecystectomy at Hospital Clinico Universidad de Chile, Santiago in Chile, a country with high As exposure, between 2001 and 2020. Tissue samples were preserved in formalin-fixed, paraffin-embedded blocks. Selected samples were retrieved, processed and submitted to inductively coupled plasma mass spectrometry (ICP-MS) to determine As concentrations. A total of 77 patients were included, including 35 GBC and 42 NCGB. The two groups were comparable, except for age (68 vs. 49 years, $p < 0.001$). Measured in 11 GBC and 38 NCGB, total As was detected in 5 GBC (14%) compared to 0 NCGB samples ($p < 0.001$). GBC group also showed higher median values of As compared to NCGB ($p < 0.001$). This pilot study provided a proof-of-concept to measure As concentrations in gallbladder samples and showed higher level of As in GBC samples compared to NCGB, paving the way for future studies aiming to investigate the impact of As on GBC, which may contribute to the prevention of this deadly disease.

PEDIATR DERMATOL. 2023 NOV-DEC;40(6):1139-1141. DOI: 10.1111/PDE.15339.

ATROPHIC VIOLACEOUS PLAQUES AS THE FIRST MANIFESTATION OF A DISORDER OF GNAS INACTIVATION

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We report the case of a 10-month-old girl who presented with failure to thrive and multiple small atrophic violaceous plaques, with no other findings

on her physical examination. The laboratory examinations, abdominal ultrasound and bilateral hand radiography performed were unremarkable. The skin biopsy revealed fusiform cells and focal ossification in the deep dermis. The genetic study showed a pathogenic variant of GNAS.

ORTHOD CRANIOFAC RES. 2023 AUG;26(3):378-386. DOI: 10.1111/OCR.12620.

INHIBITION OF THE 3-HYDROXY-3-METHYL-GLUTARYL-COA REDUCTASE DIMINISHES THE SURVIVAL AND SIZE OF CHONDROCYTES DURING OROFACIAL MORPHOGENESIS IN ZEBRAFISH

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Objectives: The 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGCR) is the enzyme controlling the rate-limiting step in the synthesis of cholesterol, sterols, and isoprenoids in the mevalonate biosynthetic pathway. Impaired function of HMGCR in zebrafish produces craniofacial malformations and orofacial cleft, mainly affecting the post-migratory neural crest cells with little earlier effect. Here we investigate morphogenetic and cellular mechanisms underlying the generation of these malformations. Methods: The morphology of chondrocytes in the lower jaw and the proliferation/apoptosis in the ethmoid plate were analysed in hmgcr1b mutants and in embryos treated with atorvastatin. In the ceratohyal of treated embryos, we measured the number and dimensions of chondrocytes. In the ethmoid plate, we performed proliferation and apoptosis assays to quantify the number of cells undergoing each process in both hmgcr1b mutants and pharmacologically treated embryos. All embryos were imaged using confocal microscopy and processed to obtain maximum intensity z-projection. Results: The shortening of the ceratohyal is produced by a moderate reduction in the number of cells combined with isometric shrinkage of the chondrocytes. At the same time, the shortening of the ethmoid plate is due to a combination of a slightly diminished proliferation with massive abnormal apoptosis at the proliferation front. Conclusion: HMGCR function is necessary for the normal survival and morphology of chondrocytes during condensation and chondrogenesis in the developing palate and jaw. Further studies are required to establish the pathways through which HMGCR acts on apoptosis, proliferation, and cell size during normal craniofacial development.

INT. J. MORPHOL. [ONLINE]. 2023, VOL.41, N.5, PP.1558-1563.

HUMORAL AND CELLULAR IMMUNOLOGY IN HUMAN PROSTATE CANCER: PLASMA CELLS AND T AND B LYMPHOCYTES

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In solid and malignant tumors, innate and adaptive immunity are combined in antitumor responses. This study aimed to analyze the activation of plasma cells and the correlation between the infiltration of B and T lymphocytes with the degree of malignancy or Gleason grade in human prostate biopsies diagnosed with cancer. Prostate cancer biopsies were obtained from the Clinical Hospital of Universidad de Chile (n=70), according to the bioethical norms of the institution. Histological sections of 5µm thickness were processed for immunohistochemistry with primary antibodies against BL and total TL (HRP/DAB). Recognition and quantification were performed under a Leica DM750 optical microscope. Microsoft Excel and GraphPad software were used for the statistical study. Correlation coefficient (Pearson) and mean comparison tests (Kruskal-Wallis and Dunn) and $p \leq 0.05$ were developed. B and T lymphocyte populations were inversely interregulated in prostate cancer (Gleason) (r= -0.46). Their relationship with Gleason grade is variable according to lymphocyte type (LB vs. Gleason r= -0.0.47 and LT vs. Gleason r= -0.21). Histological diagnosis of prostate cancer correlates with a predominance of LT. The malignancy of the pathology correlates with a predominance of LTs, according to the Gleason grade. The increased knowledge of B and T lymphocyte infiltration and plasma cell activation could be used to better target clinical trials on treatments based on immune system responses. Immunotherapy could be a new paradigm to apply better antitumor therapy strategies.

FRONT MED (LAUSANNE). 2023 OCT 6:10:1271863. DOI: 10.3389/FMED.2023.1271863. ECOLLECTION 2023.

CLINICAL AND PULMONARY FUNCTION ANALYSIS IN LONG-COVID REVEALED THAT LONG-TERM PULMONARY DYSFUNCTION IS ASSOCIATED WITH VASCULAR INFLAMMATION PATHWAYS AND METABOLIC SYNDROME

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Introduction: Long-term pulmonary dysfunction (L-TPD) is one of the most critical manifestations of long-COVID. This lung affection has been associated with disease severity during the acute phase and the presence of previous comorbidities, however, the clinical manifestations, the concomitant consequences and the molecular pathways supporting this clinical condition remain unknown. The aim of this study was to identify and characterize L-TPD in patients with long-COVID and elucidate the main pathways and long-term consequences attributed to this condition by analyzing clinical parameters and functional tests supported by machine learning and serum proteome profiling. Methods: Patients with L-TPD were classified according to the results of their computer-tomography (CT) scan and diffusing capacity of the lungs for carbon monoxide adjusted for hemoglobin (DLCOc) tests at 4 and 12-months post-infection. Results: Regarding the acute phase, our data showed that L-TPD was favored in elderly patients with hypertension or insulin resistance, supported by pathways associated with vascular inflammation and chemotaxis of phagocytes, according to computer proteomics. Then, at 4-months post-infection, clinical and functional tests revealed that L-TPD patients exhibited a restrictive lung condition, impaired aerobic capacity and reduced muscular strength. At this time point, high circulating levels of platelets and CXCL9, and an inhibited FCgamma-receptor-mediated-phagocytosis due to reduced FcγRIII (CD16) expression in CD14+ monocytes was observed in patients with L-TPD. Finally, 1-year post infection, patients with L-TPD worsened metabolic syndrome and augmented body mass index in comparison with other patient groups. Discussion: Overall, our data demonstrated that CT scan and DLCOc identified patients with L-TPD after COVID-19. This condition was associated with vascular inflammation and impair phagocytosis of virus-antibody immune complexes by reduced FcγRIII expression. In addition, we conclude that COVID-19 survivors required a personalized follow-up and adequate intervention to reduce long-term sequelae and the appearance of further metabolic diseases.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

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).

INT J MOL SCI. 2023 SEP 30;24(19):14810. DOI: 10.3390/IJMS241914810.

BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) AS A PREDICTOR OF TREATMENT RESPONSE IN MAJOR DEPRESSIVE DISORDER (MDD): A SYSTEMATIC REVIEW

Mario Ignacio Zelada, Verónica Garrido, Andrés Liberona, Natalia Jones, Karen Zúñiga, Hernán Silva, Rodrigo R Nieto

Brain-derived neurotrophic factor (BDNF) has been studied as a biomarker of major depressive disorder (MDD). Besides diagnostic biomarkers, clinically useful biomarkers can inform response to treatment. We aimed to review all studies that sought to relate BDNF baseline levels, or BDNF polymorphisms, with response to treatment in MDD. In order to achieve this, we performed a systematic review of studies that explored the relation of BDNF with both pharmacological and non-pharmacological treatment. Finally, we reviewed the evidence that relates peripheral levels of BDNF and BDNF polymorphisms with the development and management of treatment-resistant depression.

INT J MOL SCI. 2023 JUN 24;24(13):10569. DOI: 10.3390/IJMS241310569.

BDNF AND COGNITIVE FUNCTION IN CHILEAN SCHIZOPHRENIC PATIENTS

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Despite cognitive symptoms being very important in schizophrenia, not every schizophrenic patient has a significant cognitive deficit. The molecular mechanisms underlying the different degrees of cognitive functioning in schizophrenic patients are not sufficiently understood. We studied the relation between brain-derived neurotrophic factor (BDNF) and cognitive functioning in two groups of schizophrenic patients with different cognitive statuses. According to the Montreal Cognitive Assessment (MoCA) results, the schizophrenic patients were classified into two subgroups: normal cognition (26 or more) and cognitive deficit (25 or less). We measured their plasma BDNF levels using ELISAs. The statistical analyses were performed using Spearman's Rho and Kruskal-Wallis tests. We found a statistically significant positive correlation between the plasma BDNF levels and MoCA score ($p = 0.04$) in the subgroup of schizophrenic patients with a cognitive deficit ($n = 29$). However, this correlation was not observed in the patients with normal cognition ($n = 11$) and was not observed in the total patient group ($n = 40$). These results support a significant role for BDNF in the cognitive functioning of schizophrenics with some degree of cognitive deficit, but suggest that BDNF may not be crucial in patients with a normal cognitive status. These findings provide information about the molecular basis underlying cognitive deficits in this illness.

FRONT PSYCHOL. 2023 SEP 11:14:1209584. DOI: 10.3389/FPSYG.2023.1209584. ECOLLECTION 2023.

PARENTAL PRACTICES AND THEIR ASSOCIATION WITH ALCOHOL AND CANNABIS USE AMONG ADOLESCENTS IN CHILE

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

Background: Adolescent alcohol and cannabis use are common in Chile. The present study aimed to assess the relationship between perceived parenting practices and alcohol and cannabis use among adolescents in a Latin American context. Methods: We adapted and implemented a substance use prevention strategy in Chile, which included surveys of tenth-grade students from six municipalities in the Metropolitan Region of Greater Santiago. We assessed the reliability and factorial structure of the parenting scale with 16 items, which

formed part of the survey. We dichotomized parenting scores into high (above the median) and low. The association of parenting practices with alcohol and cannabis use in adolescents was assessed using multivariate multilevel regression models. Results: A total of 7,538 tenth-grade students from 118 schools were included in the study. The 16-item scale of parenting practices showed good internal consistency (Omega total = 0.84), and three factors representing Relationship between parents and adolescents, Norms and monitoring, and Parents knowing their children's friends and the parents of their children's friends. High total scores of parenting were associated with lower odds of lifetime alcohol use (OR 0.57; 95% CI: 0.49-0.65), past-month alcohol use (OR 0.63; 95% CI: 0.57-0.70), lifetime drunkenness (OR 0.64; 95% CI: 0.58-0.72), and lifetime cannabis use (OR 0.54; 95% CI: 0.47-0.61). Above median scores on each parenting subscale were associated with significantly lower odds of substance use. The strongest associations were observed for the subscale Norms and monitoring. Interactions between parenting and gender showed a significantly stronger effect of parenting practices on alcohol and cannabis use among girls. Conclusion: Different types of parenting practices were associated with a lower prevalence of adolescent alcohol and cannabis use. Improving parenting practices has the potential to prevent adolescent substance use in Chile, especially among girls.

HEALTH PROMOT PRACT. 2023 OCT 16:15248399231201551. 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

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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.

REV MED CHIL. 2023 APR;151(4):435-445. DOI: 10.4067/S0034-98872023000400435.

VALIDACIÓN DE LA ESCALA FIVE FACET MINDFULNESS QUESTIONNAIRE EN ESTUDIANTES DE MEDICINA Y MÉDICOS EN CHILE

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Antecedentes: El creciente uso de intervenciones basadas en Mindfulness, requiere instrumentos de medición estandarizados basados en el constructo para fines clínicos y de investigación. La escala Five Facet Mindfulness Questionnaire de cinco factores fue desarrollada en Estados Unidos y validada en España, y existen versiones de 39, 24 y 15 ítems (FFMQ-39, FFMQ-24 y FFMQ-15). Objetivo: Validar la escala FFMQ-24 y FFMQ-15 en Chile. Metodología: Se realizó una adaptación lingüística de la versión española del FFMQ-24 mediante 6 expertos. Se aplicó el instrumento adaptado a una muestra de 795 médicos. Se analizó la validez interna mediante cálculo de Alfa de Cronbach (?) y análisis factorial confirmatorio (CFA). Finalmente, se retuvieron 15 ítems y se mantuvo la solución de 5 factores. Luego, la escala FFMQ-15 se aplicó a una muestra de 365 estudiantes de medicina y se analizó mediante cálculo de (?) y CFA. Se evaluó la validez externa de FFMQ-15 con la escala Mental Health Continiuum-14(MHC-14). Resultados: se realizaron cambios lingüísticos. El CFA de FFMQ-24 obtuvo un ajuste bajo lo esperado para una solución de 5 factores. Se obtuvo un (?) entre .68 y .86 en todas las dimensiones. La FFMQ-15 tuvo un ajuste adecuado para 5 factores para médicos (c2=216.17, df=80, p<.01; CFI=.96; TLI=.94; RMSEA=.05 [.04, .06]; SRMR=.04) y estudiantes (c2= 163.61, df=80, p<.01; CF=.96;TLI=.94; RMSEA=.05 [.04, .07]; SRMR=.05). La validez externa con MHC-14 fue adecuada.

EUR ARCH PSYCHIATRY CLIN NEUROSCI. 2023 AUG;273(5):1201-1206. DOI: 10.1007/S00406-022-01508-3.

ENVIRONMENTAL STRESS, MINORITY STATUS, AND LOCAL POVERTY: RISK FACTORS FOR MENTAL HEALTH IN BERLIN'S INNER CITY

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This study examines whether climate change-associated environmental stressors, including air and noise pollution, local heat levels, as well as a lack of surrounding greenspace, mediate the effects of local poverty on mental health, using the 28-item General Health Questionnaire. We recruited 478 adults who were representative of eleven of Berlin's inner-city neighborhoods. The relationship of individual-level variables, neighborhood-level sociodemographic and environmental data from the Berlin Senate (Department for Urban Development, Building and Housing) to mental health was assessed in a multilevel model using SPSS. We found that neither local exposure to environmental stressors, nor available greenspace as a protective factor, mediated the effects of local poverty on variance in mental health (all p values > 0.2). However, surrounding greenspace ($r = -0.24$, $p < 0.001$), nitrogen dioxide levels ($r = 0.10$, $p < 0.05$), noise pollution (rho = 0.15, $p < 0.01$), and particle pollution ($r = 0.12$, $p < 0.001$) were associated with local poverty, which, more strongly than individual factors, accounted for variance in mental health ($\beta = 0.47$, $p < 0.001$). Our analysis indicates that the effects of local poverty on mental health are not mediated by environmental factors. Instead, local poverty was associated with both an increased mental health burden and the exposure to climate-related environmental stressors.

ENCEPHALE. 2023 DEC;49(6):654-655. DOI: 10.1016/J.ENCEP.2023.06.012.

DEINSTITUTIONALIZATION, COMMUNITY-BASED CARE AND INCARCERATION OF PEOPLE WITH SEVERE MENTAL ILLNESS: OUT OF SIGHT, OUT OF MIND?

Thomas Fovet, Adrian P Mundt, Ali Amad

Although the international literature points to a number of benefits from deinstitutionalization, such as limiting coercion, more cost-effectiveness of care systems, and better use of community care, it may be helpful to take a broader perspective on where coercion and institutionalization of people with severe mental illnesses (SMI) and/or substance use disorders frequently occur: in prisons and jails. In this comment, we propose to move beyond the inpatient/outpatient dichotomy.

SPAN J PSYCHIATRY MENT HEALTH. 2023 SEP 22:S2950-2853(23)00013-3. DOI: 10.1016/J.SJPMH.2023.06.001.

LATIN AMERICAN CONSENSUS RECOMMENDATIONS FOR THE MANAGEMENT AND TREATMENT OF PATIENTS WITH TREATMENT-RESISTANT DEPRESSION (TRD)

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Despite the abundance of literature on treatment-resistant depression (TRD), there is no universally accepted definition of TRD, and available treatment pathways for the management of TRD vary across the Latin American region, highlighting the need for a uniform definition and treatment principles to optimize the management of TRD in Latin America. Methods: Following a thematic literature review and pre-meeting survey, a Latin America expert panel comprising 14 psychiatrists with clinical experience in managing patients with TRD convened and utilized the RAND/UCLA appropriateness method to develop consensus-based recommendations on the appropriate definition of TRD and principles for its management. Results: The expert panel agreed that 'treatment-resistant depression' (TRD) is defined as 'failure of two drug treatments of adequate doses, for 4-8 weeks duration with adequate adherence, during a major depressive episode'. A stepwise treatment approach should be employed for the management of TRD - treatment strategies can include maximizing dose, switching to a different class, and augmenting or combining treatments. Nonpharmacological treatments, such as electroconvulsive therapy, are also appropriate options for patients with TRD. Conclusion: These consensus recommendations on the operational definition of TRD and approved treatments for its management can be adapted to local contexts in the Latin American countries but should not replace clinical judgement. Individual circumstances and benefit-risk balance should be carefully considered while determining the most appropriate treatment option for patients with TRD.

INFORMATION FUSION 2023; VOLUME 100, 101960 DOI.ORG/10.1016/J.INFFUS.2023.101960.

A NOVEL DEPRESSION RISK PREDICTION MODEL BASED ON DATA FUSION FROM CHILEAN NATIONAL HEALTH SURVEYS TO DIAGNOSE RISK DEPRESSION AMONG PATIENTS WITH MOOD DISORDERS

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Artificial intelligence (AI)-based techniques have been widely applied in depression research and treatment. Nevertheless, no specific predictor model for depression has been developed yet in Chile using specific Chilean characteristics (variables). The present study used data from 11525 participants of the National Health Survey (NHS) to create a model to predict risk of depression (PDRM). This model was contrasted with data from 280 outpatients diagnosed with depression. To develop the PDRM we employed classification algorithms models and fusion of data about depression from two waves of the NHS (2009–2010 and 2016–17). Validation of the model of 19 variables (questions) was done applying machine learning algorithms. Based on 2009–10 data, Recall for Naive Bayes (NB) yielded 0.92, LOGIT was 0.86 and SVM=0.84. After setting up the PDRM this predictor was contrasted with the data from patients (P) diagnosed Bipolar Disorder (140 P); Major Depressive Disorder (MDD, 140 P); and Adjustment Disorder (80 P, control). Fusion of patient's data from anamnesis and consultations was used to determine the presence or absence of each 16 variables per patient. Prediction of depression using the PDRM model detected 122 cases of depression out of the total 140 depressive cases, with a mean area under the receiver operating characteristic curve of 0.8 and a recall 0.74 (with NB). This predictive model may contribute to decision-making processes in a fast, simple and economical way.

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FENOMENOLOGÍA DE LA ANGUSTIA MORAL: IMPLICANCIAS PARA LA HUMANIZACIÓN DE LA EDUCACIÓN Y LA PRÁCTICA MÉDICA

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En el contexto de la salud, la angustia moral (AM) se refiere a las emociones negativas que surgen cuando una persona conoce el curso de acción correcto en una situación determinada pero no es capaz de seguirlo debido a impedimentos personales, jerárquicos o institucionales. La AM se ha relacionado con diversos problemas profesionales, tales como desorientación vocacional, baja motivación laboral, trato despersonalizado a los pacientes, abandono de funciones y cambios de especialidad o profesión. Si bien este fenómeno no ha sido suficientemente estudiado en Chile, se asume que existe e incluso habría aumentado durante la pandemia de COVID-19, siendo desconocidas sus repercusiones. En consecuencia, este artículo tiene como objetivos, en primer lugar, promover el estudio fenomenológico de la AM en nuestro país, considerando la importancia de prevenir su potencial impacto adverso en la salud mental de futuros profesionales, y, en segundo lugar, destacar la necesidad de incluir enfoques narrativos en la educación médica, a fin de desarrollar una aproximación más holística hacia la comprensión de los pacientes y de su condición de vulnerabilidad. En última instancia, se espera que el abordaje de las implicancias de la AM en la educación y la práctica médica contribuya con su humanización, optimizando la calidad de la atención en salud.

SCI REP. 2023 JUN 7;13(1):9275. DOI: 10.1038/S41598-023-36129-W.

A CASE STUDY OF AN INDIVIDUAL PARTICIPANT DATA META-ANALYSIS OF DIAGNOSTIC ACCURACY SHOWED THAT PREDICTION REGIONS REPRESENTED HETEROGENEITY WELL

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The diagnostic accuracy of a screening tool is often characterized by its sensitivity and specificity. An analysis of these measures must consider their intrinsic correlation. In the context of an individual participant data meta-analysis, heterogeneity is one of the main components of the analysis. When using a random-effects meta-analytic model, prediction regions provide deeper insight into the effect of heterogeneity on the variability of estimated accuracy measures across the entire studied population, not just the average. This study aimed to investigate heterogeneity via prediction regions in an individual participant data meta-analysis of the sensitivity and specificity of the Patient Health Questionnaire-9 for screening to detect major depression. From the total number of studies in the pool, four dates were selected containing roughly 25%, 50%, 75% and 100% of the total number of participants. A bivariate random-effects model was fitted to studies up to and including each of these dates to jointly estimate sensitivity and specificity. Two-dimensional prediction regions were plotted in ROC-space. Subgroup analyses were carried out on sex and age, regardless of the date of the study. The dataset comprised 17,436 participants from 58 primary studies of which 2322 (13.3%) presented cases of major depression. Point estimates of sensitivity and specificity did not differ importantly as more studies were added to the model. However, correlation of the measures increased. As expected, standard errors of the logit pooled TPR and FPR consistently decreased as more studies were used, while standard deviations of the random-effects did not decrease monotonically. Subgroup analysis by sex did not reveal important contributions for observed heterogeneity; however, the shape of the prediction regions differed. Subgroup analysis by age did not reveal meaningful contributions to the heterogeneity and the prediction regions were similar in shape. Prediction intervals and regions reveal previously unseen trends in a dataset. In the context of a meta-analysis of diagnostic test accuracy, prediction regions can display the range of accuracy measures in different populations and settings.

SERVICIO DENTOMAXILOFACIAL

INT. J. MORPHOL.41(6):1631-1639, 2023.

DEVELOPMENT OF THE GOOSE TONGUE FILIFORM PAPILLAE: COULD IT BE TOOTH-LIKE SENSE ORGANS?

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The geese's tongue filiform papillae are particularly long, and exhibit the same morphology of a tooth, evoking the lingual teeth of several fishes. In adult animals, they contain numerous mechanical Herbst's corpuscles but no taste buds. In the embryo, they appear since stage 38 and acquire their definitive shape between stages 38 and 42. They express several proteins associated with mammalian tooth development (BMP4, β-catenin, SHH, PITX2, PAX9), also known to be linked to parrot's pseudoteeth and goose's denticulations development. Neurofilaments are early present in the papillae primordia, and appear particularly numerous in adult papillae. Our results suggest that these papillae constitute a mechanical organ with a « tooth shape » derived from ancestral odontodes, whose development is controlled by numerous genes involved in classical odontogenesis.

SERVICIO DERMATOLOGÍA

AUSTRALAS J DERMATOL. 2023 NOV;64(4):E340-E347. DOI: 10.1111/AJD.14150.

TUMOUR BUDDING IN CUTANEOUS SQUAMOUS CELL CARCINOMA: A NOVEL PROGNOSIS RISK FACTOR

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Introduction: Most cutaneous squamous cell carcinomas (cSCC) have a good prognosis, there is a small group where metastasis and death occur and the evaluation of this risk is still cause for controversy. Tumour budding is a pattern of histological invasion that is an emerging risk factor in other solid tumours. Objective: To examine the association between tumour budding and other known high-risk predictors in cSCC. In addition, the impact of tumour budding on overall survival (OS) and disease-specific survival (DSS) was analysed. Method: Retrospective study. It included patients with a diagnosis of non-genital cSCC by excisional biopsy at a university hospital, between 2010 and 2020. A pathologist re-analysed their histological slides and evaluated budding. Univariate and multivariate analyses were made to study the associations. Results: 156 cSCC biopsies were found, and positive tumour budding was found in 13.5%. This correlated with worse DSS and OS. On univariate analysis, budding was correlated with the diameter, thickness of the tumour, histological grade, level of invasion, perineural and lymphovascular invasion, previous radiotherapy, recurrent tumours and lymph node metastasis (LNM). Multivariate analysis: tumour budding was associated with poorly differentiated tumours, prior radiotherapy and LNM. Conclusion: An association was found between tumour budding and most known risk factors in cSCC. We found findings that indicate that the presence of tumour budding is associated with a worse prognosis in terms of LNM, OS and DSS. This supports the results of previous work which has suggested that budding could be related to high-risk cSCC.

J CLIN NEUROPHYSIOL. 2023 NOV 1;40(7):616-624. DOI:10.1097/WNP.0000000000000929.

PAIN-RELATED VERTEX EVOKED POTENTIALS. COMPARISON OF SURFACE ELECTRICAL TO HEAT STIMULATION

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Introduction: Demonstration of nociceptive fiber abnormality is important for diagnosing neuropathic pain and small fiber neuropathies. This is usually assessed by brief heat pulses using lasers, contact heat, or special electrodes. We hypothesized that pain-related evoked potentials to conventional surface electrical stimulation (PREPse) can index Aδ afferences despite tactile Aß fibers coactivation. PREPse may be more readily used clinically than contact heat evoked potentials (CHEPS). Methods: Twenty-eight healthy subjects. Vertex (Cz-A1/A2) recordings. Electrical stimulation of middle finger and second toe with conventional ring, and forearm/leg skin with cup, electrodes. Contact heat stimulation to forearm and leg. Compression ischemic nerve blockade. Results: PREPse peripheral velocities were within the midrange of Aδ fibers. N1-P1 amplitude increased with pain numerical rating scale graded (0-10) electrical stimulation (n = 25) and decreased with increasing stimulation frequency. Amplitudes were unchanged by different presentation orders of four stimulation intensities. PREPse N1 (~130 milliseconds) and N2 (~345 milliseconds) peaks were approximately 40 milliseconds earlier than that with CHEPS. PREPse and CHEPS N1-N2 interpeak latency (~207 milliseconds) were similar. PREPse became unrecordable with nerve blockade of Aδ fibers. otorriConclusions: PREPse earlier N1 and N2 peaks, and similar interpeak N1-N2 latencies and central conduction velocities, or synaptic delays, to CHEPS are consistent with direct stimulation of Aδ fibers. The relation of vertex PREPse amplitude and pain, or the differential effects of frequency stimulation, is similar to pain-related evoked potential to laser, special electrodes, or contact heat stimulation. The relationship to Aδ was validated by conduction velocity and nerve block. Clinical utility of PREPse compared with CHEPS needs validation in somatosensory pathways lesions.

DERMATOL PRACT CONCEPT. 2023 OCT 1;13(4):E2023273. DOI: 10.5826/DPC.1304A273.

CUTANEOUS MALIGNANT MELANOMA IN CHILE: DIFFERENCES IN TUMOR THICKNESS AND OVERALL SURVIVAL BETWEEN PATIENTS FROM PUBLIC AND PRIVATE HEALTH CARE CENTERS

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Introduction: A low socioeconomic status (SES) is associated with lower survival rates in cutaneous malignant melanoma (CMM). In South America, there are few studies that analyze CMM data according to SES. Objectives: To determine the differences in microstaging and overall survival in CMM between public and private health care centers. Methods: Retrospective cohort study. Histopathological reports with a diagnosis of CMM from two public hospitals (PuH) and one private health care center (PrH) in Santiago from 2008 to 2018 were included. Patients' death certificates were obtained to estimate overall survival. Results: 1014 MMC were found. The mean age was 58.6 ± 16.8 years and 59.9% corresponded to female patients. Of these, 33.9% received treatment at PuH and 66.1% at PrH. Patients from PuH had an increased risk of having an invasive CMM and a >1 mm thickness melanoma compared to PrH (odds ratio 2.77 and 6.06, respectively). Patients with invasive CMM from the PuH were 6.29-fold more likely to die than a patient from the PrH. Conclusions: We observed a great disparity in tumor thickness between the socioeconomic status, reflecting a later detection and lower survival rate in PuH. Our results highlight a gap on which National Public Health should focus

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ACQUIRED DIGITAL FIBROKERATOMA

Oscar V Navea, Maria B Navea, Raul de la Fuente

Acquired digital fibrokeratoma is a rare, benign tumor that mostly occurs on the fingers and toes and may appear to be a supernumerary rudimentary digit. It generally affects adult men and appears as a dome-shaped papule although it can also be elongated or pedunculated. Trauma is believed to be a triggering factor in some cases. We report a male patient with an acquired digital fibrokeratoma on a finger, shaped like a cutaneous horn, and a history of minimal repeated trauma and spontaneous remissions not previously described in the literature.

CUREUS. 2023 SEP 26;15(9):E46023. DOI: 10.7759/CUREUS.46023. ECOLLECTION 2023 SEP.

PIGMENTARY DEMARCATION LINES DURING PREGNANCY WITH ERYTHEMA

Oscar V Navea, Maria B Navea, Raul de la Fuente, Marta Valenzuela

Pigmentary demarcation lines (PDL), or Voigt-Futcher lines, are lines that mark an abrupt transition between hyperpigmented skin and normal skin. PDLs are more common in Japanese and dark-skinned individuals. Eight types have been described (A-H); Type B is located on the posteromedial aspect of the lower extremities; it is more common in women and is the one most frequently associated with pregnancy. The demarcation lines of pregnancy are of unknown etiology; they appear mainly in the last trimester and disappear spontaneously months after delivery. We report a case of pregnancy-associated PDL with erythema without melanocytic pigmentation in a 23-week-gestational Latin primiparous woman.

CUREUS. 2023 DEC 10;15(12):E50286. DOI: 10.7759/CUREUS.50286. ECOLLECTION 2023 DEC.

SUPERFICIAL ANGIOMYXOMA IN AN UNCOMMON AREA: A CASE REPORT

Oscar V Navea, Maria B Navea, Raul de la Fuente

Superficial angiomyxomas, also known as cutaneous myxomas, are rare, benign soft tissue tumors that present as papulonodular or polypoid, asymptomatic, slow-growing lesions. They typically occur in the head, neck, trunk, and extremities of adults and may be isolated

tumors or part of the Carney Complex. We present a case of SA with an uncommon area of presentation and a brief discussion of the importance of ruling out the presence of systemic syndromes such as the Carney Complex.

CUREUS. 2023 SEP 26;15(9):E46026. DOI: 10.7759/CUREUS.46026. ECOLLECTION 2023 SEP.

CONCOMITANT SUBTYPES OF GRANULOMA ANNULARE IN A 66-YEAR-OLD FEMALE: A CASE REPORT

Oscar V Navea, Maria B Navea, Raul De la Fuente

Granuloma annulare (GA) is a benign, self-limited inflammatory skin condition with an unknown etiology. Although it usually presents with characteristic clinical features, a biopsy may be necessary in atypical cases to differentiate it from other granulomatous diseases. We describe a case of a 66-year-old female with two concomitant subtypes of GA, presenting with distinct clinical features but exhibiting similar histopathological findings. The patient had extensive, pruritic erythematous-violaceous lesions on her lower abdomen, buttocks, and proximal thighs, which had been progressing over the course of one year. Biopsies from the abdominal and thigh lesions showed typical histopathological features of GA, with mucin deposition, histiocytic infiltrate, and granulomatous formations. Treatment with oral antihistamines and medium-potency topical corticosteroids effectively controlled the itching but did not alter the lesion's appearance. Five months later, the patient developed new, pruritic, skin-colored, confluent papules on the internal face of her left arm, and a subsequent biopsy confirmed annular GA. Although the patient did not follow the prescribed dapsone treatment, the lesions spontaneously regressed within a year. This case emphasizes the importance of recognizing less common presentations of GA, which can mimic other, more concerning conditions. While various therapeutic options have been explored, none guarantee complete remission; however, GA typically resolves on its own over time. A better understanding of the disease's pathogenesis and the development of targeted treatments are warranted to improve management strategies for GA.

BIOENG TRANSL MED. 2023 FEB 21;8(2):E10443. DOI: 10.1002/BTM2.10443. ECOLLECTION 2023 MAR.

EFFICACY OF STEM CELL SECRETOME LOADED IN HYALURONATE SPONGE FOR TOPICAL TREATMENT OF PSORIASIS

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Psoriasis vulgaris is an inflammatory disease characterized by distinctive skin lesions and dysregulated angiogenesis. Recent research uses stem cell secretion products (CM); a set of bioactive factors with therapeutic properties that regulate several cellular processes, including tissue repair and angiogenesis. The aim of this work was to evaluate the effect of CM of Wharton's gelatin MSC (hWJCM) in a treatment based on the bioactivation of a hyaluronic acid matrix (HA hWJCM) in a psoriasiform-like dermatitis (PD) mouse model. A preclinical study was conducted on PD mice. The effect of hWJCM, Clobetasol (Clob) gold standard, HA Ctrl, and HA hWJCM was tested topically evaluating severity of PD, mice weight as well as skin, liver, and spleen appearance. Treatment with either hWJCM, HA Ctrl or HA hWJCM, resulted in significant improvement of the PD phenotype. Moreover, treatment with HA hWJCM reduced the Psoriasis Area Severity Index (PASI), aberrant angiogenesis, and discomfort associated with the disease, leading to total recovery of body weight. We suggest that the topical application of HA hWJCM can be an effective noninvasive therapeutic solution for psoriasis, in addition to other skin diseases, laying the groundwork for future studies in human patients.

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REPORTE DEL PRIMER CASO DE INFECCIÓN POR LAWSONELLA CLEVELANDENSIS EN LATINOAMÉRICA Y REVISIÓN DE LITERATURA

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Lawsonella clevelandensis es un bacilo anaerobio Gram positivo, parcialmente ácido-alcohol resistente, perteneciente al orden Corynebacteriales y considerado comensal de la piel y la cavidad bucal. En los últimos años se han reportado escasos casos de infección por este microorganismo, generalmente en pacientes inmunosuprimidos, siendo la presentación clínica más común la generación de abscesos. El aislamiento de esta bacteria es difícil ya que no crece en los medios de cultivo tradicionales, por lo que su identificación requiere habitualmente del uso de biología molecular. Presentamos el caso de una paciente de 29 años con trasplante renal y empeoramiento progresivo de la función renal en contexto de una vasculitis pauciinmune con requerimiento de mayor inmunosupresión. En el laboratorio destacaba leucocituria asintomática, con urocultivo negativo, por lo que se realizaron 7 baciloscopias en orina, con resultados positivos en 3, pero con PCR de M. tuberculosis y cultivo de micobacterias negativo. Se realizó secuenciación del gen que codifica para el ARN 16s del ribosoma bacteriano a partir de una muestra de orina, obteniéndose una secuencia compatible con Lawsonella clevelandensis. Tras el resultado, se indicó terapia con amoxicilina-ácido clavulánico por 7 meses. A conocimiento de los autores, este es el duodécimo caso de infección por Lawsonella clevelandensis descrito en la literatura médica y el primero que reporta el aislamiento del patógeno en la orina.

REV. MÉD. CHILE VOL.151 NO.6 SANTIAGO JUNE 2023 HTTP://DX.DOI.ORG/10.4067/S0034-98872023000600797

RELATO DE CASO DE INTOXICACIÓN CON SUPERWARFARINAS: UN DESAFÍO TERAPÉUTICO

Giovanna Zavadzki, José Inzunza Robles, María Fernanda San Martín, Waldo Gutiérrez Torres, José Tomás Ramos-Rojas, Jamil Gauna-Cordero, Natalia Bigossi Aguiar

La intoxicación humana por rodenticidas anticoagulantes de acción prolongada, conocidos como superwarfarinas, provoca coagulopatía de prolongado manejo. Presentamos el caso de un hombre de 42 años que ingirió una dosis tóxica de rodenticida en un intento suicida, evolucionando con epistaxis, INR de 11,6 y necesidad de hospitalización. Durante 7 días se realizaron controles seriados de pruebas

de coagulación, con optimización de diferentes dosis de suplementación de Vitamina K. El caso destaca la potencia y vida media prolongada (aproximadamente 6 semanas) de este tipo de anticoagulantes, hecho que requiere un control clínico regular y una adherencia al tratamiento satisfactoria.

SERVICIO DE PEDIATRÍA

NUTR HOSP. 2023 APR 20;40(2):273-279. DOI: 10.20960/NH.04249.

RISK OF VITAMIN D DEFICIT IN ASTHMATIC CHILDREN HOSPITALIZED IN THE NORTH AREA OF SANTIAGO

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Introduction: in recent years asthma hospitalization rate in Chilean children has doubled. Numerous studies have shown an association between hypovitaminosis D and frequent, severe asthmatic exacerbations in children. Objective: to estimate the risk of vitamin D (vitD) deficiency and insufficiency in hospitalized asthmatic children compared with patients who are monitored on an outpatient basis and do not have records of hospitalization in one year. Material and methods: an observational, analytic, and case-control study carried out in one calendar year including asthmatic children between 5 and 15 years of age. This study registered: sociodemographic and clinical data, asthma control test, severity score of hospitalization and measurements of vitD blood levels. Associations between variables were analyzed using the t-test and chi-squared test. The risk for hypovitaminosis D and deficiency was calculated through logistic regression. The data was fed into the Stata 14 software. Results: a total of 117 patients, 9 ± 2.7 years old, were admitted, 64% were male and 51% presented with malnutrition by excess. Six out of ten children presented moderate asthma and 55 % had a poor control of their pathology; 73.5% presented hypovitaminosis D (insufficiency and deficiency), hospitalized patients had 2.8 times more risk of presenting vitD deficiency, adjusted according to seasonality and age (95 %CI, 1.07-7.5, $p < 0.05$) without being associated with a higher severity score of hospitalization. Conclusion: Most of the asthmatic children in the sample presented with hypovitaminosis D, with a higher percentage of deficiency in hospitalized patients, which is not associated with greater severity of hospitalization.

SERVICIO TRAUMATOLOGÍA

FOOT ANKLE ORTHOP. 2023 JAN 27;8(1):24730114221148172. DOI: 10.1177/24730114221148172. ECOLLECTION 2023 JAN.

SHORT-TERM RESULTS OF HEMIARTHROPLASTY OF THE ANKLE JOINT FOR TALAR-SIDED CARTILAGE LOSS

Manuel J Pellegrini, Franco Mombello, Aaron Cortes, Felipe Chaparro, Cristian Ortiz, Giovanni Carcuro

Background: Ankle hemiarthroplasty is a 1-piece implant system replacing the talar side of the tibiotalar joint. Hemiarthroplasty offers limited bone resection and may provide easier revision options than joint-ablating procedures. Methods: Prospective, multicenter, noncomparative, nonrandomized clinical study with short term follow-up on patients undergoing hemiarthroplasty of the ankle. Radiologic and functional outcomes (Foot and Ankle Outcome Score FAOS, Foot and Ankle Ability Measure [FAAM], Short Form-36 Health Survey [SF-36], Short Musculoskeletal Functional Assessment [SMFA], and visual analog scale [VAS] pain scores) were obtained at 3 and 12 months and the last follow-up (mean 31.9 months). Results: Ten patients met the inclusion criteria. Three were converted to total ankle replacement at 14, 16, and 18 months. Pain VAS scores improved on average from 6.8 to 4.8 (P = .044) of the remaining 7 at a mean of 31.9 months' follow-up. For these 7 in the Survival Group, we found that SF-36 physical health component improved from 25.03 to 42.25 (P = .030), SMFA dysfunction and bother indexes improved from 46.36 to 32.28 (P = .001), and from 55.21 to 30.14 (P = .002) in the Survival Group, and FAAM sports improved from 12.5 to 34.5 (P = .023). Conclusion: Patients undergoing hemiarthroplasty of the ankle joint for talar-sided lesions had a 30% failure rate by 18 months. Those who did not have an early failure exhibited modest pain reduction, functional improvements, and better quality of life in short-term follow-up. This procedure offers a possible alternative for isolated talar ankle cartilage cases.

BR J DERMATOL. 2023 MAR 30;188(4):533-541. DOI: 10.1093/BJD/LJAC128.

ACCESS TO PSORIASIS TREATMENT IN BRAZIL AND CHILE: A CROSS-SECTIONAL MULTICENTRE GLOBAL HEALTHCARE STUDY ON PSORIASIS

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Background: Sufficient data on access to systemic treatment for patients with psoriasis living in Latin America (LA) including Brazil and Chile are lacking. Understanding the availability and limiting factors of access to treatments can help to improve patient care and decrease long-term healthcare costs. Objectives: In association with the Global Psoriasis Atlas, this cross-sectional survey study analysed the availability and insurance reimbursement of systemic treatments for adult patients with psoriasis in Brazil and Chile. Methods: A multicentre, cross-sectional Global Healthcare Study on Psoriasis was performed in Brazil and Chile in 2020. For each eligible adult patient with psoriasis, doctors and nurses completed a 48-item questionnaire about clinical aspects of psoriasis including the Psoriasis Area Severity Index (PASI), body surface area (BSA) score and the Dermatology Life Quality Index (DLQI), as well as the availability of systemic treatments and insurance reimbursement status. Between-country differences were compared with Wilcoxon rank sum tests for continuous variables, and a $\chi 2$-test or Fisher's exact test, where appropriate, for categorical variables. The median and interquartile range (IQR) was calculated for non-normal distributed data. Results: A total of 1424 patients with psoriasis from 43

centres [27 centres in Brazil (n = 826) and 16 in Chile (n = 598)], were included with a mean (SD) age of 49.1 (16.3) and 49.2 (15.1) years, respectively. Unstratified analyses revealed that patients with psoriasis in Chile had more severe disease than those in Brazil [PASI 11.6 vs. 8.4 (P < 0.001) and BSA 14.7 vs. 12.0 (P = 0.003), respectively]. For patients with moderate-to-severe psoriasis, defined as PASI and/or BSA ≥ 10, systemic nonbiologic drugs were available (81.2% in Brazil and 65.3% in Chile, P ≤ 0.001), but only 37.0% of patients in Brazil and 27.3% in Chile received biologics (P = 0.01). Lack of availability and/or lack of insurance reimbursement for biologic drugs for patients with moderate-to-severe psoriasis was reported for 22.2% (50 of 225) in Brazil and 67.9% (148 of 218) in Chile (P < 0.001). Patients with no access to biologic therapies due to lack of availability/insurance reimbursement had a median PASI of 9.15 (IQR 3.00-14.25) in Brazil and 12.0 (IQR 5.00-19.00) in Chile (P = 0.007), as well as a median BSA of 7.0 (IQR 3.00-15.00) and 12.0 (IQR 5.00-22.50) (P = 0.002), and median DLQI of 11.0 (6.00-15.00) and 21.0 (6.50-25.00) (P = 0.007), respectively. Conclusions: Chilean patients had significantly more severe psoriasis compared with Brazilian patients in our study. While nonbiologic treatments for moderate-to-severe psoriasis were available in both LA countries, there is a high need for improvement in access to more effective psoriasis treatments including biologics. Our results highlight a significant gap between treatment recommendations in international psoriasis guidelines and real-world situations in Brazil and Chile.

J KNEE SURG. 2023 MAR;36(4):389-396. DOI: 10.1055/S-0041-1735312.

GONYAUTOXINS 2/3 LOCAL PERIARTICULAR INJECTION FOR PAIN MANAGEMENT AFTER TOTAL KNEE ARTHROPLASTY: A DOUBLE-BLIND, RANDOMIZED STUDY

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The purpose of this study was to compare the efficacy of periarticular infiltration of gonyautoxin 2/3 (GTX 2/3) and a mixture of levobupivacaine, ketorolac, and epinephrine for pain management after total knee arthroplasty (TKA). Forty-eight patients were randomly allocated to receive periarticular infiltration of 40 µg GTX 2/3 (n = 24) diluted in 30 mL of sodium chloride 0.9% (study group) or a combination of 300 mg of levobupivacaine, 1 mg of epinephrine, and 60 mg ketorolac (n = 24) diluted in 150 mL of sodium chloride 0.9% (control group). Intraoperative anesthetic and surgical techniques were identical for both groups. Postoperatively, all patients received patient-controlled analgesia (morphine bolus of 1 mg; lockout interval of 8 minutes), acetaminophen, and ketoprofen for 72 hours. A blinded investigator recorded morphine consumption, which was the primary outcome. Also, the range of motion (ROM) and static and dynamic pain were assessed at 6, 12, 36, and 60 hours after surgery. The incidence of adverse events, time to readiness for discharge, and length of hospital stay were also recorded. The median of total cumulative morphine consumption was 16 mg (range, 0-62 mg) in the GTX 2/3 group and 9 mg (range, 0-54 mg) in control group, which did not reach statistical difference (median test, p = 0.40). Furthermore, static and dynamic pain scores were similar at all time intervals. GTX 2/3 was inferior in range of motion at 6 and 12 hours; nevertheless, we noted no difference after 36 hours. No differences between groups were found in terms of complications, side effects, or length of hospital stay. No significant differences were found between groups in terms of breakthrough morphine requirement. However, local anesthetic use resulted in an increased ROM in the first 12 hours. This prospective randomized clinical trial shows that GTX 2/3 is a safe and efficient drug for pain control after TKA; nevertheless, more studies using GTX 2/3 with larger populations are needed to confirm the safety profile and efficiency. This is level 1 therapeutic study, randomized, double-blind clinical trial.

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SEARCHING FOR THE BEST TREATMENT FOR RAMP LESIONS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Ramp lesions are a common occurrence in patients with anterior cruciate ligament (ACL) tears. These lesions can be difficult to diagnose due to their concealed nature, and their treatment is crucial due to the stabilizing function of the medial meniscocapsular region. The optimal treatment option for ramp lesions varies depending on the size and stability of the lesion. The purpose of this study was to evaluate the best treatment option for ramp lesions based on the stability of the lesion, including no treatment, biological treatment, and arthroscopic repair. We hypothesize that stable lesions have a favorable prognosis with techniques that do not require the use of meniscal sutures. In contrast, unstable lesions require appropriate fixation, either through an anterior or posteromedial portal. This study is a systematic review and meta-analysis with a level of evidence IV. The study used Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for a systematic review of clinical studies reporting outcomes of ramp lesion treatment. The PubMed/MEDLINE database was searched using Mesh and non-Mesh terms related to ramp lesions, medial meniscus ramp lesions, and meniscocapsular injuries. The inclusion criteria encompassed clinical studies in English or Spanish that reported the treatment of ramp meniscal lesions, with a follow-up of at least six months and inclusion of functional results, clinical stability tests, radiological evaluation, or arthroscopic second look. The analysis included 13 studies with 1614 patients. Five studies distinguished between stable and unstable ramp lesions using different criteria (displacement or size) for assessment. Of the stable lesions, 90 cases received no treatment, 64 cases were treated biologically (debridement, edge-curettage, or trephination), and 728 lesions were repaired. There were 221 repaired unstable lesions. All different methods of repair were registered. In stable lesions, three studies were included in a network meta-analysis. The best-estimated treatment for stable lesions was biological (SUCRA 0.9), followed by repair (SUCRA 0.6), and no treatment (SUCRA 0). In unstable lesions, seven studies using International Knee Documentation Committee Subjective Knee Form (IKDC) and 10 studies using Lysholm for functional outcomes showed significant improvement from preoperative to postoperative scores after repair, with no differences between repairing methods. We recommend simplifying the classification of ramp lesions as stable or unstable to determine treatment. Biological treatment is preferred for stable lesions rather than leaving them in situ. Unstable lesions, on the other hand, require repair, which has been associated with excellent functional outcomes and healing rates.

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CONCORDANCE IN RADIOLOGICAL PARAMETERS OF DIFFERENT KNEE VIEWS AFTER TOTAL KNEE ARTHROPLASTY

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Background Total knee arthroplasty (TKA) is a cost-effective treatment for the end-stage of knee osteoarthritis. Despite the improvements in this surgery, a significant percentage of patients still report dissatisfaction after knee arthroplasty. Radiological results have been used to predict clinical outcomes and satisfaction after knee replacement. This study aims to evaluate the concordance of a set of radiographic views to assess alignment on total knee arthroplasty. Methods A concordance study was designed with 105 patients (130 TKA) that underwent conventional total knee arthroplasty cruciate-retaining design recruited for the study and scheduled for their annual radiograph control. Measurements were performed on the following radiograph after total knee replacement: full-length standing anteroposterior and lateral radiograph, anteroposterior standing, lateral and axial knee view, and the knee "seated view". A musculoskeletal radiologist and a knee surgeon were recruited to perform the radiological measurement and then estimate the interobserver agreement. Results There was an excellent correlation between Limb Length (LL), Hip-knee-ankle angle (HKA), Sagittal mechanical tibial component alignment (smTA), extension lateral and medial joint space (eLJS and eMJS), 90º flexion lateral and medial joint space (fLJS and fMJS) and Sagittal anatomic lateral view tibial component alignment (saLTA); the good correlation between Mechanical lateral femoral component alignment (mLFA), Sagittal anatomic tibial component alignment (saTA), Sagittal anatomic lateral view femoral component alignment 2 (saLFA2), Patella Height (PH); and moderate to poor correlation for the rest of measurements. Conclusion Excellent and good concordance can be achieved for radiographic measurements in different knee views to assess results after TKA. These findings must encourage future studies to address functional and survival outcomes using all knee views and not just one plane.

CUREUS. 2023 SEP 29;15(9):E46203. DOI: 10.7759/CUREUS.46203. ECOLLECTION 2023 SEP.

INCREASE IN POSTOPERATIVE BODY MASS INDEX IN PATIENTS AFTER TOTAL KNEE ARTHROPLASTY

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Objectives The aim of this is to investigate the changes in body mass index (BMI) following knee arthroplasty and to evaluate their impact on patient-reported outcomes and functional evaluations. Methods This observational study included 90 patients who underwent total knee arthroplasty (TKA) and were followed up for a median period of 2.6 years. BMI measurements were recorded before and after surgery, and patient-reported outcomes and functional evaluations were assessed using standardized scales and tests. Results Following TKA, BMI increased statistically significantly (Wilcoxon signed-rank test, $p < 0.000$). In addition, half of the patients experienced an increase in BMI, with 32% moving up in their BMI category. However, there were no clinically significant differences in patient-reported outcomes or functional evaluations between the group that gained BMI and the group that maintained or lost BMI. Conclusion This study reveals that patients tend to have increased BMI following TKA. However, these BMI changes do not significantly impact patient-reported outcomes or functional evaluations. It underscores the importance of patient education regarding healthy lifestyle habits, including diet and physical activity, to address postoperative weight gain effectively.

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LATIN AMERICAN FORMAL CONSENSUS ON THE APPROPRIATE INDICATIONS OF EXTRA-ARTICULAR LATERAL PROCEDURES IN PRIMARY ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

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Objectives: To create a practice guideline for the appropriate indications of an extra-articular procedure in primary anterior cruciate ligament reconstruction (ACLR). Methods: The formal consensus method described by the Haute Autorité de Santé was used. The Latin American Society of Arthroscopy, Articular Replacement, and Sports Injuries (SLARD) recruited three groups of experts on ACLR. Initially, the steering group, consisting of eight surgeons, performed a systematic review of the literature and elaborated on 192 scenarios for primary ACLR. The rating group, composed of 23 surgeons, rated each scenario in two rounds, with an in-between in-person meeting for discussion. Median scores and agreement levels were estimated to classify each scenario as inappropriate, uncertain or appropriate for adding anterolateral reconstruction. Finally, the lecture group, consisting of 10 surgeons, revised each stage of the method, results and interpretation. Results: Of the scenarios, 11.97% were rated as appropriate for adding an extra-articular lateral procedure, 7.81% as inappropriate and 80.21% as uncertain. The key recommendations for the addition of extra-articular lateral techniques were as follows: it is appropriate when the patient is under 25 years of age, has high-grade physical examination findings, practises a pivoting sport and has hyperlaxity; meanwhile, it is inappropriate when the patient has low-grade physical examination findings, has normal laxity and does not practise a pivoting sport. Conclusions: The appropriate indications of extra-articular lateral procedures in primary ACLR were determined on the basis of the best available evidence and expert opinion following a formal consensus method.

J CLIN MED. 2023 SEP 21;12(18):6096. DOI: 10.3390/JCM12186096.

SIMILAR PATIENT SATISFACTION AND QUALITY OF LIFE IMPROVEMENT ACHIEVED WITH TKA AND THA ACCORDING TO THE GOODMAN SCALE: A COMPARATIVE STUDY

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Background: Total knee arthroplasty (TKA) and total hip arthroplasty (THA) are effective treatments for severe knee and hip osteoarthritis. Historically, TKA has been associated with lower satisfaction than THA, but recent advances in knee surgery have led to lower dissatisfaction

rates. This study aimed to compare the satisfaction and self-reported improvement in the quality of life of two cohorts of patients who underwent TKA and THA, respectively. Methods: This observational study compared two previously published cohorts of patients who underwent THA and TKA in a single university center. The Goodman scale was used to assess satisfaction and self-perception of improved quality of life after TKA and THA at a minimum one-year follow-up. Propensity score matching was used to balance age, gender, and follow-up between groups. Significance was set at 0.05. Results: The study included a total of 105 THAs and 131 TKAs. Both groups had high levels of satisfaction with pain relief, ability to do house/yard work, and overall satisfaction, with above 90% satisfaction rates. Regarding improvement in quality of life, both groups had 86% of patients reporting improvement as "much better." After propensity score matching, no significant difference was found between THA and TKA for any of the comparisons made using the Goodman scale. Conclusions: The study showed that both TKA and THA resulted in high levels of satisfaction and improvement in quality of life. There was no significant difference in satisfaction rates between TKA and THA, contrary to the historical trend of lower satisfaction rates for TKA.

MEDICINA (KAUNAS). 2023 MAR 31;59(4):693. DOI: 10.3390/MEDICINA59040693.

A CROSS-SECTIONAL, RETROSPECTIVE, AND COMPARATIVE STUDY BETWEEN DELIRIUM AND NON-DELIRIUM PSYCHIATRIC DISORDERS IN A PSYCHOGERIATRIC INPATIENT POPULATION REFERRED TO CONSULTATION-LIAISON PSYCHIATRY UNIT

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Background and objectives: Delirium is the most prevalent psychiatric disorder in inpatient older people. Its presence is associated with higher rates of institutionalization, functional disability and mortality. This study aims to evaluate delirium in a hospitalized psychogeriatric population, focusing on which factors predict the appearance of delirium, the impact it generates and the diagnostic concordance between non-psychiatric physicians and psychiatrists. Material and methods: This is an observational, cross-sectional, retrospective, and comparative study. We obtained data from a sample of 1017 patients (≥65 years) admitted to general hospital and referred from different services to the consultation-liaison psychiatry (CLP) unit. Logistic regression was performed using delirium as the dependent variable. To estimate the concordance of the diagnoses, the Kappa coefficient was used. To assess the impact of delirium, an ordinal regression, Wilcoxon median test and Fisher's test were performed. Results: Delirium is associated with a higher number of visits, OR 3.04 (95% CI 2.38-3.88), longer length of stay and mortality, OR 2.07 (95% CI, 1.05 to 4.10). The model to predict delirium shows that being >75 years old has an OR of 2.1 (95% CI, 1.59-2.79), physical disability has an OR of 1.66 (95% CI, 1.25-2.20), history of delirium has an OR of 10.56 (95% CI, 5.26-21.18) and no use of benzodiazepines has an OR of 4.24 (95% CI, 2.92-6.14). The concordance between the referring physician's psychiatric diagnosis and the psychiatrist CLP unit showed a kappa of 0.30. When analysing depression and delirium, the concordance showed Kappa = 0.46. Conclusions: Delirium is a highly prevalent psychiatric disorder, but it is still underdiagnosed, with low diagnostic concordance between non-psychiatric doctors and psychiatrists from CLP units. There are multiple risk factors associated with the appearance of delirium, which must be managed to reduce its appearance.

J EXP ORTHOP. 2023 JUL 26;10(1):73. DOI: 10.1186/S40634-023-00641-9.

ANTERIOR KNEE PAIN AND SIT-UP TESTS PREDICTS PATIENTS' SATISFACTION AND IMPROVEMENT IN QUALITY OF LIFE AFTER ANTERIOR STABILIZED TOTAL KNEE REPLACEMENT WITHOUT PATELLAR RESURFACING

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Purpose: The purpose of this study was to assess patient satisfaction and identify risk factors for dissatisfaction after anterior stabilised conventional total knee arthroplasty (TKA) without patellar resurfacing, using the Goodman score. Methods: We conducted a cross-sectional study using data from our institutional database from 1 January 2018 to 1 March 2021. Patients who underwent TKA with the Vanguard® Cruciate Retaining Anterior Stabilized Knee System (Zimmer Biomet, Warsaw, Indiana, USA) without patellar replacement were included. Patients with other bearing surfaces (posterior stabilised or medial congruent) or diagnosed with infection or instability were excluded. Patients' reported outcomes, body mass index (BMI), passive range of motion, the timed up-and-go test, sit-up test, and algometry were assessed. Patients were also asked if they had anterior knee pain. Satisfaction was assessed using the Goodman scale, and logistic multivariate regression was used to identify variables associated with dissatisfaction and perceived improvement in quality of life. Results: A total of 131 TKA patients were included in the study. The median satisfaction score was 100 (interquartile range [IQR], 87.5 to 100), with the 75-point threshold at the 90th percentile according to Section A of Goodman. Section B of Goodman showed that 113 TKA patients (86.26%) reported "great improvement" or "more than I ever dreamed." Multivariate logistic regression revealed that anterior knee pain (OR 5.16, 95% CI 1.24 to 21.39), the sit-up test (OR 0.63, 95% CI 0.49 to 0.81), and BMI (OR 0.84, 95% CI 0.70 to 0.99) were significantly associated with patient dissatisfaction and a worse perceived improvement in quality of life. The receiver operating characteristics curve for the models had areas under the curve of 0.83 (95% CI 0.69 to 0.97) and 0.82 (95% CI 0.70 to 0.94), respectively. Conclusion: Anterior stabilised TKA without patellar resurfacing can achieve 90% satisfaction and 86% improvement in quality of life. To improve these results, it is essential to prevent and treat anterior knee pain and enhance quadriceps strength.

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PRÓTESIS UNICOMPARTIMENTAL DE RODILLA

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In a patient with severe unicompartmental knee osteoarthritis where conservative treatments have been exhausted, with painful symptoms located on the affected side and with a reducible axis, the unicompartmental knee prosthesis (UKP) is the first option for

our work group. Within the study to confirm the diagnosis and plan the surgery, weight-bearing knee x-rays, Rosenberg x-rays, and teleradiographs of the lower extremities stand out. The objective of surgery is to replace the affected area, restoring the anatomy with an adequate balance of soft tissues. Regarding alignment, the challenge is not to overload the opposite side or that of the prosthesis. There are mobile and fixed plates and although the clinical and survival results are similar, in recent years with the incorporation of robotic surgery, the balance has tipped towards the use of fixed plates. The clinical and functional results are better and there are fewer complications than when total knee prostheses (TKP) are used in the same type of patients. The survival studied in registries is lower than for TKP, but when used in high-flow centers where the percentage of UKP is close to a third of the total with strict patient selection, the duration is as good as in PTR.

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GENTAMICINCOATED TIBIAL NAIL IS AN EFFECTIVE PREVENTION METHOD FOR FRACTURE-RELATED INFECTIONS IN OPEN TIBIAL FRACTURES

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Fracture-related infection (FRI) is a common complication following open tibia fracture (OTF), especially in patients with high-energy trauma or comorbidities. The use of gentamicin-coated nail (GCN) has been proposed as a local adjuvant to prevent FRI in high-risk patients. Hypothesis: The incidence of FRI is expected to be lower in OTF treated with a GCN, alongside with no detrimental effects on fracture healing time. Objectives: This study aimed to evaluate the effectiveness of GCNs as a definitive fixation method and prophylaxis for FRI in OTFs. Secondary outcomes included non-union rates and time to healing. Methods: The study design was a mixed cohort, including a prospective group of patients treated with GCN (Expert Tibial Nail PROtect™, Depuy Synthes, Johnson&Johnson Company Inc, New Jersey, USA) and a retrospectively evaluated group treated with non-gentamicin-coated nail (NGCN). Patients with at least 12 months of follow-up were included. The treatment protocol consisted of timely administration of antibiotics, surgical debridement, and early soft-tissue coverage. Exclusion criteria included protocol infringement, traumatic amputation, and loss of follow-up. Statistical analysis was performed using Stata v14.0, with a significance level of $p < 0.05$. Results: The study included 243 patients, 104 in GCN group and 139 NGCN group. External Fixator use was higher in the NGCN group, but this did not significantly affect the FRI rate. GCN use was associated with a significantly lower incidence of FRI (2.88% GCN group vs. 15.83% NGCN group, OR 0.16, $p < 0.01$). Furthermore, GCN use was found to be a protective factor against tibial non-union (OR 0.41, $p = 0.03$). There were no adverse effects attributed to locally administered gentamycin. The NGCN cohort had a higher incidence of polytrauma, although the difference was not statistically significant. A longer time to heal as well as more FRI and Non-union according to the progression in Gustilo-Anderson classification was observed in the GCN group. Conclusion: Our findings suggest that GCN is an effective prophylactic method to reduce the risk of FRI in open tibial fractures at 12-month follow-up, as well as, probably derived from this protective effect, leading to lower fracture consolidation times when compared with cases treated without GCN.

FOOT ANKLE INT. 2023 SEP;44(9):905-912. DOI: 10.1177/10711007231184844.

ACUTE DELTOID INJURY IN ANKLE FRACTURES: A BIOMECHANICAL ANALYSIS OF DIFFERENT REPAIR CONSTRUCTS

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Background: The importance of the deltoid ligament in the congruency and coupling of the tibiotalar joint is well known. The current trend is to repair it in cases of acute injuries in the context of ankle fractures; however, there is limited information on how it should be reconstructed. The objective of this study was to compare different deltoid ligament repair types in an ankle fracture cadaveric model. Methods: Sixteen cadaveric foot-ankle-distal tibia specimens were used. All samples were prepared as a supination external rotation ankle fracture model. Axial load and cyclic axial rotations were applied on every specimen using a specifically designed frame. This test was performed without deltoid injury, with deltoid injury, and after repair. The reconstruction was performed in 4 different ways (anterior, posterior, middle, and combined). Medial clear space (MCS) was measured for each condition on simulated weightbearing (WB) and gravity stress (GS) radiographs. Reflective markers were used in tibia and talus, registering the kinematics through a motion analysis system to record the tibiotalar uncoupling. Results: After deltoid damage, in all cases the MCS increased significantly on GS radiographs, but there was no increase in the MCS on WB radiographs. After repair, in all cases, the MCS was normalized. Kinematically, after deltoid damage, the tibiotalar uncoupling increased significantly. All isolated repairs achieved a similar tibiotalar uncoupling value as its baseline condition. The combined repair resulted in a significant decrease in tibiotalar uncoupling. Conclusion: Our results show that deltoid repair recovers the tibiotalar coupling mechanism in an ankle fracture model. Isolated deltoid repairs recovered baseline MCS and tibiotalar uncoupling values. Combined repairs may lead to overconstraint, which could lead to postoperative stiffness. Clinical studies are needed to prove these results and show clinically improved outcomes.

FOOT ANKLE SURG. 2023 JAN;29(1):90-96. DOI: 10.1016/J.FAS.2022.11.001.

DOES A FIBULA-SPARING APPROACH IMPROVE OUTCOMES IN TIBIOTALOCALCANEAL ARTHRODESIS?

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Background: Tibiotalocalcaneal (TTC) arthrodesis is considered a salvage procedure for either complex deformity or arthritis about the hindfoot, and can be performed via fibula-resection (FR) or fibula-sparing (FS) approaches. The primary aim of this study was to investigate differences in outcomes in FR versus FS TTC arthrodeses. Methods: This was a retrospective cohort study reviewing outcomes of TTC arthrodesis at a single institution. Patients who underwent a TTC arthrodesis from 2005 to 2017 and had minimum two-year follow-up

were included. Preoperative diagnosis, pre- and post-operative radiographic coronal alignment, fixation methods, and complications were compared between groups. Results: 107 patients (110 ankles) underwent TTC arthrodesis, with a mean age of 57.0 years (sd, 14.0 years). The mean clinical follow-up was 50.7 months (range, 24-146) and mean radiographic follow-up was 45.8 months (range, 6-146 months). Pre-operative diagnoses included arthritis (N = 40), prior non-union (N = 21), Charcot neuro-arthropathy (N = 15), failed total ankle arthroplasty (N = 15) and avascular necrosis of the talus (N = 19). Sixty-nine ankles comprised the FS group and 41 comprised the FR group. There was no significant difference in the non-union rate between groups (29% FR vs 38% FS, p = 0.37), complication rate (59% FR vs 64% FS, p = 0.59), or post-operative coronal standing radiographic alignment (89.6 degrees FR, 90.5 degrees FS, p = 0.26). Logistic regression analyses demonstrated a pre-operative diagnosis of failed TAA was associated with post-operative nonunion (OR:3.41,CI:1.13-11.04,p = 0.03). Pre-operative indication for TTC arthrodesis of arthritis alone was associated with a decreased risk of non-union (OR:0.27,CI:0.11-0.62,p = 0.002). Conclusion: TTC arthrodesis is a successful surgical option for complex hindfoot deformity, arthritis, and limb salvage regardless of surgical approach. We did not detect a difference in the union rate, incidence of complications, or coronal plane radiographic alignment in fibula-sparing versus fibula-resection constructs. Patients with a pre-operative indication for surgery of arthritis may be at decreased risk of developing non-union.

SERVICIO UROLOGÍA

NEUROUROL URODYN. 2023 NOV;42(8):1603-1627. DOI: 10.1002/NAU.25187.

ICS-SUFU STANDARD: THEORY, TERMS, AND RECOMMENDATIONS FOR PRESSURE-FLOW STUDIES PERFORMANCE, ANALYSIS, AND REPORTING. PART 2: ANALYSIS OF PFS, REPORTING, AND DIAGNOSIS

Peter F W M Rosier, Andrew Gammie, Juan Pablo Valdevenito, John Speich, Phillip Smith, Sanjay Sinha; members of the ICS Working Group PFS23

Aims: The Working Group (WG), initiated by the International Continence Society (ICS) Standardisation Steering Committee and supported by the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction, has revised the ICS Standard for pressure-flow studies of 1997. Methods: Based on the ICS standard for developing evidence-based standards, the WG developed this new ICS standard in the period from May 2020 to December 2022. A draft was posted on the ICS website in December 2022 to facilitate public discussion and the comments received have been incorporated into this final release. Results: The WG has recommended analysis principles for the diagnosis of voiding dysfunction for adult men and women without relevant neurological abnormalities. New standard terms and parameters for objective and continuous grading of urethral resistance (UR), bladder outflow obstruction (BOO) and detrusor voiding contraction (DVC) are introduced in this part 2 of the standard. The WG has summarized the theory and recommendations for the practice of pressure-flow study (PFS) for patients in part 1. A pressure-flow plot is recommended for the diagnosis of every patient, in addition to time-based graphs. Voided percentage and post void residual volume should always be included in PFS analysis and diagnosis. Only parameters that represent the ratio or subtraction of pressure and synchronous flow are recommended to quantify UR and only parameters that combine pressure and flow in a product or sum are recommended to quantify DVC. The ICS BOO index and the ICS detrusor contraction index are introduced in this part 2 as the standard. The WG has suggested clinical PFS dysfunction classes for male and female patients. A pressure-flow scatter graph including every patient's pdet at maximum flow (pdetQmax) with maximum flow rate (Qmax) point should be included in all scientific reports considering voiding dysfunction. Conclusion: PFS is the gold standard used to objectively assess voiding function. Quantifying the dysfunction and grading of abnormalities are standardized for adult males and females.

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DEFINING BLADDER OUTLET OBSTRUCTION AND DETRUSOR UNDERACTIVITY IN FEMALES WITH OVERACTIVE BLADDER: ARE WE FORGETTING ABOUT THE FREE UROFLOWMETRY?

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Introduction: Both detrusor underactivity (DU) and bladder outlet obstruction (BOO) can coexist in patients with overactive bladder. Definitions of both DU and BOO are based on pressure-flow study (PFS) data. However, invasive urodynamics study can differ from a natural micturition, in fact, discrepancies between free uroflowmetry (UFM) and PFS have been largely described. Our goal is to assess the correlation of free-flowmetry and PFS among patients with OAB and to evaluate how different definitions of DU/BOO are able to discriminate patients with different free UFMs. Methods: A retrospective review of urodynamics performed at a single institution was conducted. Females with OAB who voided more than 150 mL in both UFM and PFS were included. Parameters from both voiding episodes were compared with nonparametric test. Two definitions of DU were applied; PIP1: Pdet@Qmax+Qmax < 30 and Gammie: Pdet@Qmax < 20 cmH2 O, Qmax < 15 mL/s, and BVE < 90% (Bladder voiding efficiency). Also, two definitions of obstruction were chosen; Defretias: Pdet@Qmax ≥25 cmH2 O and Qmax ≤ 12 mL/s and Solomon-Greenwell female BOO index ≥ 18. Patients who matched with each definition were compared to those who did not, to assess if any definitions were able to discriminate different noninvasive uroflowmetries. Results: A total of 195 patients were included. Overall, mean age was 55 ± 12 years, 90.8% had mixed urinary incontinence, and 39% complained of at least one voiding symptom. Globally, Qmax and BVE correlated poorly between UFM and PFS, showing that most of the variation corresponded to a systematic error. Twenty-two individuals were found to have DU, they had a difference of 13 mL/s on both maximum flows. Fifty-four patients showed BOO, with a difference between their Qmax of 19 mL/s. Among the four definitions analyzed, only PIP1 and Defreitas were able to discriminate patients with actually a lower Qmax on the free UFM. Conclusions: Patients with overactive bladder seem to have a systematic discordance between the urine flow of the free and invasive studies. Current definitions of DU and BOO, which are based on the PFS parameters, are not consistently able to discriminate patients who actually void deficiently on the free UFM.

NEUROUROL URODYN. 2023 NOV;42(8):1590-1602. DOI: 10.1002/NAU.25192.

ICS-SUFU STANDARD: THEORY, TERMS, AND RECOMMENDATIONS FOR PRESSURE-FLOW STUDIES PERFORMANCE, ANALYSIS, AND REPORTING. PART 1: BACKGROUND THEORY AND PRACTICE

Peter F W M Rosier, Juan P Valdevenito, Phillip Smith, Sanjay Sinha, John Speich, Andrew Gammie; Members of the ICS Working Group PFS

Aims: The working group (WG) initiated by the International Continence Society Standardization Steering Committee and supported by the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction has revised the (1997) ICS Standard for pressure flow studies. Methods: Based on the ICS standard for developing evidence-based standards, the WG developed this new ICS standard in the period from May 2020 to December 2022. A draft was posted on the ICS website in January 2023 to facilitate public discussion and the comments received have been incorporated into this final release. Results: The WG summarizes the theory and recommends the practice and the terms used for the diagnosis of voiding dysfunction for adult female and male patients without relevant neurological abnormalities, in part 1 of this standard. The WG has also recommended standard principles and parameters for objective and continuous grading of urethral resistance and detrusor voiding contraction on the basis of pressure flow studies in part 2. The recommendations for practice in this part have also the aim to increase the understanding of the physiology as well as the psychology of voiding. The potential effects of the laboratory situation of the test on the voiding as well as the role of the urodynamicist in this regard are discussed. The WG has recommended to use for diagnosis only the voidings that are considered representative by the patient. Conclusion: A pressure flow study is the gold standard to assess voiding function and to quantify dysfunction. This part of the standard explains the clinical background, gives recommendations for the execution of a pressure flow study and lists relevant terms, parameters, and units of measurements.