

ABSTRACTS

El material que se presenta a continuación proviene de los datos recolectados por la Revista de nuestro Hospital.

Abstracts presentados en congresos internacionales 2019

DEPARTAMENTO DE RADIOLOGÍA

EUROPEAN CONGRESS OF RADIOLOGY - VIENA, AUSTRIA

CORRESPONDENCE ANALYSIS BETWEEN DIFFERENT REFERENCE LINES USED IN MAGNETIC RESONANCE DEFECOGRAPHY OF PELVIC ORGANS PROLAPSE OR THE MEASUREMENT OF PROLAPSE OF PELVIC ORGANS WITH POPQ

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Purpose: The aim of this study was to evaluate which of the reference lines: pubococcygeal (PCL), mid-pubic (MPL) or H (HL), commonly used in Magnetic Resonance Defecography (MRD) for evaluation of pelvic floor dysfunction, has better correspondence with the Pelvic Organ Prolapse Quantification system (POPQ). Methods and Materials: Observational, cross-sectional study. POPQ stage and demographic data was obtained of fifty-six patients in which MRDs was performed. The MRDs were reviewed by four expert radiologist and prolapsed was measured using PCL, MPL and HL. A bivariate correspondence analysis and quantification of the inertia of the two dimensions under study was performed between each line and the POPQ. Results: The mean age was 45.2 ± 11.1 years. The analysis of the anterior compartment only obtained an adequate correspondence between PCL and HL on POPQ stages I-II. For the middle compartment there is a slight correspondence between PCL and POPQ stages 0-II, there is also correspondence between the MPL and POPQ stages 0-I, with greater correspondence in patients without prolapse. For the posterior compartment no correspondence was obtained for any of the lines. Conclusion: There is no adequate correspondence between MRD reference lines and POPQ when evaluating the pelvic floor as a whole. When analyzed by compartments, there is better correspondence with PCL and HL in the anterior compartment, and for PCL and MPL in the middle. There is no correspondence for the posterior. These results make us propose that the analysis of MRDs should.

DEPARTAMENTO DE OTORRINOLARINGOLOGÍA

42ND ANNUAL MIDWINTER MEETING ARO – BALTIMORE, EEUU

APATHY IN PRESBYCUSIS IS RELATED WITH BRAIN ATROPHY AND FUNCTIONAL LOSS

Chama Belkhiria ; Melissa Martínez; Simon San Martin; Alexis Leiva; Maricarmen Andrade; Paul H. Delano; Carolina Delgado

Background: Presbycusis is associated with cognitive decline (CD) in the elderly and is recognized as one of the principal modifiable risk factors for dementia. Late onset neuropsychiatric symptoms (NPS) are also associated with dementia and apathy is the most prevalent NPS. We hypothesized that presbycusis and apathy would have an additive negative effect on the aging brain and would be related to brain volume loss and cognitive and functional decline. Objectives: Study the interrelations between presbycusis and apathy on brain structure, cognitive and functional performance Methods: The ANDES (Auditory and Dementia study) is a prospective cohort of healthy Chilean hispano-mestizo elders ≥ 65 years, "cognitively" normal (MMSE >24) with different levels of hearing loss without hearing aids. Patients were evaluated with comprehensive neuropsychological assessment, neuropsychiatric evaluation using the neuropsychiatry inventory questioner (NPI-Q) and apathy evaluation scale (AES), functionality in activities of daily living (ADL) and pure tone average (PTA). Results: 110 subjects were recruited; mean age and education were 74 ± 5.5 and 9.5 ± 4.2 years, mean PTA= 26 ± 12 . 56 subjects had normal auditory thresholds (controls) (PTA= 17 ± 5) and 54 had presbycusis: 35 mild (PTA= 30 ± 4) and 19 moderate (PTA= 47 ± 8). Presbycusis patients were significantly older than controls, without differences in cognitive, neuropsychiatric or functional assessment. Once adjusted by age and education, the PTA was correlated with apathy, sleep disorders and functional impairment but not with cognitive measurements.

Presbycusis patients but not controls, had significant positive correlations between apathy and impairment in ADL and brain volume loss in several brain regions: accumbens, cingulate cortex, orbitofrontal cortex, insular cortex, amygdala, precuneus, superior temporal and total grey matter. Conclusions: Presbycusis patients had more NPS and functional impairment than controls, which is related with volume loss in frontal/subcortical, limbic and temporal regions. Hearing loss and apathy interaction are predisposing functiona.

THE ROLE OF MEDIAL OLIVOCOCHLEAR TRANSMISSION DURING SELECTIVE ATTENTION TO VISUAL STIMULI WITH AUDITORY DISTRACTORS Paul H. Delano

The mammalian auditory efferent system is a unique neural network that originates in the auditory cortex and projects to the cochlear receptor through the olivocochlear bundle. It has been proposed to function as a top-down filter of peripheral auditory responses during selective attention to cross-modal stimuli. In the last years, we have been studying the role of olivocochlear transmission in animal models, including chinchillas and the α -9 nicotinic receptor subunit knock-out mice. Experiments performed in chinchillas show that selective attention to visual stimuli reduces auditory-nerve responses to auditory distractors, while cochlear microphonic responses are enhanced. These findings suggest that the medial olivocochlear fibers are activated during selective attention to visual stimuli. Next, we show that selective attention to visual stimuli with auditory distractors is altered in α -9 nicotinic receptor knock-out (KO) mice, as they made less correct responses and made more omissions than wild type (WT) mice in presence of auditory distractors. Moreover, we evaluated the effects of contralateral noise on auditory nerve responses in alpha-9 KO and WT mice by measuring the amplitude of wave I from auditory brainstem responses with and without contralateral broadband noise. We found that alpha-9 KO mice have a reduced olivocochlear reflex strength, and that the individual magnitude of the olivocochlear reflex correlates with the number of correct responses made by WT and KO mice. Taken together, our results, demonstrate that an intact medial olivocochlear transmission aids in ignoring auditory distractors during selective attention to visual stimuli, probably by suppressing auditory-nerve responses through medial olivocochlear activation.

COCHLEAR AND AUDITORY-NERVE FUNCTIONS ARE ASSOCIATED TO COGNITIVE DECLINE IN ELDERS Paul H. Delano

Epidemiological evidence shows an association between age-related hearing loss and cognitive decline in elderly people. Presbycusis subjects with audiometric hearing thresholds (PTA) worse than 40 dB are more likely to develop dementia. The mechanisms that connect this epidemiological association are unknown. Here we propose that the amplitude of auditorynerve responses at supra-thresholds levels (80-90 dB), which has been used as a proxy of the loss of synapses between inner hair cells and auditory nerve neurons, is an important factor linking presbycusis and cognitive decline. Methods: The ANDES (Auditory and Dementia study) project is a prospective cohort of Chilean hispano-mestizo elders ≥ 65 years, "cognitively" normal (MMSE >24) with different levels of age-related hearing impairment. A total of 112 people have been evaluated with comprehensive neuropsychological and audiological evaluations, including: audiometric thresholds (0.25 to 8 kHz), amplitudes and latencies of auditory brainstem responses (ABR) waves I and V obtained at 80-90 dB nHL, distortion product otoacoustic emissions (DPOAEs). Results: 99 participants (60 women) complied with the inclusion criteria, with a mean age of 73.9 ± 5.2 years, and a mean education of 9.4 ± 4.1 years. The mean pure tone average (PTA) for the right ear was 29.3 ± 12.1 dB HL. Mean HHIE-S was 7.00 ± 7.3 points, while average MMSE was 28.1 ± 1.3 (range between 24 and 30 points). In the group of normal hearing subjects, the amplitude of the left ABR wave I and of the left amplitude ratio between wave I and V correlated with the Trail Making Test A (TMT-A) time (Spearman test, $r=-0.45$, $p=0.04$; $r=-0.52$, $p=0.02$ respectively), while there was no correlation in the amplitude of DPOAEs and in the contralateral noise effects on DPOAEs from the left ear. In addition, the amplitude of the right ABR wave I and the right wave I/V ratio correlated with the Frontal Assessment Battery (FAB) score (Spearman test, $r=-0.471$, $p=0.03$; $r=-0.541$, $p=0.01$), while there were non-significant correlations between the amplitude of DPOAEs and the contralateral noise effects in the right DPOAEs with the FAB score. Conclusions: These results suggest that hidden hearing loss is associated to slower processing speed and diminished frontal functions in elderly humans. Funded by Anillo ACT1403, Fondecyt 1161155 and ICM P09-015F.

LOW-FREQUENCY OSCILLATORY MODULATION OF THE COCHLEAR AMPLIFIER BY SELECTIVE ATTENTION Constantino Dragicevic; Bruno Marcenaro; Marcela Navarrete; Luis Robles; Paul Delano

Evidence show that selective attention to visual stimuli modulates the gain of cochlear responses, probably through auditory-cortex descending pathways. At the cerebral cortex level, amplitude and phase changes of neural oscillations have been proposed as a correlate of selective attention. However, whether sensory receptors are also influenced by the oscillatory network during attention tasks remains unknown. Here, we searched for oscillatory attention-related activity at the cochlear receptor in humans. We used an alternating visual/auditory selective attention task and measured electroencephalographic activity simultaneously to distortion product otoacoustic emissions (a measure of cochlear receptor-cell activity). In order to search for cochlear oscillatory activity, the otoacoustic emission signal, was included as an additional channel in the electroencephalogram analyses. We found the presence of low frequency (<10 Hz) brain and cochlear amplifier oscillations during periods of selective attention to visual and auditory stimuli. Notably, switching between auditory and visual attention modulates the amplitude and the temporal order of brain and inner ear oscillations. These results extend the role of oscillatory activity network during cognition in neural systems to the receptor level.

TOP-DOWN MODULATION OF OTOACOUSTIC EMISSIONS AND EARLY AUDITORY EVOKED POTENTIALS BY VISUAL WORKING MEMORY LOAD

Bruno Marcenaro; Alexis Leiva; Vladimir Lopez; Constantino Dragicevic; Paul H. Delano

Selective attention requires focusing on relevant stimulus but also avoiding distracting stimulus from other sensory modalities. A growing line of evidence show that attention and working memory mechanisms are closely related, so that early modulation of sensory processing can impact subsequent working memory performance. Here, we ask whether distortion product otoacoustic emissions (DPOAEs), a sub product of the cochlear amplifier in the cochlea, and early cortical auditory evoked potentials N1 and P2 are modulated by selective attention and visual working memory load. Twenty subjects (twelve male, age range 20-31, mean age 25.2 years) with normal hearing performed a visual change detection task with varying working memory load (high load= 4 objects; low load = 2 objects). Auditory stimulus (frequency range 1250-2200 Hz) were delivered simultaneously with the task to measure DPOAEs, and N1-P2 evoked potentials. Individual visual working memory capacity was assessed using behavioral results. Results show that the amplitude of DPOAEs are modulated by working memory load and that working memory performance is correlated with P2 amplitude. This study helped to clarify the role of auditory efferent pathway in the regulation of cochlear responses and understand how early stimulus processing is related with working memory.

STRUCTURAL CINGULATE CORTEX CHANGES ARE ASSOCIATED TO COCHLEAR AGING

Chama Belkhiria; Rodrigo Vergara; Simon San Martin; Alexis Leiva; Bruno Marcenaro; Melissa Martínez; Carolina Delgado; Paul H. Delano

Introduction: Age-related hearing loss or presbycusis is characterized by bilateral progressive hearing loss and impaired speech understanding especially in noisy environments. Several studies in humans have found brain structural changes in patients with hearing loss, including grey matter volume reduction in the right temporal lobe and correlations between hearing impairment and smaller gray matter volume in the auditory cortex. However, whether cognitive decline and the atrophy of brain regions in presbycusis patients are specifically associated to the cochlear receptor cell loss is unknown. We hypothesized that cochlear amplifier dysfunction in presbycusis is a major contributor for cognitive decline and structural brain changes in elderly population. Methods. 96 patients aged over 65 years were included from cross-sectional data from the ANDES cohort. These subjects had mini mental state examination (MMSE) score over 24 and were evaluated by neuropsychological and audiological evaluations, including pure tone audiometric (PTA) thresholds and distortion product otoacoustic emissions (DPOAEs). Data were divided into three groups: (i) a control group with normal hearing levels, (ii) presbycusis group with preserved cochlear function (PCF) and (iii) a group with presbycusis and cochlear dysfunction (CD). Grey matter volumes and cortical thickness were calculated from 3-Tesla MRI wholebrain T1-weighted images using automatic Freesurfer segmentation. Results. The patients mean age was 73.62 ± 5.34 years, with 63 female and with an average hearing of 25.35 ± 10.91 dB. When comparing structural differences between hearing impairment groups, the parahippocampus volume and the anterior and posterior cingulate cortex thickness were significantly more atrophied in the CD group. Only in the CD group there were significant correlations between cingulate cortex atrophy and impairment in working memory, episodic memory, language and visuoconstructive abilities. Conclusions. Cochlear dysfunction was associated with brain structural changes mainly in non-auditory areas and was associated with impairment in cognitive domains beyond auditory processing. Our findings suggest that the presbycusis patients with loss of outer hair cells have more severe alterations in the neural structures related to the effortful network than those with more preserved cochlear amplifier function. The absence of DPAOE in mild presbycusis patients could be an early risk factor.

THE OLIVOCOCHLEAR REFLEX STRENGTH IS CORRELATED WITH BEHAVIORAL PERFORMANCE IN A VISUAL SELECTIVE ATTENTION TASK WITH BROADBAND NOISE DISTRACTORS BUT NO WITH DISTRESS CALLS IN CHINCHILLAS.

Macarena Bowen; Gonzalo Terreros; Macarena Ipinza; Felipe N. Gomez-Moreno; Luis Robles; Paul Delano.

Background. The auditory efferent network comprises descending projections from the auditory cortex to the superior olivary complex, from where medial olivocochlear (MOC) bundle emerges ending in the outer hair cells of the cochlea. MOC function can be assessed by measuring the effects of contralateral acoustic stimulation (CAS) on the amplitude of distortion product otoacoustic emissions (DPOAEs). One of the possible functions of the efferent system is the modulation of cochlear sensitivity during selective attention to visual stimuli. In this work, we studied the relationship between MOC reflex variability and visual attention performance, hypothesizing that inter-subject variability of MOC reflex is related to the capability of avoiding auditory distractors. For this, we analyzed the effect of two types of auditory distractors: (1) broad-band noise (BBN) as an irrelevant artificial stimulus and (2) chinchilla distress vocalizations as relevant ecological stimuli. Methods. We measured the MOC reflex using contralateral BBN in ten awake chinchillas. After that initial measure, chinchillas were trained in a two-choice visual discrimination task. The behavioral performance was evaluated in a 12 days protocol divided into three blocks of 4 days: without auditory distractors (base-line), with BBN and with four different male chinchilla vocalizations ($F_0 = 537 - 854$ Hz), as auditory distractors. Results. CAS-induced DPOAE amplitude changes had an average of 0.75 ± 1.23 dB across all frequencies. During the presentation of vocalization auditory distractors a significant increase in latency of correct responses was observed between the first day with vocalization (2025.11 ± 493.4 ms) and day 3 base-line (1373.81 ± 314 ms), day 3 and 4 of BBN (1416.62 ± 570.1 , 1381.43 ± 386.6 ms) and day 4 of vocalization (1513.9 ± 569.3 ms) (RMANOVA on Ranks, Tukey post-hoc, $p < 0.05$). Significant Spearman correlations among MOC reflex magnitudes and behavioral performance during first day with noise as distractor – latency of responses

($r=0.7$, $p=0.03$) and accuracy ($r=-0.8$, $p<0.01$) – were found. Discussion. Our results show a correlation between MOC strength and behavioral performance during selective attention to visual stimuli only when using BBN as auditory distractor. Unexpectedly, vocalizations did not correlate with MOC strength, but affect behavioral performance by decreasing accuracy and increasing the latency of responses.

EXTENDED FRONTAL SINUS ENDOSCOPIC APPROACH.

Cristofer Salazar, Cristobal Chavez, Karen Garcia, Rodolfo Nazar, Alfredo Naser, Catalina Avila

Introduction: Nasosinus endoscopic surgery has increased its use in recent years. Depending on the type of lesion, as well as its location within the frontal sinus, the endoscopic approach is the best choice for most cases. Objectives: Describe and analyze the clinical and epidemiological characteristics of patients undergoing extended endoscopic frontal sinus surgery in the otolaryngology service of the Clinical Hospital of the University of Chile (HCUCH). Material and methods: Retrospective, descriptive study, including patients with otolaryngological pathology who have undergone extended endoscopic surgery of frontal sinus, between 2013 and 2018 in HCUCH. Epidemiological variables, clinics, results and complications were analyzed. Results: The series consists of 60 patients, with an average age of 44.5 years; 28 men and 32 women. The most frequent diagnoses that motivated this intervention were: Chronic Rhinosinusitis with Nasal Polyps. (36.6%) and non polyps chronic rhinosinusitis (23.3%). All patients were studied with nasal endoscopy and images, with computed tomography being the choice. In the preoperative analysis with images, anatomy of the frontal sinus is very variable. No intra-surgical complications were reported. During the postoperative period, only 1.7% of patients progressed with complications, septal perforation was the only one. In the follow-up period, one patient required revision surgery. Discussion and conclusion: Those patients with frontal sinus pathology should be evaluated in a complete way, with anamnesis, physical examination and images, to select properly. It's a safe procedure, but should be performed in a center with specialized otolaryngologists, with adequate surgical instruments.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

27TH EUROPEAN CONGRESS OF PSYCHIATRY – VARSOVIA, POLONIA

OUR CONSCIOUS EXPERIENCE

J. Saavedra, C. Zarate

Background and aims.– Human beings exist as long as they interact with their environment. Existence is meaningful and transcends the self in an irreducible experience through the interaction I-the self; I-the other. Humans confront the necessity of giving sense to their existence, configuring and adapting their own history. Past experiences, act as background for the current experience and the next ones to come. Objective: elucidate the configuration of existence through the interaction of I-the self; I-the other through ontology. Methods.– Analyzing the conscious experience from an occidental, oriental and philosophical vision, perspective in an attempt of coming together poles objected in the vacuity of the TAO; with the purpose of developing the human experience in the surrounding universe. Results.– During life, human beings exist in a continuum, as organisms that develop and satisfy their needs within society. This dialectic between the self, existence and environment does not necessarily imply human beings are aware of their existence. Thus, the irreducible phenomenon of becoming conscious is achieved by having contact with our own corporality, and our being in relation to the universe. As a result, we experience and interpret our existence again towards new interactions with the external world, interpersonal relations, and our inner self. Conclusions.– Conscious experience is an active phenomenon, that develops intuitive and reflexively, such as in the first phenomenological reduction, where psychic content and the theory are hold in parentheses, thus transcending the own psyche.

FEELINGS OF THE PSYCHIATRIST OR THERAPIST FOR PATIENT'S, MATTER?

C. Zarate, R. Alejandra

Background and aims.– Countertransference (CT) includes a full range of cognitive, affective and behavioral responses that psychiatrists experiment with their patients. Recent evidence indicate that CT can help understand patient's psychological reality, and also be a prognostic indicator of treatment (1,2) Objective.– Evaluate the relationship between observers and interviewer's CT and the patient's degree of psychopathology, and gender differences. Methods.– An adapted Countertransference Questionnaire (CTQ), (3) adapted and validated by us, was applied to a group of psychiatry residents and faculty after observing the first psychodynamic, through a one way mirror during the years 2013–2017. Patients' clinical severity was measured using Clinical Global Impression Scale (CGI). Our adapted CTQ grouped in seven factors. Results.– We find out that factors of the CTQ show variability in scores depending on the patient severity (CGI). We also observe differences in CGI score ad gender of observers according CTQ factors. These results are in agreement with our hypothesis. Conclusions.– The factor 1 of CTQ presents a significant low score in the patients with low and high severity (CG 2,6) with a p value $\leq 0,05$. F2 shows significant difference regarding the patients' severity too. Our findings also show significant different CGI by gender in F1 and F2. Factor 1 measures empathy and involvement, factor 2 rejection and distance. These results raise questions and a further challenges and research as a work group.

DEPARTAMENTO DE ANESTESIOLOGÍA Y MEDICINA OPERATORIA

CONGRESO IARS - MONTREAL, CANADÁ

LOW ALPHA POWER FROM ELECTROENCEPHALOGRAPHIC ACTIVITY IS ASSOCIATED WITH THE DEVELOPMENT OF ACUTE CONFUSIONAL STATE

Rodrigo Gutiérrez, Jose Ignacio Egaña, Ivan Saez, Fernando Reyes, Constanza Briceño, Mariana Venegas, Isidora Lavado, Antonello Penna

Postoperative acute confusional state (PACS) is a frequent complication in elderly patients. This disorder may manifest as postoperative delirium (POD), or as a milder disorder called postoperative subsyndromal delirium (POSSD). Both types of delirium are associated with poor outcomes^{3,4}. Intraoperative electroencephalogram (EEG) may be capable of identifying patients at risk for PACS during surgery. The goal of this study was to characterize and differentiate intraoperative EEG markers in the frequency domain in patients who developed PACS and those who did not. **METHODS:** After approval of the local ethics committee at the Hospital Clínico de la Universidad de Chile, we conducted an observational study in elderly patients scheduled for elective major abdominal surgery. All patients signed the informed consent form. Exclusion criteria were history of dementia, encephalopathy, pre-operative delirium, alcohol or drug abuse, major psychiatric disorder, and contraindication to receiving sevoflurane-based anesthesia. Anaesthesia care was provided according to the clinical judgement of the attending anesthesiologist. Intraoperative EEG data were recorded with a 16-channel EEG and analyzed with MATLAB and EEGlab. PACS was detected with the confusion assessment method⁵, and the power spectra (1-40 Hz) were compared between patients. The relative powers of the delta (1-4 Hz), theta (5-8 Hz) and alpha (9-12 Hz) bands were also calculated. To characterize the topography of frequency domain changes, the 16-channel data were divided into 3 electrode regions of interest: frontal (Fp1 and Fp2), occipital (O1, Oz, and O2), and the average of the 16 channels (global EEG). We calculated that a sample size of 40 patients would be required to identify differential anaesthesia-induced states in patients who developed PACS and those who did not, given a 30% incidence of PACS⁵, at least a 30% difference in the relative power in any band, 20% loss of patients, an alpha error of 0.05, and a power of 80%. **RESULTS:** PACS was diagnosed in 48% (14/29) of patients: 2 patients developed POD and 12 POSSD. These 14 patients were older (76.4±5.2 years vs. 69.3±7.8 years, $p=0.008$) and had a lower preoperative Montreal Cognitive Assessment score (24.5 (22.8-27.3) vs. 28.0 (26.8-29.0), $p=0.004$) than those who did not develop PACS (non-PACS). No other difference was found in the baseline demographic characteristics (Table 1). There were no detectable power spectrum differences before anesthesia between the groups with and without PACS. However, the EEG spectral analysis showed that patients who went on to develop PACS had a lower intraoperative alpha power during anesthesia (Figure 1). Moreover, PACS was associated with relatively lower alpha and higher delta powers, independent of anesthetic dose (Figure 2). Finally, relative alpha power had a high ability to identify the patients who developed PACS, with an area under the curve of 0.90 (CI 0.78-1) in the ROC analysis (Figure 3), with a better discrimination ability than other known risks factors, such as age or preoperative cognitive performance. As anaesthetic dose and physiological variables are potential confounding factors underlying cognitive differences, the MACage values and physiological characteristics of the two groups were compared. MACage did not differ between the PACS and non-PACS patients as shown in Table. Thus, anaesthetic dose did not explain the differences in relative alpha or delta power. MACage was significantly correlated with relative alpha power in patients with PACS ($r=0.64$, $p=0.013$), but not in non-PACS subjects ($r=0.31$, $p=0.29$), suggesting that relative alpha power was dose-dependent for sevoflurane in PACS patients only (Figure 4). **CONCLUSIONS:** A relatively low intraoperative alpha-band power and high delta-band power were associated with increased risk for PACS, independent of anaesthetic dose. Interestingly, no power spectrum differences between the PACS and non-PACS groups were apparent before anaesthesia induction. It is likely, therefore, that the effect of anaesthesia unmasks susceptibility to POD or POSSD, although more studies are needed to elucidate the mechanism underlying these associations. Undoubtedly, intraoperative EEG with spectral analysis is a promising tool for identifying patients at risk for PACS.

REMIFENTANIL-INDUCED HYPERALGESIA IS NOT PREVENTED BY ACETAZOLAMIDE IN PATIENTS UNDERGOING TOTAL THYROIDECTOMY

Rodrigo Gutiérrez, Felipe Contreras, Alonso Blanch, Jose Ignacio Egaña, Daniela Bravo, Daniel Rappoport, Patricio Cabané, Patricio Gac, Francisco Rodriguez, Antonello Penna

Acute administration of remifentanil may activate N-methyl-D-aspartate (NMDA)-dependent pronociceptive systems¹, reducing the nociceptive thresholds and leading to the opioid-induced hyperalgesia (OIH). However, studies in animal models suggest that OIH might also be mediated by impaired anionic homeostasis in spinal lamina I neurons due to a down-regulation of the K-Cl co-transporter KCC2. Restoring the anionic homeostasis with the administration of acetazolamide, a carbonic anhydrase inhibitor, reversed the OIH in mice (2). The aim of this clinical trial was to test whether preoperative administration of 250 mg of acetazolamide during sevoflurane-remifentanil anesthesia diminishes the postoperative OIH in patients undergoing total thyroidectomy. **METHODS:** After approval of the local ethic committee at the Hospital Clínico de la Universidad de Chile, we conducted a randomized, double-blind, placebo-controlled clinical trial between December 2016 and September 2018. All participants sign the informed consent. We included patients between 18 and 65 years, ASA I or II, scheduled to total thyroidectomy. Exclusion criteria were: chronic pain, previous thyroidectomy, analgesic use in the last 48 h and body mass index >30. Patients were randomly allocated to the acetazolamide (ACTZ) group (administration of 250 mg of ACTZ 2 h before surgery) or to the control group (administration of placebo). Mechanical pain thresholds (MPT) were measured before and after surgery (at 2 and 12-18h after surgery) using hand-held von Frey filaments in the forearm as previously described³. Anesthesia was standardized: induction with propofol 2 mg/kg-1 and

followed with rocuronium 0.6 mg/kg-1. Two minutes before of the propofol injection, remifentanyl infusion was initiated using Minto's model. After tracheal intubation, patients were ventilated to normocapnia with 50% oxygen and without nitrous oxide. Anesthesia was maintained with remifentanyl at a target effect-site of 4.5 0.5 ng/ml, and sevoflurane at an end-tidal concentration of 0.8 MAC corrected for age. Thirty minutes before the anticipated end of surgery, a 0.1 mg/kg-1 bolus dose of morphine was given intravenously and then a morphine PCA device was connected. The primary endpoint was to detect a decrease in the MPT at 12-18h in the ACTZ group respect to control group. Based on previous results (3), the number of patients needed to find a decrease in a 20g in the MPT was 17 per group, with a power of 0.80 and an α of 0.05. Assuming a dropout rate of 30%, we calculated a sample size of 22 patients per group. Secondary outcomes were the occurrence of hyperalgesia (defined as a decrease in the MPT), pain evaluated with a numeric pain rating scale (NPRS) and morphine consumption during the first 24 h after surgery. Variables were expressed as mean (SD) or median (IR) as appropriate. The analysis of the von Frey measurement, NPRS, and morphine consumption was performed using two-way ANOVA. RESULTS: Three patients were lost in the follow-up. Therefore, 47 patients completed the study (Figure 1). Both groups were comparable in the baseline characteristics and intraoperative variables (Table 1). Baseline MPT were similar in both groups. There were no differences in the MPT at 12-18h between both groups. Compare to baseline, the MPT at 12-18 hours diminished in both groups (Figure 2). Fourteen of 23 patients (60%) develop hyperalgesia in the control group compare to 11 of 23 patients (48%) in the ACTZ group ($p = 0.5$). Finally, we found no differences in the postoperative pain (Figure 3a) or in morphine consumption (Figure 3b). CONCLUSIONS: Acetazolamide does not prevent OIH in patients undergoing total thyroidectomy.

DEPARTAMENTO DE MEDICINA

SECCIÓN DE GASTROENTEROLOGÍA

THE 2019 ANNUAL ILTS MEETING - TORONTO, CANADA

IMPACT OF THE MELD ERA IN LIVER ALLOCATION IN CHILE: ARE CANDIDATES WITH HEPATOCELLULAR CARCINOMAS BEEN BENEFICIATED DUE TO THE EXCEPTION POINTS?

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Background: Since October 2011 the MELD score system was adopted in Chile for liver allocation. However there are many circumstances, including Hepatocellular carcinoma (HCC) where the MELD does not reflect mortality or probability to dropout from the waiting list (WL). Our normative assign 20 extra points plus one additional point per month for candidates with HCC. Objectives: To evaluate the dropout rate of the waiting list (WL) and survival post-liver transplantation (LT) between cirrhotic patients (CP) listed by MELD scores, patients listed with HCC and patients listed by other exceptions (non-HCC). Methods: Retrospective analysis of the WL of adult candidates (>15 years old) for elective cadaveric and living-donor LT of in Chile, from October 2011 until December 2017. Analysis of the dropout rate of WL and survival post-LT were carried out including Kaplan-Meier curves compared with log-rank test Results: In this period, 730 candidates were listed. Mean age was 53.9 ± 12.0 years; 55.8% were men. The principal etiologies were NASH (29.5%), Alcoholic Liver Disease (16.2%) and Autoimmune (11.8%). We analyzed three groups of candidates: CP 301 (41.3%), HCC 195 (26.7%) and non-HCC 233 (32%). We registered 352 LT (48.2%). Mean time in WL was 311 days: 244 days in CP, 381 days in HCC and 313 in non-HCC. The annual dropout rate was significantly higher in CP compared with candidates with HCC, and non-HCC exceptions (45.5%; 33.1% and 29.3%, respectively, $p < 0.001$). Survival post-LT was 86.1% at 1-year and 84.6% at 5-year, without differences among the three groups ($p = 0.411$). Conclusion: Exceptions generate inequities in dropout rate, disadvantaging patients without exceptions. Therefore, the extra scoring assignment must be carefully adjusted. Prioritization for LT using the MELD score system has not decreased the dropout rate in Chile (persistent low donor's rate).

SECCIÓN DE INFECTOLOGÍA

29TH EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY & INFECTIOUS DISEASES - AMSTERDAM, HOLANDA

CHILEAN STRAINS OF CLINICAL ORIGIN OF NON-O1, NON-O139 VIBRIO CHOLERAE CARRY THE GENES VCSN2, VCSC2, VCSV2, VSPD, TOXR2 Y VOPF FROM SECRETION SYSTEM T3SS2 PRESENT IN AN ISLAND OF PATHOGENICITY

M. Ulloa, G. Osorio, C. Sanhueza, L. Porte, J. Dabanch, A. Fica, I. Briceño, M. Lafourcade, F. Silva, L. Castillo

Background: The virulence factors of the *Vibrio cholerae* non-O1, non-O139 strains are not clearly known. The strain of septicemic origin NNI *Vibrio cholerae* non-O1, non-O139 was sequenced previously by the Illumina platform. A fragment of the pathogenicity island VPal-7 of *V. parahaemolyticus* was detected in its genome. Aim: To detect the virulence genes *vcsN2*, *vcsC2*, *vcsV2*, *vspD*, *toxR2* y *vopF* in Chilean strains of *V. cholerae* non-O1, non-O139. Methods: A total of 9 Chilean strains of clinical origin of *Vibrio cholerae* non-O1, non-O139 isolated between 2006-2012 were analyzed by conventional PCR assays for type III secretion genes encoded on that island: *vcsN2*, *vcsC2*, *vcsV2*, *vspD*, *toxR2* and *vopF*. Additionally, the presence of the virulence genes *hylA* and *rtxA* was determined. In addition, REP-PCR and ERIC-PCR assays were performed. Results: most (6/9) Chilean *V. cholerae* non-O1, non-O139 strains contain the type III secretion genes *vcsN2*, *vcsC2*, *vcsV2*, *vspD*, *toxR2* and *vopF*, encoded in an island of pathogenicity. In addition, all (9/9) the strains contain the virulence genes *hylA* and *rtxA*. Conclusion: These results strongly suggest the possibility that those strains possess an important virulence potential in humans.

EVALUATION OF CEFTAROLINE RESISTANCE (CPT-R) IN CHILE ACROSS TIME AND A COMPARISON OF CLSI VS. EUCAST BREAKPOINTS IN METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

Ayesha Khan, Lina M. Rivas, Maria Spencer, Jose RW. Martínez, Marusella Lam, Pamela Rojas, Lorena Porte, Francisco Silva, Stephanie Braun, Francisco Valdivieso, Margareta Mülhauser, Mónica Lafourcade, William R. Miller, Patricia Garcia, Cesar A. Arias, Jose M. Munita

Background: CPT-R in MRSA is associated with clonal complex (CC) 5 lineages. Chile, with wide dissemination of the CC5 Chilean-Cordobes clone, has high MRSA rates. In 2019, CLSI revised the breakpoints (BPs) keeping susceptible (S, minimum inhibitory concentration [MIC mg/L] ≤ 1), added susceptible dose-dependent (SDD, MIC 2-4), removed intermediate (MIC 2); resistant (R) is now MIC ≥ 8 . EUCAST S is MIC ≤ 1 , but R differentiates among pneumonia (MIC > 1) and nonpneumonia (NP) isolates (MIC > 2). We evaluated CPT-R across time and agreement between agencies for broth microdilution (BMD), E-test and Disk Diffusion (DD). Methods: Hospital- (HA; n=320, 10 centers) and community-associated (CA, n=37) clinical MRSA isolates collected between 1999-2018 were confirmed with MALDI-TOF, ceftoxitin DD, and mecA PCR. CPT susceptibilities were evaluated by BMD, E-test and DD (5 and 30 mg) across revised and old CLSI or EUCAST BPs. We determined essential and categorical agreement (EA, CA), very major, major and minor errors (VME, ME, MiE). Results: The MIC₅₀/MIC₉₀ of HA-MRSA with BMD was 2/2 mg/L (64% of isolates considered CPT non-susceptible) and 0.5/0.5 mg/L for CA-MRSA. MIC₅₀/MIC₉₀ was 1/1.5 with E-test. Strains collected in 1999-2008 (n=161) and 2009-2018 (n=159) both had a MIC₅₀/MIC₉₀ of 2/2. The EA of E-test with BMD was 82%; results of CA-VME-ME-MiE were 51-0-0-48% using the new CLSI BPs or 51-81-0-45% using EUCAST or old CLSI BPs. For BMD, CA-VME-ME-MiE between new CLSI and EUCAST was 95-0-0-5 with 100% CA for E-test. Under NP EUCAST BPs, R isolates increase from 5 to 21% by BMD and 0 to 8% by E-test. CA-VME-ME-MiE between new CLSI and NP EUCAST BPs for BMD is 79-0-0-21 and for E-test is 91-0-0-8. For DD vs BMD, CA-VME-ME-MiE is 55-0-1-44 with new CLSI BPs, 53-63-1-43 with old CLSI and 36-6-35-51 with EUCAST. With EUCAST DD (5ug CPT) as reference vs CLSI DD (30ug CPT), CA-VME-ME-MiE is 25-70-0-38. Conclusion: CPT nonsusceptibility is frequent in the CC5 HA-MRSA clone circulating in Chile across time. All methods had poor performance against BMD, but revision of CLSI BPs decreased error rates. E-test under called the MIC. CLSI DD (under called nonsusceptibility) and EUCAST DD (overcalled resistance) are drastically discordant. Respiratory isolates evaluated under NP BPs increased rates of resistance.

ID WEEL CONGRESS 2019 - WASHINGTON, USA

IN VITRO ACTIVITY OF CEFTOLOZANE/TAZOBACTAM (C/T) AGAINST ENTEROBACTERIACEAE AND PSEUDOMONAS AERUGINOSA CIRCULATING IN CHILE

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Background: The widespread dissemination of carbapenem-resistant (CR) *P. aeruginosa* and Enterobacteriaceae has created a major global public health crisis. C/T is a recently approved therapeutic which consists of the combination of a novel cephalosporin (ceftolozane) and tazobactam (a β -lactamase inhibitor). C/T has shown good activity against a wide range of multidrug-resistant (MDR) Gram negatives, being particularly interesting as an alternative for MDR *P. aeruginosa*. We aimed to determine the activity of C/T against clinical strains of Enterobacteriaceae and *P. aeruginosa* recovered in 4 large clinical centers from Chile. Methods: We analyzed 434 isolates of Enterobacteriaceae (347 *E. coli*, 66 *K. pneumoniae*, 21 Enterobacter cloacae complex) and 57 *P. aeruginosa* collected during 2017 from 4 tertiary care institutions in Santiago, Chile. Identification was performed as per each local clinical microbiology lab. Susceptibility testing was performed by broth microdilution using customized Sensititre plates (Trek). Carba-NP was performed to screen for carbapenemase production. Susceptibilities were analyzed as per 2019 CLSI breakpoints. Results: The MIC₅₀/90 for C/T against Enterobacteriaceae and *P. aeruginosa* were 1/4 $\mu\text{g/mL}$ and 2/16 $\mu\text{g/mL}$, respectively. In Enterobacteriaceae, susceptibility to C/T reached 92% in *E. coli* (Fig 1A), 91% in *E. cloacae* complex (Fig 1B) and 70% in *K. pneumoniae* (Fig 1C). Remarkably, C/T remained active against 58% (33/57) of CR Enterobacteriaceae (Fig 2A). Among Carba-NP-negative CR isolates (46%, 26/57), susceptibility to C/T was 54% (Fig 3 A-C). In *P. aeruginosa*, the overall susceptibility to C/T was 81% (Fig 1D), maintaining activity against 69% (25/36) of CR strains (Fig 2B). Importantly, susceptibility to C/T in CR *P. aeruginosa* isolates with a negative Carba-NP (67%, 24/36) was 83% (20/24) (Fig 3D). Conclusion: In this multicenter study, we observed that C/T was highly active against clinical isolates of Enterobacteriaceae and *P. aeruginosa*. Of note, C/T remained active against a large proportion of CR clinical strains. Moreover, the activity of C/T was particularly high against CR *P. aeruginosa* isolates with a negative Carba-NP.

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Ayesha Khan – Lina Rivas – Maria Spencer – Jose Martínez – Marusella Lam – Pamela Rojas – Lorena Porte – Francisco Silva – Stephanie Braun – Francisco Valdivieso – Margareta Mülhauser – Mónica Lafourcade – William Miller – Patricia Garcia – Cesar Arias – Jose Munita

Background: CPT-R in MRSA is associated with clonal complex (CC) 5 lineages. Chile, with wide dissemination of the CC5 Chilean-Cordobes clone, has high MRSA rates. In 2019, CLSI revised the breakpoints (BPs) keeping susceptible (S, minimum inhibitory concentration [MIC mg/L] ≤ 1), added susceptible dose-dependent (SDD, MIC 2-4), removed intermediate (MIC 2); resistant (R) is now MIC ≥ 8 . EUCAST S is MIC ≤ 1 , but R differentiates among pneumonia (MIC > 1) and nonpneumonia (NP) isolates (MIC > 2). We evaluated CPT-R across time and

agreement between agencies for broth microdilution (BMD), E-test and Disk Diffusion (DD). Methods: Hospital- (HA; n=320, 10 centers) and community-associated (CA, n=37) clinical MRSA isolates collected between 1999-2018 were confirmed with MALDI-TOF, cefoxitin DD, and mecA PCR. CPT susceptibilities were evaluated by BMD, E-test and DD (5 and 30 mg) across revised and old CLSI or EUCAST BPs. We determined essential and categorical agreement (EA, CA), very major, major and minor errors (VME, ME, MiE). Results: The MIC₅₀/MIC₉₀ of HA-MRSA with BMD was 2/2 mg/L (64% of isolates considered CPT non-susceptible) and 0.5/0.5 mg/L for CA-MRSA. MIC₅₀/MIC₉₀ was 1/1.5 with E-test. Strains collected in 1999-2008 (n=161) and 2009-2018 (n=159) both had a MIC₅₀/MIC₉₀ of 2/2. The EA of E-test with BMD was 82%; results of CA-VME-ME-MiE were 51-0-0-48% using the new CLSI BPs or 51-81-0-45% using EUCAST or old CLSI BPs. For BMD, CA-VME-ME-MiE between new CLSI and EUCAST was 95-0-0-5 with 100% CA for E-test. Under NP EUCAST BPs, R isolates increase from 5 to 21% by BMD and 0 to 8% by E-test. CA-VME-ME-MiE between new CLSI and NP EUCAST BPs for BMD is 79-0-0-21 and for E-test is 91-0-0-8. For DD vs BMD, CA-VME-ME-MiE is 55-0-1-44 with new CLSI BPs, 53-63-1-43 with old CLSI and 36-6-35-51 with EUCAST. With EUCAST DD (5ug CPT) as reference vs CLSI DD (30ug CPT), CA-VME-ME-MiE is 25-70-0-38. Conclusion: CPT nonsusceptibility is frequent in the CC5 HA-MRSA clone circulating in Chile across time. All methods had poor performance against BMD, but revision of CLSI BPs decreased error rates. E-test under called the MIC. CLSI DD (under called nonsusceptibility) and EUCAST DD (overcalled resistance) are drastically discordant. Respiratory isolates evaluated under NP BPs increased rates of resistance.

SECCIÓN DE INMUNOLOGÍA

17TH EUROPEAN MEETING ON HIV & HEPATITIS - ROMA, ITALIA

USE OF RAPID HIV ANTIBODY TESTS IN CHILE AS PREVENTION STRATEGY

Ferrer Pablo, Afani Alejandro, Bastias Carla

Introduction: Today Chile has the highest rate of new HIV infections in Latin America. Although in Chile the first rapid test for HIV was registered in 1999, it has never been used massively in the general population as a prevention strategy for HIV infection. Method: 4th generation rapid HIV test (BTNX, Ontario Canada) and an anonym epidemiologic survey were realized to 1337 people in Santiago between November 28 of 2017 and March 31 of 2018. In accordance with the national HIV/AIDS law, a complete confirmation process was made to the people who were reactive in the rapid test. Results: A total of 1,337 people were tested of which 20 were reactive for antibodies against HIV. The 20 people were confirmed as HIV positive by the confirmation algorithm carried out by the Institute of Public Health of Chile (ISP-Chile), the technical agency mandated at the national level to confirm all new cases of HIV infection that are being screened in Chile. Of the 20 people detected, 18 were men with an average age of 32.4 years and 2 were women with an average age of 42.5 years. According to these data, the current prevalence of HIV in the people studied is 1.5%. A total number of 1200 surveys were collected. Responders were 52% male and 48% women. During the last year: only 20% of the respondents answered that they had always used condom, only 40% reported having had an HIV test and same period time the average number of sexual partners was 3. An 80% responded that they would be willing to use a drug as pre-exposure prophylaxis. A 90% of the respondents answered that the test was not carried out for the following reasons: difficult access, lack of time, lack of interest, excessive price and fear of the result. Conclusions: In Chile during the five-year period 2010-2015 new cases of HIV have increased up to 96% in the age group that goes from 14 to 29 years. This reality has the country in a situation of epidemiological alert. The prevalence of 1.5% reported by our work is three times higher than that estimated by UNAIDS for Chile. This discrepancy has its origin in the difficult access that the population has to the diagnosis of HIV, which is performed exclusively in public and private health centers. Our experience tells us that massive testing by means of rapid fourth-generation tests is an excellent opportunity to bring the diagnosis closer to people. The limited use of condoms by the majority of the population studied is evidence that could explain the high number of new HIV cases in Chile.

17TH EDITION OF THE EUROPEAN AIDS CONGRESS -BASELEA, SUIZA

ISLATRAVIR EFFICACY AND SAFETY FOR SELECTED DEMOGRAPHIC AND BASELINE SUBGROUPS FROM A PHASE 2 TRIAL IN TREATMENT NAÏVE ADULTS WITH HIV-1 INFECTION

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1University of Paris, Hôpital Saint-Louis, Paris, France 2Bichat Hospital, AP-HP, Paris, France 3University of Chile, Santiago, Chile 4North Texas Infectious Diseases Consultants, Dallas, USA 5Hospital Hernán Henríquez Aravena of Temuco, Temuco, Chile 6Orlando Immunology Center, Orlando, USA 7Merck & Co., Inc., Kenilworth, USA. Purpose: Islatravir (ISL, MK-8591) is the first nucleoside reverse transcriptase translocation inhibitor (NRTTI) in development for treatment of HIV-1 infection. We analyzed the week 48 results of a Phase 2 ISL trial in treatment naïve adults with HIV-1 infection by pre-specified subgroups for efficacy and safety. Method: In this randomized, double-blind, dose-ranging trial, participants were initially assigned to receive ISL (0.25 mg, 0.75 mg, or 2.25 mg) with doravirine (DOR, 100 mg) and lamivudine (3TC, 300 mg) or a fixed-dose combination of DOR, 3TC, and tenofovir disoproxil fumarate (DOR/3TC/TDF) once daily. Participants receiving ISL who achieved HIV-1 RNA<50 copies/mL at Week 20 or later stopped taking 3TC at their next visit and continued DOR+ISL at initial dosage; most participants stopped 3TC at Week 24. Efficacy endpoints included the overall proportion of participants at week 48 with HIV-1 RNA<50 copies/mL. For the current analysis, efficacy results were summarized within

pre-specified subgroups (age, sex, race, region, baseline HIV-1 RNA, baseline CD4+ T-cell count) using the Observed Failure Approach (excludes participants with data missing for reasons other than lack of efficacy). Results: 121 participants received study drug and were included in analyses (mean age 31 yr, 92.6% male, 76.0% white, 49.6% Hispanic or Latino, 22% HIV-1 RNA>100,000 copies/mL, median CD4+T-Cell Count 456 cells/mm³). At week 48, 92.9% (26/28), 93.1% (27/29), 85.7% (24/28), of participants achieved HIV-1 RNA<50 copies/mL in the 0.25 mg, 0.75 mg, 2.25 mg dose of ISL respectively, compared to 92.9% (26/28) with DOR/3TC/TDF. Across the pre-specified and selected demographic and baseline subgroups, proportions of participants with HIV-1 RNA<50 copies/mL at week 48 were comparable between all treatment arms (Figure 1). In the safety analysis, similar adverse event rates between treatment groups were observed across subgroups. Conclusions: At week 48, across all baseline subgroups, the ISL regimens demonstrated similar efficacy and safety comparable to DOR/3TC/TDF.

FAR FROM 90–90–90 GOALS IN LATIN AMERICA

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Purpose: One year away from 90–90–90 WHO goals, a final 52% of viral suppression among people living with HIV (PLWH) in Latin America (LA) was reported by UNAIDS in 2017, based upon estimations and information provided by governments. The objective of our study was to measure rates of retention in ART and virological suppression (VS) in LA by independent data collection from HIV Care Centers. Method: We collected data from 34 HIV centers on charge of 62,375 out of 499,020 patients under control in 8 LA countries. Patients admitted to care in 2016 were followed up and one-year outcomes were registered in grouped sex and age stratified sheets. The continuum of care was built starting from UNAIDS PLWH estimations, the number of patients under control following an elicitation procedure (1st 90 includes diagnosed and linked) and the results of follow up for retention and suppression. Sensitivity analysis was carried out according to the expected PLWH under control in each country. Results: From 7,820 patients admitted to care in 2016, 252 died in the first year (3.2%) and 224 transferred out were censored for analysis. 85.4% of patients were retained in ART at one year (77.3% to 93.2%) and 90.0% of them achieved VS below 1,000 copies/mL (61.0% to 96.3%). The final 90–90–90 rate ranged from below 40% in Venezuela, Guatemala and Peru to 57.9% in Argentina with an average of 46.9% for the 8 countries. Conclusion: Our independent data collection shows that rates of retention in ART and VS in LA are close to the goals. Nevertheless, we are far to achieve the final 90–90–90 in LA being the main gap insufficient testing and linkage to care. Our results are valuable to focus and intensify the treatment as prevention efforts.

SECCIÓN DE NEUMOLOGÍA

CONGRESO EUROPEO ENFERMEDADES RESPIRATORIAS - MADRID, ESPAÑA

INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES ASSOCIATED WITH MYOSITIS AUTOANTIBODIES: CLINICAL CHARACTERISTICS FROM A MULTICENTER LATIN-AMERICAN COHORT.

José Ernesto Juárez León, María Laura Alberti, Verónica Wolff, Felipe Reyes, Francisco Paulin, Leandro Fassola, Fabian Caro, Gabriel Carballo, Tamara Palavecino, Juan Carlos Díaz, Ivette Buendía Roldán, Mayra Mejía, Matías Florenzano, Jorge Rojas Serrano

Background: IIP with incomplete established criteria for CTD are an increasingly recognized group of patients and myositis autoantibodies are a common feature. Aims: To describe clinical characteristics and lung function evolution of a multicenter cohort of patients with a clinical diagnosis of IPAF with myositis autoantibodies. Methods: Retrospective multicenter cohort study (Argentina, Chile and Mexico). Baseline and follow-up records of individuals with IPAF diagnosis according to 2015 ATS/ERS criteria with myositis autoantibodies during November 2016 to November 2018 were collected. Multivariate analyses were performed to evaluate the relationship between lung function improvement (FVC ≥10%) and clinical variables. Results: 44 patients were identified with IPAF diagnosis, 77% were women with mean age (SD) 56.2 (15.1) years. ANA were present in 90% with nucleolar, fine speckled, and speckled patterns being the most frequent. The most common autoantibody was Ro-52 (50%) followed by Ku (38%) and PM-Scl-75 (26%). Most cases debuted with inflammatory patterns on HRCT at diagnosis: OP (43%) and NSIP (66%). Treatment was not standardized across centers, but corticosteroids plus MMF was the most frequent regimen (44%). Male gender was the best predictor for lung function improvement after treatment initiation (OR 17.4, p=0.02), while the rest of clinical variables included in our analyses were not. Conclusions: IPAF with myositis autoantibodies may portend a different prognosis and treatment response in comparison with other group of autoantibodies. Patients may benefit of early introduction of immunosuppressive regimens in the long-term.

MULTICENTRIC LATIN AMERICAN STUDY OF 211 PATIENTS WITH INTERSTITIAL LUNG DISEASE AND MYOSITIS RELATED ANTIBODIES

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INTRODUCTION: ILD is a common manifestation of patients with myositis related antibodies (MRA). The aim of our study is to describe the clinical and radiological features of a group of patients with ILD and MRA, and their association with the initial pulmonary function (PF). METHODS: Descriptive study of a multicentric cohort of patients evaluated between 2016-2018 in 3 ILD clinics in Argentina, Chile and

México. Descriptive statistics, univariate and multivariate analysis were performed. RESULTS: 184 patients presented initial ILD diagnosis or simultaneous with connective tissue disease (CTD). The majority were women, with a mean age of 57±12 years. Anti-Synthetase (AS) antibodies were the most frequent (Jo-1, PL-12, PL-7). Main CTD diagnoses were AS syndrome and ILD with autoimmune features (IPAF). Main extra-thoracic symptoms, more frequent HRCT patterns and PFTs are described in Table 1. Worse PF was defined as FVC <70% and/or DLCO <50%. ILD as initial diagnosis (OR 2.21; p 0.045) and NSIP/OP (OR 2.67; p 0.011) were associated with worse PF. Better PF was associated with dermatomyositis rash, arthritis (OR 2.47; 2.38 p <0.05) and ANA+ (OR 2.95; p 0.004). CONCLUSIONS: AS antibodies, NSIP and NSIP/OP patterns were the most frequent data, as reported in other cohorts. Worse PF could be related to the absence of extra-thoracic symptoms and "classic" antibodies of CTD, causing a delay in ILD diagnosis.

IDIOPATHIC PULMONARY FIBROSIS: MORTALITY TRENDS IN CHILE

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Introduction: The mortality rates of Idiopathic pulmonary fibrosis (IPF) are increasing in Europe and United States, but in Latin-American there are only some studies from Brazil and Argentina and they report low mortality rates. The aim of this study was to estimate the trends of IPF mortality rates in Chile. Material and methods: Descriptive ecologic study, deaths secondary to IPF (International Classification of Diseases 10: J84.0, J84.1, J84.8, J84.9) in patients of > 45 years old between 2002 and 2015 were obtained from a secondary database of the Ministry of Health of Chile and the population of the same age and period was obtained from the National Institute of Statistics, allowing to determine IPF mortality rates by each year, month and geographical location (region). The statistical analysis used was the Prais model. Results: A progressive increase in the IPF mortality rates in Chile was observed. It ranges from 18.5 per 100.000 in 2002 to 24.6 per 100.000 in 2015, with a slope trend of 0.27 per year (p = 0.013). Also, there were significant differences between geographical regions (p = 0.04), and higher rates of mortality were observed during winter months. Conclusions: The mortality of IPF in Chile is higher than the reported by other Latin-American studies and there is a significant increase on the mortality rates. Further research is needed to confirm whether the results are associated to actual increase on the mortality rates or linked to better diagnosis of IPF in addition to further epidemiologic studies to determine factors influencing both the death rates and upward trend. The results can then be used to evaluate what public intervention may be needed.

SECCIÓN DE REUMATOLOGÍA

ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY - MADRID, ESPAÑA

CHARACTERIZATION OF PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF) AND ITS COMPARISON WITH PATIENTS WITH SCLERODERMA-RELATED INTERSTITIAL LUNG DISEASE AND WITH IDIOPATHIC FIBROSIS

Karen Vergara, Silvana Saavedra, Felipe Reyes, Annelise Goecke, Caterina Chesta, Sebastian Chavez

Background: Diffuse parenchymal pulmonary diseases, called interstitial lung diseases, are a heterogeneous group of disorders that are classified together due to clinical, radiographic, physiological or similar pathological manifestations 1. The diagnosis of idiopathic interstitial pneumonias requires the exclusion of known causes of interstitial pneumonia. Identifying an underlying etiology is important for clinical perspectives because it impacts prognosis and treatment 2. A recent number of studies has shown that many patients diagnosed as idiopathic interstitial pneumonia have clinical elements that suggest an underlying autoimmune process without meeting established diagnostic criteria for connective tissue disease 3,4. Objectives: Our objectives were to characterize the clinical findings of patients who meet the IPAF criteria and compare them with the clinical characteristics of patients with scleroderma-related interstitial lung disease and patients with idiopathic pulmonary fibrosis. Methods: We retrospectively reviewed 254 patients hospitalized at the Hospital Clínico de La Universidad de Chile between January 2012 and June 2018 who had ICD-10 diagnosis of J84 (Other respiratory diseases principally affecting the interstitium) and J99.1 (Respiratory disorders in other diffuse connective tissue disorders). The electronic medical record was reviewed retrospectively to extract pertinent data. We applied IPAF criteria to this 254 patients. We then characterized the clinical, serological and morphological features of the IPAF cohort and compared outcomes to other ILD cohorts: scleroderma-related interstitial lung disease and idiopathic pulmonary fibrosis (IPF). Results: Of 254 patients screened, 17 patients met the IPAF criteria. Mean age was 60 years with a female predominance. The most frequent pattern by high-resolution computed tomography was NSIP present in 46.7%. The median of Forced Vital Capacity was 82%, and median of DLCO was 50%. 14 patients (82%) were treated with corticosteroids. 11 Patients (64%) used other immunosuppressants: 6 patients azathioprine, 4 mycophenolate and 1 patient used cyclophosphamide. One patient received a lung transplant in IPAF cohort. We identified 2 deaths in IPAF cohort, 6 in scleroderma-related interstitial lung disease and 30 in IPF cohort. IPAF cohort survival was worse than Scleroderma cohort and better than the IPF cohort. Conclusion: Our IPAF cohort is similar to the cohorts described in other studies, in relation to the age of diagnosis, female predominance and High-resolution Computed Tomography pattern. Also the trend in survival was similar to others previously described. Our study has limitations, the first one is related to the retrospective nature of the reviewed cohorts. Further prospective studies should be conducted for a more comprehensive evaluation of the evolution of these diseases and the impact of the treatments used.

PREVALENCE OF ANXIETY/DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS AT THE UNIVERSITY OF CHILE'S CLINICAL HOSPITAL AND THEIR ASSOCIATIONS WITH DISEASE ACTIVITY INDEXES AND QUALITY OF LIFE

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Background: Rheumatoid Arthritis is a chronic inflammatory disease with great impact in quality of life. Anxiety and depression could be frequently present in RA patients and may impact the disease activity evaluation. However psychological evaluation or therapy are not part of the standard of care of RA patients. Objectives: To evaluate the prevalence of anxiety/depression in rheumatoid arthritis patients in control at the University of Chile's Clinical Hospital and to investigate the association of anxiety/depression with disease activity and quality of life. Methods: The Hospital Anxiety Depression Scale (HADS) was applied to measure depression and anxiety in a cross-section patients with RA meeting the ACR/EULAR 2010 criteria in control at the University of Chile's Clinical Hospital. All patients included gave their inform consent. Demografic characteristics, Disease variables and activity, measure as DAS28-VHS, DAS-28 CRP, CDAI and SDAI and HAQ were evaluated at the same time. Spearman correlation, Fisher exact test, Chi-Square and Kruskal-Wallis test were used according to variables at evaluation. Statistical analysis was perform by Stata v12.1 sftware. The study was approved by the Hospital Ethic Review board. Results: 122 patients were enrolled in the study between december 2017 and December 2018. 103 (84.45%) were female. 56 (46%) had depression and/or anxiety according to HADS. 24% of the patients (n=24) had only depression. The severity of the depression symptoms was mild in 71%, moderate in 21% and severe in 8% of the patients. 42%, 40% and 18% of the patients with anxiety (n=55) had mild, moderate and severe anxiety symptoms respectively. The disease activity was significantly higher in patients with as compared to those without anxiety/depression, measure with all of the following indexes: DAS28-VHS (4.33 vs 2.75, $p<0.001$), DAS-28 CRP (4.13 vs 2.75, $p<0.001$), CDAI (15 vs 7 $p<0.001$) and SDAI (17 vs 7.5, $p<0.001$). The HAQ was also significantly higher in patients with anxiety/depression (1.18 vs 0.29, $p<0.01$). Conclusion: Depression/anxiety symptoms was very frequent in our cohort of RA patients. The disease activity measure with different indexes and the HAQ was significantly higher in the patients with depression/anxiety. It is possible that psychological factors influence the RA treatment outcomes. Therefore screening and therapy of anxiety and depression should be consider in the regular management of RA patients.

POSITIVE MRI OF THE SPINE AS IMAGING CRITERION IN THE ASAS CLASSIFICATION CRITERIA FOR AXIAL SPONDYLOARTHRITIS

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Background: MRI is a useful tool for the evaluation of patients with chronic back pain suspected of axial spondyloarthritis. As defined by ASAS classification criteria, MRI suggestive of axial spondyloarthritis is based on the presence of inflammatory lesions in the sacroiliac joints. However inflammatory lesions in the spine may also occur. A consensus definition for a positive MRI-spine was developed by OMERACT MRI working group. In this consensus a positive MRI-spine is described as the presence of ≥ 3 inflammatory lesions in the corner of the vertebrae (bone marrow edema lesions), whereas each lesion needs to be present on ≥ 2 consecutive slices. Objectives: The purpose of this study was to evaluate the presence of spinal inflammatory lesions on MRI performed between January, 2015 and December, 2015 in the Universidad de Chile Clinical Hospital. Methods: Data from MRI performed between January, 2015 and December, 2015 in the Universidad de Chile Clinical Hospital was collected. The patients were derived by a physician as part of the study of chronic back pain. Results: A total of 118 MRI were performed in this period, from which 8 showed evidence of spinal involvement without sacroileitis. The finding in MRI were: 3 patients with enthesitis of spinal ligaments, 2 patients with spondylodiscitis and 3 patients with bone marrow edema in the corner of the vertebrae. However, no patients fulfilled the OMERACT criteria for a positive MRI-spine (≥ 3 corner based inflammatory lesions). Patients with inflammatory lesions in the corner of vertebrae only showed 1 or 2 bone marrow edema sites. When we hypothetically added this criteria (assuming 2 bone marrow edema sites as a positive MRI-spine) to the ASAS-criteria for axial spondyloarthritis, only one patient could be classified via the imaging arm. Conclusion: Adding a positive MRI-spine as an imaging criterion to the ASAS-criteria for axial spondyloarthritis did not resulted in newly classified patients in this cohort. A combination of MRI-spine and MRI-SI had no incremental value compared with MRI-SI alone.

PREVALENCE AND SAFETY OF BIOLOGIC THERAPY IN A CHILEAN COHORT OF RHEUMATOID ARTHRITIS PATIENT, A RETROSPECTIVE STUDY

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Background: Interstitial lung disease (ILD) is a common extra-articular condition in rheumatoid arthritis (RA). New-onset ILD or ILD worsening has also been reported as a possible consequence of biologic therapy. These associations are based on case reports. The present study evaluated ILD prevalence and exacerbation among users of abatacept (T-cell inhibitor), rituximab (B-cell inhibitor), and anti-TNF α agents in a cohort of adult RA patients. Objectives: In the present study, we aimed to assess the safety of biologic therapy in patients with ILD associated to RA and patients without a history of ILD. Methods: Data from RA patients beneficiaries of the Ley Ricarte Soto (LRS) program, at the Hospital Clínico de La Universidad de Chile, who received abatacept, rituximab, or anti-TNF α agents for at least a year, were reviewed. Results: Seventy four patients were reviewed retrospectively between January 2016 and December 2018 (55 female; mean disease duration, 7 years; mean age, 55 years). Mean (SD) DAS 28 ESR was 6.9 (± 0.1) previously to initiate therapy. RA was

seropositive in 65 patients (87.8%). Eighteen patients (24.3%) had been previously diagnosed with ILD, with a median duration of 4 years. Most common patterns of RA-associated ILD were UIP (n=5 [46%]) and CPFE (n=3 [23.1%]). Patients with ILD at baseline as compared to patients without history of ILD were more frequently males (27.8% vs 7.5%, $p < 0.05$), had an older age (64 + 12 vs 52 + 13, $p < 0.005$), a higher positivity of anti-cyclic citrullinated protein antibodies (CCP) (87.5% vs 80%, $p < 0.005$) and a more frequent history of smoking (50% vs 28%, $p < 0.005$). The treatment received by patients with RA-associated ILD previously to start biologics under LRS program were: methotrexate [MTX] (n=5), leflunomide [LFN] (n=14), sulfasalazine [SSZ] (n=8), etanercept [ETN] (n=1), adalimumab [ADA] (n=1), abatacept ABA (n=3) and rituximab [RTX] (n=1). When the patients were enrolled to LRS program 83.3% received abatacept, 11.1% anti-TNF α agents and 5.5% rituximab. All patients with RA-associated ILD remained stable at 1 year follow-up. RA patient without ILD who started biologic therapy did not had ILD at 1 year follow-up. Conclusion: There were no significant differences in the risk of complications between patients with a baseline history of ILD receiving different biologic agents. The present study found that male sex, older age, seropositive RA and patients with a history of smoking, were at increased risk for developing ILD. These data are largely consistent with those of the existing literature. Patients without a history of ILD did not develop pulmonary complications, but these data may be affected by the short follow-up window. Further studies are needed to evaluate the risk of RA-associated ILD and its complications.

AMERICAN COLLEGE OF RHEUMATOLOGY ANNUAL MEETING 2019 - ATLANTA, USA

SAFETY OF BIOLOGICAL DMARD IN PATIENTS WITH INTERSTITIAL LUNG DISEASE FROM A CHILEAN COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background/Purpose: Interstitial lung disease (ILD) is a common pulmonary manifestation of rheumatoid arthritis (RA) that may be related to the inflammatory process itself, to infectious complications, and/or to the therapy. Biological disease-modifying antirheumatic drugs (bDMARD) have dramatically improved the outcome of RA, but an increasing number of reports have described the potential lung toxicity of this group of drugs. Methods: Retrospective cohort study using data from RA patients beneficiaries of the Ley Ricarte Soto program, at the Hospital Clínico Universidad de Chile, was conducted to assess ILD prevalence and exacerbation, among users of abatacept (ABA), rituximab (RTX), and anti-TNF α agents. Clinical findings and laboratory data were collected from medical records. The presence or progression of ILD on HRCT was evaluated by a rheumatologist, a pneumonologist and a radiologists who have expertise in assessing ILD, all part of the Rheumatic Lung Group at our Hospital. Results: 126 RA patients were included; 85% female, mean (SD) age 55 (13.4) years, mean disease duration 11 (8.7) years. RA was seropositive in 108 patients (85.7%). DAS28 ESR was 6.1 (1.2) previously to initiate bDMARDs. A total of 30 patients (23.8%) had been previously diagnosed with ILD, most common patterns on HRCT were UIP (n=10[33%]) and bronchiolar abnormalities (n=4[13.3%]). Patients with as compared to without ILD at baseline were more frequently males (53 vs 15%, $p < 0.05$), had an older age (62.6 + 11.9 vs 55 + 13.4, $p < 0.005$), a higher positivity of anti-CCP (73 vs 47.6% $p < 0.005$) and a more frequent history of smoking (43 vs 21%, $p < 0.005$). The patients with a history of ILD were also, significantly more likely to receive ABA (n=24 [82.8] % versus n=35 [36.1%] without ILD; $p < 0.001$) and significantly less likely to receive anti-TNF therapy (n=3 [10.3%] versus n=57 [58.7 %] without ILD; $p < 0.001$). Only 6 patients received RTX, two of them with history of ILD. All patients with RA-associated ILD remained stable at 28 month follow-up. In the group of patients without a history of ILD, only one developed an organizing pneumonia that responded well to corticosteroids and was not related to the biological therapy. Conclusion: Our data show that, in a real-world setting, there were no significant differences in the risk of complications between patients with or without a baseline history of ILD receiving different biologic agents. In our Cohort, bDMARDs were not associated with new ILD either. These data may be affected by the short follow-up window and the preference for the use of ABA, over anti-TNF α agents, as initial biological therapy in RA-ILD.

IGG4-RELATED DISEASE, CLINICAL SERIES ON CHILEAN PATIENTS

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Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic fibroinflammatory condition that can affect almost any organ. Gold standard for diagnosis, biopsy, can show lymphoplasmacytic infiltration, storiform fibrosis, obliterative phlebitis and IgG4+ plasma cell infiltrate. High serum IgG4 levels is observed only in 50% of patients. Disease is more frequent in males, around 60 years old, affecting one or multiple organs with subacute development of tumors or organomegaly. Lymphadenopathies are common, and 40% of patients have a history of allergies. Umehara's diagnostic criteria (2012), based on clinical features, serum IgG4 levels and histopathology are the most accepted. Disease was described in 2003, and Chilean reports are scarce. We describe clinical, laboratory, histopathology findings, and treatment on Chilean IgG4-RD patients. Methods: We analyzed retrospectively clinical records of 48 patients with IgG4-RD from nine medical centers. Patients with possible, probable and definitive diagnosis, according to Umehara criteria, were included. Results: Our cohort was 56% male, with a mean age of 52 (18-76) years. Histological confirmation of IgG4-RD was obtained in 44 of 45 patients who underwent a biopsy. Twenty-three percent of patients had allergic background, 27% had eosinophilia and 43% had elevated plasma levels of IgG4 (≥ 135 mg/dl). The clinical involvement was: pleural and lung disease 38%, kidney 27%, orbital pseudotumor 25%, lymphadenopathy 21%, retroperitoneal fibrosis 19%, aortitis 19%, sialoadenitis 17%, pancreas 17%, pericardium 15% and meninges in 8%. There were three patients with hypophysitis and two with mediastinal fibrosis. Multiple organ involvement (≥ 2 organs), observed in 69%, was significantly

more frequently in males ($p < 0.05$). There was a statistically significant association between renal disease and low complement levels ($p < 0.01$). All patients who had renal or pulmonary disease had multiple organ involvement. Multiple organ involvement was not related with immunosuppressive treatment requirement. Pathology confirmation, in 44 patients, showed: lymphoplasmacytic infiltrate in 43 (98%), storiform fibrosis in 29 (66%) and none had obliterative phlebitis. All tissues had diagnostic IgG4 (+) immunohistochemical staining. Storiform fibrosis was present in all lung and kidney biopsy, but only half of salivary gland, orbital and retroperitoneal tissue. Regarding treatment, all patients received glucocorticoids. In 30 patients (63%) was required immunosuppressive treatment: azathioprine, followed by methotrexate and mycophenolate mofetil were drugs most used. Rituximab was used in 8 patients. Clinical response was good, but one patient dies because extensive mediastinal disease. Conclusion: IgG4-RD in Chilean patients is similar that described elsewhere. In most of patients serum levels of IgG4 were normal, then biopsy was essential to diagnosis. Multiple organ involvement was frequent, being pleuropulmonary, kidney, orbital and lymph node most usual localizations. Renal and pulmonary localization occurred always in context of multiorgan disease.

MYOSITIS RELATED ANTIBODIES AND INTERSTITIAL LUNG DISEASE: VARIABLES ASSOCIATED WITH BASELINE LUNG FUNCTION AND FUNCTIONAL IMPROVEMENT: RESULTS FROM A MULTICENTRIC LATIN-AMERICAN COHORT

Veronica Wolff, Maria Laura Alberti, Felipe Reyes, Ernesto Juarez, Jorge Rojas-Serrano, Fabian Caro, Ivette Buendia, Mayra Mejia, Matias Florenzano, Francisco Paulin

Background/Purpose: Idiopathic inflammatory myopathies (IIM) comprise a group of autoimmune diseases associated to different myositis related antibodies (MRA), that determine distinct phenotypes but share some symptoms, including myositis, skin rash and high prevalence of interstitial lung disease (ILD), the latter being particularly associated with some MRA. Some patients with MRA and ILD will fulfill IIM classification criteria, but others will not and may be classified as ILD with autoimmune features (IPAF). The aim of our study is to describe the clinical and radiological features of a group of patients with ILD and MRA, and their association with baseline and longitudinal pulmonary function (PF). **Methods:** Descriptive study of a multicentric cohort of 211 patients evaluated between 2016-2018 in 3 multidisciplinary ILD clinics in Argentina, Chile and México. Every patient was confirmed to have ILD by thoracic high-resolution computed tomography (HRCT). Descriptive statistics, univariate and multivariate analysis were performed. **Results:** 211 patients were included, (Chile = 119, México = 50 and Argentina = 42). Most patients were women (77,4%), mean age of 57 \pm 12 years. In 146 patients (70%) ILD was diagnosed first, in 43 patients (18%) ILD and connective tissue disease (CTD) were diagnosed simultaneously, and CTD was diagnosed first in 25 patients (12%). Mean interval between ILD and CTD diagnosis was 7.6 months (Table 1). Anti-Synthetase (AS) antibodies were the most frequent (Jo-1, PL12, PL-7), followed by Ro-52, PM-Scl 75-100 and Ku. Most frequent CTD diagnoses were AS syndrome and IPAF. Most prevalent HRCT patterns were non-specific interstitial pneumonia /organizing pneumonia overlap (NSIP/OP) and NSIP (Table 1). Worse baseline PF was defined as forced vital capacity (FVC) $<$ 70% and/or diffusion capacity of carbon monoxide (DLCO) $<$ 60% at debut. Worse baseline PF was associated to ILD alone as initial diagnosis, NSIP/OP HRCT pattern, absence of dermatomyositis rash and absence of positive ANA and Ro (uni/multivariate analysis, Table 2). Functional improvement was defined as an increase of FVC greater than 10% in follow up. 121 patients with $>$ 3 months of follow-up were included. Functional improvement was associated with absence of ILD as the first manifestation of disease and absence of sclerodactily, presence of OP HRCT pattern and mechanic's hands (uni/multivariate analysis, Table 3). First line immunosuppressive treatments consisted in corticosteroids (CS) associated with a CS sparing agent like mycophenolate mofetil, azathioprine, cyclophosphamide, leflunomide, tacrolimus or rituximab (Table 1). **Conclusion:** In our MRA-ILD cohort, AS antibodies and AS Syndrome were the most common findings, followed by IPAF. NSIP and NSIP/OP were the most prevalent HRCT patterns. Worse baseline PF could be related to the absence of extra-thoracic symptoms and "classic" antibodies of CTD (e.g ANA, Ro), causing delay in diagnosis and treatment. On the contrary, better functional improvement could be related to the presence of extra-thoracic signs that allow an opportune diagnosis and therapy, and more acute-subacute forms of ILD, as OP HRCT pattern.

TREATMENT WITH DEXAMETHASONE AND MONOPHOSPHORYL LIPID A REMOVES DISEASE-ASSOCIATED TRANSCRIPTIONAL SIGNATURES IN MONOCYTE-DERIVED DENDRITIC CELLS FROM RHEUMATOID ARTHRITIS PATIENTS AND CONFERS THE ABILITY TO MODULATE CD4+ T CELL RESPONSES

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Background/Purpose: Tolerogenic dendritic cells (ToDCs) are promising tools for therapy of autoimmune diseases such as rheumatoid arthritis (RA). Here we characterise ToDCs from RA patients modulated with dexamethasone and monophosphoryl lipid A (MPLA) concerning gene expression, phenotype, cytokine profile, migratory properties and T cell-stimulatory capacity to explore their suitability for autologous cellular therapy. **Methods:** ToDCs were generated from monocytes of 9 RA patients, meeting 2010 ACR/EULAR criteria, and 10 healthy controls, using dexamethasone for tolerization and MPLA for activation (MPLA-tDCs). The phenotype of MPLA-tDCs and their migratory behaviour towards lymphoid chemokines were analysed by flow cytometry and transwell assays. Cytokine secretion of MPLA-tDCs and their ability to activate autologous antigen-specific T cells was determined by flow cytometry and ELISA. Genome-wide transcriptional analysis was performed and differential expression was defined by a false discovery rate of ≤ 0.05 . **Results:** MPLA-

tDCs derived from RA patients, exhibited characteristics of semi-mature DCs (Fig 1), such as: reduced expression of costimulatory and coactivation molecules and the capacity to migrate in response to ligands of lymph node homing chemokine receptors CCR7 and CXCR4. These cells displayed an anti-inflammatory cytokine profile inducing hyporesponsiveness and IL-10 secretion of autologous CD4+ T cells specific to synovial antigens. Global transcriptome analysis demonstrated that treatment with dexamethasone and MPLA overcame RA-associated effects on gene expression profiles of monocyte-derived DCs (Fig 2). Figure 1.pdf Figure 1. MPLA-tDCs from rheumatoid arthritis patients and healthy controls display low expression of maturation markers and high TLR2 Conclusion: Monocyte-derived DCs of RA patients have the potential to develop stable tolerogenic features when modulated with dexamethasone and MPLA, irrespective of disease status. The ability of MPLA-tDCs to impair T cell responses to synovial antigens validates their potential for the treatment of RA.

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ANNUAL CONGRESS ESICM LIVES 2019 - BERLÍN, ALEMANIA

ELECTRICAL IMPEDANCE TOMOGRAPHY PREDICTS LUNG STRAIN DETERMINED BY COMPUTED TOMOGRAPHY: A TRANSLATIONAL PROOF OF CONCEPT STUDY

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Background and study objective. Mechanical ventilation can induce lung injury, phenomenon known as VILI. An important mechanism of the VILI is the excessive global strain. Even more, regional strain is spatially correlated with regional inflammation. Information on regional strain could help to develop protective ventilatory strategies. The standard for this evaluation is computed tomography (CT), which does not allow continuous assessment and exposes to radiation. Electrical impedance tomography (EIT) is able to monitor changes in regional lung ventilation and it could become a surrogate for CT-measured strain. Objectives. To compare the global and regional strain measured by CT with the change in electrical impedance (ΔZ) adjusted by anthropometric measurements in pigs and ARDS patients. Méthodes. The study was approved by Ethics Committee. Three pigs, mechanically ventilated using VT of 250 and 500 mL, underwent whole-lung CT at end-inspiration and end-expiration with PEEP 10 and 20 cmH₂O, before and after lung injury induction. Eleven ARDS patients also underwent whole-lung CT during at end-expiration and end-inspiration with PEEP 5 and best PEEP according EIT. A biomechanical analysis was employed to construct 3D maps of the volumetric strain. CT and EIT examinations were performed simultaneously. Strain maps were divided into 4 regions of interest "ROI" (Upper and Lower, Right and Left), coinciding spatially with the regions upon which inflation was calculated for EIT. Due to repeated measures in pigs and humans, linear mixed effect models were performed to predict lung strain and aeration measured by CT from ΔZ obtained by EIT, adjusting for known confounders. For all models, individual pigs or humans were considered as random effects, and PEEP as repeated measures. Diagnostic performance of EIT-based predictions of lung strain was evaluated by the Lin's concordance coefficient (LCC) and Bland-Altman Graph. Results. In pigs, linear association for global strain was accurate ($R = 0.974$, p -valor < 0.001), and large positive relations were found at different regions of interest. In humans, linear association at global, as well as in many lung ROI were high and positive with $R > 0.932$. Agreement of lung strain measured by CT and predicted by EIT-based models were excellent in overall terms in humans (LCC > 0.95). Conclusion. The change in electrical impedance provides a noninvasive assessment of global and regional strain, without radiation at bedside.

SERVICIO DE UROLOGÍA

XXXVIII CONGRESO CONFEDERACIÓN AMERICANA DE UROLOGÍA - BUENOS AIRES, ARGENTINA

VAPORIZACIÓN PROSTÁTICA CON LÁSER THULIUM (THUVAP), UNA TÉCNICA EFECTIVA Y SEGURA PARA EL MANEJO DEL CRECIMIENTO PROSTÁTICO BENIGNO (CPB) DE MEDIANO VOLUMEN

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Introducción. El desarrollo de la cirugía prostática endoscópica con láser se ha posicionado como una técnica segura y eficaz para el tratamiento del crecimiento prostático benigno (CPB)¹. La vaporización prostática con laser Thulium (ThuVap) ha sido descrita como una forma segura para el tratamiento del CPB². Hasta el momento, hay pocas series descritas de ThuVap en Latinoamérica. Nuestro objetivo es describir los resultados y complicaciones de una serie de pacientes tratados con ThuVap. Materiales y Métodos. Revisión prospectiva de pacientes operados mediante ThuVap entre los años 2016 y 2019 en un único centro. Se registraron variables demográficas, quirúrgicas y funcionales pre y post operatorias. Resultados. Se registraron 80 pacientes. La edad promedio fue de 66 ± 9 años, PSA preoperatorio promedio $4,07 \pm 3,66$ ng/dL, Qmax promedio $10,7 \pm 1,9$ mL/s, volumen prostático $77,7 \pm 38$ mL. El tiempo quirúrgico promedio fue de $93,8 \pm 46,1$ min. El promedio de días con sonda vesical fue de 3 ± 2 días, y el promedio de días de hospitalización fue de $2,6 \pm 1,8$ días. El Qmax promedio a los 3 meses fue de $22,6 \pm 8,6$ mL/s. Hubo 10 pacientes con complicaciones post operatorias (12,5%), de las cuales solo 1 requirió hospitalización (1,2%). Conclusiones. La vaporización prostática con láser Thulium se presenta como una opción segura y

eficiente para el manejo de CPB de mediano volumen.

ENUCLEACIÓN PROSTÁTICA CON LASER THULIO Y HOLMIO: COMPARACIÓN DE RESULTADOS CON ADENOMECTOMÍA PROSTÁTICA TRANSVESICAL

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Introducción. El desarrollo de la cirugía prostática endoscópica con laser se ha posicionado como una técnica segura y eficaz para el tratamiento del crecimiento prostático benigno (CPB). La enucleación endoscópica con láser compete con la cirugía prostática abierta para el tratamiento de próstatas de gran tamaño (mayores de 80 gramos) con beneficios en términos de reducción del sangrado, de los días de hospitalización y retorno a las actividades cotidianas. El objetivo de este trabajo es comparar resultados intra y post operatorios entre enucleación prostática laser (EPL) con Holmio y Thulio y adenomectomía prostática transvesical (ADTV). **Materiales y Métodos.** Revisión retrospectiva de pacientes sometidos a enucleación prostática con laser (HoLEP y ThuLEP) y a ADTV entre 2016 y 2019. Se incluyeron variables demográficas y datos perioperatorios. **Resultados.** Se incluyeron 102 pacientes (51 ADTV, 25 HoLEP y 26 ThuLEP). Los grupos fueron comparables en edad (66+ 8 años), PSA preoperatorio (4,65 ng/mL), y tamaño prostático (96 =79-120 gr.). El tiempo operatorio de EPL fue 130 minutos vs 80 minutos para ADTV ($p<0,0001$). La velocidad de resección fue de 0,65 gr/min para EPL vs 1,36 gr/min para ADTV. El tiempo de sonda uretral post operatorio fue 3.0 vs 7.0 días ($p<0,0001$) y los días de hospitalización de 2.0 vs 7.0 días ($p<0,0001$) a para EPL y ADTV respectivamente. Hubo 16/51 complicaciones en ADTV vs 15/51 en EPL. Según la clasificación de Clavien-Dindo, en EPL el 93,3% de las complicaciones fueron grado I y una grado II. En ADTV el 83,3% fueron grado I y hubo dos grado III. **Conclusiones.** La enucleación prostática con laser para próstatas de gran tamaño es una técnica segura con similar tasa de complicaciones, pero un tiempo quirúrgico más prolongado que ADTV. Sin embargo, presenta significativamente menos días de uso de sonda y de hospitalización.

EVALUACIÓN DEL NUEVO URETEROSCOPIO DIGITAL DESCARTABLE WISCOPE: PRIMEROS 100 CASOS

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Introducción: La utilización de ureteroscopios flexibles desechables para el tratamiento de litiasis ureterales y renales está en aumento. Nuestro grupo evaluó la efectividad medida con la tasa libre de cálculos y tiempo operatorio, así como la seguridad medida por las complicaciones inmediatas y tardías, del nuevo equipo digital Wiscope de OTU Medical. **Método:** Estudio retrospectivo durante un periodo de 11 meses. Se registraron las características clínicas de los pacientes, los datos intraoperatorios, la presencia de complicaciones y tasa libre de cálculos. Se excluyeron pacientes donde se realizó cirugía endoscópica intrarrenal combinada y evaluación de tumores de vía urinaria superior. **Resultados:** Se realizaron 105 procedimientos. El 62% fueron mujeres, el 70% de los pacientes tenían piedras únicas, en este grupo la ubicación fue de un 23% cáliz inferior, 22% cáliz medio, 12% cáliz superior, 19% en la pelvis renal y 24% en el uréter proximal. El tamaño y densidad promedio de litiasis fueron 14,5 mm y 1008 UH respectivamente. En el 30% pacientes tenían litiasis múltiples con diferentes ubicaciones, en este grupo el tamaño promedio por sumatoria de diámetros máximos fue de 30,2 mm. Se utilizó láser de holmio de 30 w, la energía promedio fue de 13,5 kJ y la fibra más utilizada fue la de 272 um (88%). El tiempo operatorio promedio fue de 76 min. El 45% de los pacientes tenía doble jota previo, y el 87% quedó con doble jota posterior al procedimiento. En el 48% de los casos se evaluó la tasa libre de cálculos, siendo un TC sin contraste el método más frecuente en el 88% de este grupo. Hubo litiasis residual significativa en el 48% de los estudiados. El 76% de los casos se realizaron de forma ambulatorio, y presentaron complicaciones el 16%, mayormente infecciones y dolor por el catéter. 12 pacientes consultaron en el servicio de urgencia y 7 pacientes requirieron rehospitalización de urgencia. No tenemos complicaciones tardías reportadas. **Conclusión:** Wiscope es seguro y efectivo en el tratamiento de litiasis urinarias. Consideramos que su utilización es fácil con una curva de aprendizaje similar a otros equipos con características parecidas disponibles en el mercado.

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

29 WORLD CONGRESS ON ULTRASOUND - BERLÍN, ALEMANIA

ASSESSMENT OF FETAL RIGHT VENTRICULAR SYSTOLIC FUNCTION: NOMOGRAMS OF FRACTIONAL AREA CHANGE BY 2D-ECHOCARDIOGRAPHY

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Objectives. Right ventricular (RV) fractional area change (FAC) is a 2D-echocardiographic parameter to assess RV global systolic function. Fetal reference ranges are not yet available. Our aims were: to study prenatal RV FAC feasibility and reproducibility and to construct nomograms for RV FAC and end-diastolic and end-systolic RV areas throughout gestation. **Methods.** Prospective cohort study including 602 low-risk singleton pregnancies undergoing a fetal echocardiography from 18-41 weeks of gestation. RV end-diastolic and end-systolic areas were measured following standard recommendations for ventricular dimensions and strict landmarks to identify the phases of the cardiac cycle. RV FAC was calculated as: $[(ED \text{ area} - ES \text{ area}) / ED \text{ area}] \times 100$. RV FAC intra- and inter-observer reproducibility was

evaluated in 45 fetuses by calculating the interclass correlation coefficient (ICC). Parametric regressions were tested to model each parameter against gestational age (GA) and estimated fetal weight (EFW). Results. RV areas and FAC were successfully obtained in ~99% of fetuses with acceptable reproducibility [FAC ICC (95% confidence interval): 0.69 (0.44-0.83)]. Nomograms were constructed for RV end-diastolic and end-systolic areas and FAC. RV areas showed a quadratic and logarithmic increase with GA and EFW, respectively. In contrast, RV FAC showed a slight quadratic decrease throughout gestation (figure 1). The best models for RV areas and FAC were a second degree polynomial. Conclusions. RV FAC is a feasible and reproducible parameter to assess RV systolic function in fetal life. We provide nomograms adjusted by both GA and EFW.

FETOPLACENTAL DOPPLER IDENTIFIES SMALL FETUSES WITH INCREASED CONCENTRATIONS OF CORD BLOOD ERYTHROPOIETIN

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Objectives. Chronic hypoxia is a powerful stimulus for the synthesis of erythropoietin (EPO) in the fetus resulting in an increase in erythrocyte production and in an increase in the oxygen-carrying capacity. We sought to describe the association between fetoplacental Doppler with cord blood EPO in small for gestational age (SGA) fetuses. **Methods.** A nested case-control study within a prospective cohort study including 124 controls (birthweight > p10) and 209 SGA cases (BW < p10). Cases and controls were followed-up with fetal biometry and fetoplacental Doppler. Cord blood concentrations of EPO were determined at delivery as a surrogate of chronic intrauterine hypoxia. Logistic regression predictive models evaluating the performance of fetal biometry and fetoplacental Doppler for the identification of chronic hypoxia were appraised. **Results.** Cord blood plasmatic EPO concentrations were significantly higher in SGA fetuses compared to controls (29.8 [17.2–58.7] vs 22.4 pg/mL [14.3–52.4], $p=0.05$). In 87 (41.6%) of SGA fetuses, EPO was above 90th centile. Among SGA fetuses, those with cord blood EPO concentrations above >90th centile presented non-significant differences in EFW centile [3 (1–9) vs 3 (1–8), $p=0.6$] and ductus venosus z-score [0.11 (-0.91–0.95) vs. -0.33 (-0.95–0.56), $p=0.3$], but higher uterine artery (UtA) z-score [1.42 (-0.58–2.95) vs 0.30 (-0.64–1.25), $p=0.01$] and lower cerebroplacental (CPR) ratio z-score [-1.17 (-1.87–0.31) vs -0.50 (-1.02–0.16), $p=0.0001$] than those with EPO <90th centile. Univariate regression analysis demonstrated that in SGA fetuses, MCA and CPR were significantly associated with higher concentrations of EPO. After multivariate analysis, MCA Doppler <5th centile and UtA Doppler >95th centile were the strongest predictors of cord blood EPO >90th percentile (OR=3.1 (1.62–5.9) and 18.8 (2.36–149.5) respectively). **Conclusions.** Uterine artery and MCA Doppler showed a strong association with increased cord blood EPO supporting its prognostic role in SGA.

FETOPLACENTAL DOPPLER FOR THE IDENTIFICATION OF CARDIAC DYSFUNCTION IN SMALL-FOR-GESTATIONAL-AGE FETUSES

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Objectives. Fetal cardiovascular dysfunction has been described as an adaptive mechanism to placental insufficiency with adverse short and long term consequences. However, only a proportion of small for gestational age (SGA) fetuses will present this cardiovascular adaptation. The objective of this study was to describe the association between fetal biometry parameters and fetoplacental Doppler with cardiac dysfunction in SGA fetuses. **Methods.** Nested case-control study including 192 AGA pregnancies (BW > 10th centile) and 240 SGA cases (BW < 10th centile). Cord blood concentrations of B-type natriuretic peptide (BNP) were determined at delivery to assess cardiac dysfunction. Logistic regression analyses evaluating the performance of fetal biometry and fetoplacental Doppler for the identification of fetal cardiac dysfunction were appraised. **Results.** Cord blood plasma BNP concentrations in AGA and SGA were 11.5 [6.61–18.02] and 18.3 [8.98–33.08] pg/mL, respectively ($p < 0.0001$). In 57 (23.8%) of SGA, BNP was above 90th centile. SGA fetuses with CB BNP >90th centile presented lower EFW centile [2 (0–5) vs. 4 (1–9), $p=0.001$], higher uterine artery (UtA) z-score [2.02 (-0.46–3.17) vs. 0.25 (-0.81–1.22), $p=0.001$] and lower cerebroplacental ratio z-score [-1.46 (-2.12–0.55) vs. -0.55 (-1.13–0.11), $p < 0.0001$] than those with BNP <90th percentile. Ductus venosus (DV) was also higher in this group [0.48 (-0.52–1.20) vs. -0.36 (-1.02–0.48), $p=0.005$]. Univariate regression analysis demonstrated that in SGA all fetoplacental Doppler parameters, but DV, an EFW < 3rd centile and delivery < 34 weeks were highly associated with fetal cardiac dysfunction (BNP >90th centile). Multivariate analysis demonstrated that UtA Doppler >95th centile, MCA <5th percentile and delivery < 34 weeks were the strongest predictors of BNP >90th percentile (OR = 2.4 (1.16–5.13), 7.19 (1.59–32.39) and 8.8 (2.50–30.96), respectively). **Conclusions.** UtA and MCA Doppler are significantly associated with fetal cardiac dysfunction among SGA fetuses.

IS FIRST TRIMESTER SALIVA PROGESTERONE LEVEL ASSOCIATED WITH SPONTANEOUS PRETERM DELIVERY?

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Objectives. The aim of this pilot study was to determine whether first trimester saliva progesterone (SPr) is altered during the first trimester of pregnancy and its role as a screening test for spontaneous preterm delivery (sPTD). **Methods.** Saliva progesterone together with maternal characteristics and biophysical markers (cervical length and uterine artery Doppler) were assessed at 11-14 weeks' gestation in a nested case-control study which included 30 women who later developed sPTD and 57 matched controls delivering at term. Saliva samples were centrifuged, and the supernatants were frozen at -80°C until samples were analysed. The distribution of measured SPr and biophysical markers in the term and sPTD groups were compared. Logistic regression analysis was used to evaluate if any variable was

significantly associated with sPTD. Results. The mean value of SP_r in the first trimester of pregnancy was significantly lower in women who delivered prematurely compared to controls (426.3 ± 24.7 pg/mL vs 512.3 ± 26.3 pg/mL, $p=0.037$), being also lesser in those women who delivered below 34 weeks (387.0 ± 41.0 pg/mL vs 511.8 ± 25.8 pg/mL, $p=0.050$). Neither cervical length nor uterine artery Doppler were associated with sPTD. Logistic regression analysis demonstrated that a combination of maternal characteristics and SP_r provided a significant contribution in the prediction of sPTD before 34 and 37 weeks, being the detection rate, at a fixed 10% false positive rate, at around 45% and 20%, respectively. Conclusions. This pilot study concluded that saliva progesterone level is reduced during the first trimester of pregnancy in women who later delivered prematurely, and it might be particularly useful in predicting preterm delivery before 34 weeks of gestation.

AGENESIS OF THE DUCTUS VENOSUS: PRENATAL DIAGNOSIS, PERINATAL OUTCOMES AND SYSTEMATIC REVIEW OF LITERATURE

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Objectives. The aim of this study is to describe the prenatal diagnosis and perinatal outcomes in fetuses with agenesis of the ductus venosus (ADV) and to perform a systematic review of literature. Methods. Retrospective descriptive study of all cases with prenatal diagnosis of ADV, occurring between 2011 and 2018 in three tertiary centres. We reviewed patient data of all ADV cases. We also conducted literature search of ADV in MEDLINE, PUBMED, and SCIELO, data bases. Series with 10 or more cases were included. Results. Ten articles were reviewed and our cases were included in the analysis. A total of 283 cases of ADV were included, 36 ours and 247 previously published. In our series mean maternal age was 34 years (16-43 y) and mean gestational age at diagnosis was 17 weeks (11-37 w). ADV was diagnosed at 11-14 screening in 17 patients (47%), 11 with increased nuchal translucency. 19 (53%) were diagnosed at the second-trimester ultrasound, 17 had a major abnormality associated. Shunt was intrahepatic in 22 patients, extrahepatic in 14. In the extra hepatic group, 11 communicated directly to inferior vena cava, 2 to right atrium, and 1 to the iliac vein. Chromosome analysis was performed in 19 of 36 cases; 12 of the fetuses were aneuploid (9 Turner syndrome and 3 Down's syndrome). As for perinatal results, of 36 patients 9 died; 30 had some anomaly (aneuploidy or major abnormality associated), and 6 were healthy. Conclusions. ADV is a rare condition and is associated with aneuploidies, especially Turner Syndrome. It is highly associated with major abnormalities; especially cardiac malformations and it is associated with poor perinatal outcomes (especially extrahepatic). Systematic review, including our series, shows similar perinatal outcomes.

ULTRASOUND REFERENCE RANGES FOR FETAL PRENASAL THICKNESS AND ITS ROLE AS SCREENING TEST FOR CHROMOSOMAL ABNORMALITIES AT 16–25 WEEKS OF GESTATION

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Objectives. Aims of this study were to establish prenasal thickness (PNT) reference ranges throughout gestation and to evaluate its value for screening for chromosomal defects in a Chilean population. Methods. To determine PNT reference ranges for our population, the fetal profile was examined in 3,904 consecutive euploid singleton pregnancy between 16 to 41 weeks gestation since April 2010 to October 2016. The data was log transformed and fitted using a second-order polynomial equation; To determine the role of PNT as second trimester screening test for fetal aneuploidy, 3,249 pregnant women who underwent a routine ultrasound scan at 16–25 weeks gestation were included. Detection rate (DR), false positive rate (FPR) and likelihood ratio (LR) for increased PNT (>95th percentile) were obtained. Results. There was a positive correlation between PNT and gestational age ($r^2=0.38$; $p<0.001$, second-order polynomial). Nomograms including the 5th, 50th and 95th percentiles were created for each gestational age. Expected PNT increased from 2.7 mm at 16 weeks to 7.6 mm at 41 weeks. In the group of patients who were scanned between 16 to 25 weeks, there were 33 cases with chromosomal abnormalities, being 19 trisomy 21, 8 trisomy 18 and 3 trisomy 13. The PNT was increased in 4.9% of the 3,216 chromosomally or phenotypically normal fetuses and in 57.9% of the 19 fetuses with trisomy 21, being, therefore, the positive LR around 12. By contrast, the PNT was increased in just two of the 11 cases of trisomy 18 and 13. With a 5% false positive rate, the detection rate for trisomy 21, combining PNT and maternal age, was 68.4%. Conclusions. PNT increases throughout gestation in chromosomally normal fetuses, although this is much thicker in abnormal karyotype, and particularly in trisomy 21. PNT might be included as a second trimester soft marker for chromosomal abnormalities.

VEIN OF GALEN ANEURYSM: PRENATAL DIAGNOSIS, PERINATAL OUTCOMES AND SYSTEMATIC REVIEW OF LITERATURE

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Objectives. The aim of this study is to describe the clinical behaviour of pregnancies with prenatal diagnosis of Vein of Galen aneurysm (VGA), and perform systematic review of literature. Methods. We performed a retrospective descriptive study of all cases with prenatal diagnosis of VGA, occurring between 2010 and 2018 in three tertiary centres. We reviewed patient data of all VGA cases. We also conducted literature search of VGA in MEDLINE, PUBMED, and SCIELO, data bases. Series with 5 or more cases were included. Results. Three articles were reviewed and our cases were included in the analysis. A total of 57 cases of VGA were included, 8 ours and 49

previously published. In our series mean gestational age at diagnosis was 32.3 weeks (25-36 weeks). At time of diagnosis 6/8 present heart failure and only 1/8 with an associated brain injury. Perinatal outcomes of our series and systematic review are showed in table 1. Conclusions. VGA is a rare malformation with high perinatal mortality, most frequently due to heart failure. However, survival patients have a good prognosis. To identify prognostic factors is relevant to manage and counseling patients with prenatal diagnosis of VGA.

DOPPLER EVALUATION OF SYSTOLIC TO DIASTOLIC DURATION RATIO IN NORMAL FETUSES FROM 18 TO 41 WEEKS OF GESTATION

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Objectives. The systolic (S) to diastolic (D) duration ratio (S/D) has been proposed as a useful index to assess ventricular function in some pediatric cardiopathies. Prenatal reports on S/D are scarce and nomograms are not available. We aimed to establish normal values for left (LV) and right ventricular (RV) S/D ratios in normal fetuses and to investigate its relation to heart rate (HR), gestational age (GA) and estimated fetal weight (EFW). **Methods.** Prospective cohort study including 602 low-risk singleton pregnancies (GA 18-41 weeks). Spectral Doppler signals of LV and RV inflow were obtained. D was defined from E-wave onset to A-wave termination and S from A-wave end to the onset of the next E-wave. Relations between S/D ratios and HR, GA and EFW were analysed by uni and multivariate regression. Interclass correlation coefficient (ICC) was used to assess intra and inter-observer reproducibility in 45 fetuses. **Results.** S/D ratios were successfully obtained in 95% of fetuses with good reproducibility (ICC>0.85). HR range was 114-171bpm. LV and RV S/D ratios were significantly correlated to HR but not GA or EFW. With increasing HR, the S/D ratio increased exponentially in the LV and quadratically in the RV (figure 1). **Conclusions.** S/D is a feasible and reproducible parameter to evaluate biventricular function in fetal life. We provide fetal reference ranges of LV and RV S/D ratios for HR. Future studies will assess its clinical utility in fetal cardiac pathologies.

PRENATAL DIAGNOSIS OF CORRECTED TRANSPOSITION OF GREAT ARTERIES: 13-CASE SERIES AND SYSTEMATIC REVIEW OF LITERATURE

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Objectives. The aim of this study is to describe the clinical behaviour of pregnancies with corrected transposition of the great arteries (CTGA) and perform systematic review of literature. **Methods.** We perform a retrospective descriptive study of all CTGA cases occurring during a 19-year period in three tertiary care hospital. We also conducted literature search of CTGA in MEDLINE, EMBASE, Europe PMC and Scielo. All series with ten or more cases were included in the analysis. **Results.** Five articles were reviewed and our cases were including in the analysis. A total of 115 cases of CTGA were included, 13 ours and 102 previously published. In our series, maternal age was 31,6 years (23 to 40), gestational age to diagnosis was 26,6 (21 to 34), and there were no isolated cases. All born alive and three had BAV. Perinatal and one year follow up outcomes of our series and systematic review are showed in table 1. **Conclusions.** CTGA is an infrequent congenital heart disease. Prenatal diagnosis is possible in cases with other cardiac malformations. Our series and systematic review, shows similar findings, diagnosis during second trimester, most associated to others cardiac malformations. Most of the cases born alive, and after complex interventions and its frequent the association to complete AV, it has a high survival rate at year.

PRENATAL DIAGNOSIS OF CONGENITAL HIATAL HERNIA: CASE REPORT

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A twenty-seven-year-old nulliparous woman with a 35.2-week normal pregnancy, was referred to us with the diagnosis of abdominal solid mass. We identified in the upper and posterior wall of the abdomen a hyperechogenic image, that goes until lower part of mediastinum, we suspected CHH (figure 1). Also, during the screening, we identified horseshoe kidneys. Fetal MRI confirm this finding. Patient had a vaginal delivery at 39 weeks of pregnancy. During the first month of extrauterine life, both diagnoses of CHH and horseshoe kidney were confirmed with a gastrointestinal contrast study and abdominal ultrasound respectively. Prenatal diagnosis of CHH is unusual and in the literature, there are only eight case reports as prenatal diagnosis. In every case, the condition was identified during the third trimester. All cases had the stomach involved and five of them presented volvulus. Six patients were taken to surgical repair; two patients were not intervened, having conservative treatment; and fundoplication was done in five patients. Differential diagnosis of a solid mass in the fetal thorax is hard to distinguish from other congenital anomalies as diaphragmatic hernia, esophageal duplication, neuroenteric cyst or a microcystic adenomatoid lung malformation. Our case shows that the prenatal detection of CHH can result in an early neonatal diagnosis and planned corrective surgery, which can reduce long term morbidity.

PRENATAL DIAGNOSIS OF THYMIC HYPERPLASIA: CASE REPORT

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We present a case of fetus with thymic hyperplasia. At present, this is the first case of prenatal diagnosis of thymic hyperplasia reported in the literature. A 28-year-old primiparous woman with spontaneous and healthy pregnancy. In a routine third trimester scan, we find at the thoracic level in the cut of three vessels, anterior mediastinum homogeneous hypoechoic image of regular edges with a transverse diameter and a total area over 95 centiles (figure 1), confirmed by MRI, suggestive of thymic hyperplasia. Caesarean section was

performed at 38 weeks of pregnancy, obtaining a normal term newborn. A chest x-ray and echocardiography was performed after birth, reporting hyperplasia of the thymus. At 72 hours, laboratory studies were performed including blood biometry, liver function tests, TORCH, c-reactive protein, parvovirus B19 and lymphocyte populations, which were within normal ranges. Hyperplasia of the thymus is rare and is detected incidentally in a routine ultrasound in postnatal life. In this case normal hemodynamics, no images of thymus tumour or evidences of bacterial or viral fetal infection were found. Fetal surveillance and termination of pregnancy at term are suggested. The follow-up studies was carried out in postnatal life, including image and laboratory studies, blood count, C-reactive protein, TORCH profile and study of lymphocyte subpopulations, all was normal. In our case no clinical repercussion was observed either in the fetal life or in the newborn. At our knowledge this is the first reporting of prenatal diagnosis thymic hyperplasia.

PRENATAL DIAGNOSIS OF LARGE ENTERIC DUPLICATION: CASE REPORT

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We report a clinical case of large enteric duplication. Patient was referred to our centre at 32 weeks of pregnancy with the diagnosis of abdominal tumour. Ultrasound examination showed in the upper third of the fetal abdomen large mixed homogeneous image of 71 x 27 mm, with well defined walls that mimic austras, colour Doppler shows just few vessels in its walls. And the wall presents an image of two layers, an internal echogenic and an external non-echogenic; no other malformations were found. Diagnosis of enteric duplication of ileum segment, was made. MRI was performed and showed same size and location image with meconium inside, confirming the diagnosis of enteric duplication. Enteric duplication is a rare congenital malformation that can arise at any point of the gastrointestinal tract. The most frequent segment of duplication is the ileum (more than 40% of cases). A third of the cases present associated malformations. Our case is, to our knowledge, the largest isolated enteric duplication reported. Prenatal diagnosis is important to refer the patient to third level centre, and to made a elective minimal invasive neonatal surgery.

FETAL DIAGNOSIS OF ANOMALOUS RENAL VEIN SHUNT INTO AZYGOS VEIN

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Azygos vein is formed at 7 to 10 weeks from last menstrual period, derived from the supracardinal system, with a cranial drainage into the superior vena cava. Renal vein anomalies are relatively rare, usually detected during adulthood by routine assessments indicated for other symptoms. Although most of these anatomical variations are asymptomatic and with lack of clinical significance, their unknown existence might generate surgery risks like hemorrhage, nephrectomy, and even death. In this report, we present a case of an anatomic variant of the left renal vein with azygos vein shunt. Because of this variant, the azygos vein showed a tortuous and dilated shape due to venous congestion. A 24-year-old healthy nulliparous woman with a normal 11–14 weeks, and 20–24 weeks scans. During a routine third trimester ultrasound at 27+1 weeks, the presence of Azygos vein was identified at 3-vessels trachea view and confirmed at longitudinal view of aorta. No other cardiac or extracardiac anomalies were identified. In a follow-up ultrasound with advanced echocardiography at 32+2 weeks, azygos vein dilatation was observed, with a 2 mm diameter, at expense of a left renal vein shunt identified with 4Dflow® (figure 1). During follow-up scans, no signs of congestive heart failure was observed. A spontaneous vaginal delivery was assisted at 39+2 weeks of gestation, obtaining a healthy female newborn, birthweight 3,322 grams, with a 1min and 5min APGAR of 9 and 10, respectively. At first month of life an abdominal Doppler assessment confirmed the diagnosis of anomalous left renal vein drainage into azygos. A neonatal echocardiography and karyotype were performed, both with normal result. In conclusion, although venous anomalies are relatively unusual and mostly with a lack of clinical significance, a very detailed understanding of antenatal vascular development is of utmost importance for antenatal diagnosis and follow-up.

ROLE OF CEREBROPLACENTAL RATIO IN NORMAL GROWING FETUS FOR THE DETECTION OF ABNORMAL PERINATAL OUTCOMES

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Objectives. To evaluate the role of third trimester cerebroplacental ratio (CPR) in predicting abnormal perinatal outcomes in fetuses growing over the 10th centile. Methods. This was a retrospective study of 1,190 non-small fetuses attending the fetal medicine unit for a routine third trimester ultrasound at 35-41 weeks' gestation. All foetuses had an estimated fetal weight greater than 10th centile at the time of the scan. Abnormal CPR results were defined as those values bellow 5th percentile for gestational age. To calculate the detection rate of CPR either alone or combined with other variables for the prediction of abnormal perinatal outcomes, an univariate or multivariate logistic regression analysis was used. Abnormal perinatal outcomes were defined as a composite outcome: new-born weight bellow 10th centile, neonatal death, abnormal intrapartum fetal heart rate, Apgar score <7, abruption placentae and postpartum admission to neonatal unit. Results. There were 166 pregnancies with normal growing fetuses who had altered CPR. This group was associated with lower rate of gestational age at delivery and higher proportion of small gestational age new-born < 10th centile (18.9% vs 8.4%; $p < 0.05$) and abnormal intrapartum fetal heart rate (3.6% vs 1.1%; $p < 0.05$). On the other hand, the incidence of abnormal perinatal outcomes was 12,6% ($n = 151$). The CPR <5th centile detection rate was 21.5% for a false positive rate of 10%, however a combined model including maternal age, parity, estimated fetal weight and CPR had a sensitivity of 46.4%. Conclusions. This study confirm that CPR performed in normal growing fetuses is associated with higher rate of abnormal perinatal outcomes.

COMBINED PREDICTIVE MODEL OF BIRTHWEIGHT AT DIAGNOSIS OF EARLY AND LATE ONSET PRE-ECLAMPSIA

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Objectives. To analyse the combined predictive role of uterine artery (UtA) Doppler, maternal characteristics and fetal biometry for estimation of birthweight in patients with diagnosis of pre-eclampsia (PE). **Methods.** Retrospective cohort study of patients with fetal ultrasound and UtA Doppler assessment at diagnosis of global (g-PE), early-onset (e-PE) and late-onset PE (l-PE) and complete perinatal outcome. Maternal characteristics were obtained before ultrasound and stored at a dedicated database. Fetal biometry and Doppler values were expressed as z-score to overcome the gestational age. Spearman test was used for correlation between birthweight z-score and UtA z-score. A multivariate linear regression analysis for birthweight prediction combining maternal characteristics, fetal biometry and UtA Doppler was determined for g-PE, e-PE and l-PE. **Results.** A total of 143 singleton pregnancies with PE were assessed with UtA Doppler at diagnosis. Of these, 52 (36.4%) were e-PE and 91 (63.6%) were l-PE. Correlation of birthweight z-score and UtA z-score for g-PE, e-PE and l-PE was -0.41 ($p < 0.0001$), -0.21 ($p = 0.04$) and -0.50 ($p = 0.0002$), respectively. For g-PE, the best birthweight predictive model included UtA z-score, estimated fetal weight (EFW) z-score, maternal smoking habit and diabetes mellitus background ($r = 0.88$; $p < 0.0001$). For e-PE, the best model included EFW z-score, previous PE background and smoking habit ($r = 0.87$; $p < 0.0001$). For l-PE, the best model included UtA z-score and fetal abdominal circumference z-score ($r = 0.80$; $p < 0.0001$). **Conclusions.** Uterine artery Doppler is a good predictor of birthweight in patients with pre-eclampsia, mainly in those that delivered after 34 weeks of gestation. These results bring new evidence on the role of placental dysfunction in l-PE.

DEPARTAMENTO DE CIRUGÍA

48 WORLD CONGRESS OF SURGERY - CRACOVIA, POLONIA

FAILED NISSEN FUNDOPLICATION: CONVERSIÓN TO TOUPET FUNDOPLICATION PLUS ROUX-EN-Y DISTAL GASTRECTOMY

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Introduction: Nissen fundoplication fails due to different causes as was described before. The clinical manifestation is the combination of dysphagia, retrosternal pain and reflux. Endoscopic and radiological findings include esophagitis, Barretts's esophagus and hiatal hernia. Revisional procedures are more complex, also associated with postoperative complication and high rate of re failures. **Objective** Report post-operative outcome of patients submitted to revisional surgery performing conversion of Nissen to Toupet fundoplication combined with distal gastrectomy with Roux -en Y- gastrojejunostomy. **Materials & Methods:** Prospective cohort of 18 patients. Inclusion criteria were patients with previous Nissen fundoplication for treatment of pathological gastroesophageal disease that developed dysphagia, heartburn or retrosternal pain, in whom a pathological reflux disease was detected in the upper endoscopy, 24 hr pH esophageal monitoring and barium radiological esophagogram. Also, all patients were tested with esophageal manometry prior to surgery. The surgery performed was conversion of Nissen to Toupet fundoplication combined with distal gastrectomy with Roux -en Ygastrojejunostomy. All the pre-operative tests were repeated 1 year post-operative. The follow-up is 100%. **Results:** The results pre and post-operative are respectively as follow: retrosternal pain 27.8% and 0% ($p = 0.016$), stenosis of the cardias 38.9% and 5.6% after surgery ($p = 0.016$), hiatal hernia 50% and 5.6% ($p = 0.016$), LESp= 10.6 mmHg and 15mmHg ($p = 0.036$), %time<4pH 9.4 and 1.4 ($p = 0.004$), DeMeester score 48.3 and 8.1 ($p = 0.008$). The postoperative complications were 27.8%, all complications were Clavien-Dindo < 2. There was no mortality in the cohort **Conclusion:** The surgical approach tested is safe and effective for management of failed Nissen fundoplication.

UPPER GASTROINTESTINAL BLEEDING DUE TO DUODENAL GASTROINTESTINAL STROMAL TUMOR MANAGED BY PARTIAL DUODENECTOMY WITH PANCREATIC PRESERVATION.

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Introduction: Gastrointestinal stromal tumor are low frequency tumors. Duodenal location is rare constituting 3-5 % of total GIST. The common clinical presentation is bleeding detected by upper digestive endoscopy. Surgical resection is the treatment of choice. **Materials & Methods:** The purpose is to present the diagnostic workup, the technique of partial duodenectomy with pancreatic preservation for duodenal GIST and outcome. (Case report) **Results:** Result: endoscopy only demonstrated bleeding of second portion of duodenum, but angioTC identified suspicion of duodenal bleeding and laparotomy was indicated which confirmed a local tumor of second-third portion of duodenum. Complete third portion of duodenum below the papila was resected with preservation of pancreatic head and digestive tract was reconstructed by Roux-en-Y latero-lateral duodeno-jejunostomy. Biopsy confirmed low grade malignant GIST. Outcome was uneventfully. Patient is alive 7 years after operation. **Conclusion:** Conclusion: partial duodenectomy with pancreatic preservation is possible to perform safety in selected patients.

INCISIONAL HERNIA. OUR EXPERIENCE AT A UNIVERSITARY CENTER

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Introduction: Incisional hernia (IH) is the most common sequel after abdominal surgery, and may represent serious risk to develop late morbidity. Mesh repair is at present the gold standard with less recurrence than primary repair. Open, laparoscopic and robotic techniques has been described. Mesh position may be onlay, inlay, sublay or IPOM. Literature recomend open sublay mesh, but in our experience open onlay mesh according our protocols have demonstrated excellent results. The purpose of the present study is to report the experience in the treatment of incisional Hernia (IH), at our university center. **Materials & Methods:** 672 patients, with IH, were attended at the Clinic Hospital, University of Chile, between 2012 and 2016. Computerized data base give prospectively records of: demography, comorbidities, type of surgery and herniorraphy performed. Kind of mesh employed, and post operatory morbidity. (30 days). Elective surgery was restricted to patients with BMI below 32. morbimortality were analized. **Stadistic analysis:** Chi square. **Results:** : Demography: 72% female and 28% male. 57% below 65 years. BMI mean 27 kg/m². Comorbidities: Hypertension 43%, Diabetes 15%, Hypothyroidism 6%, CPO 2.3%. Primary surgery: Biliary 33%, Gynecologic 15%, Coloproctological 17%, gastric 15%, Exploratory laparotomy 7%. Emergency surgery 5%, Elective 95% Repair: without mesh 3%, with mesh: 86% Onlay, 7% Sublay, 2% Inlay and 2% Intraperitoneal. Laparoscopic 8% Polypropylene mesh in 85%. Postoperative morbidities: wall hematoma 1%, enterotomy 2%, (recognized and repaired at the same surgery), and enterocutaneous fistulae 0.1%. 97% of the patients did not present any morbidity; the present series did NOT presented mortality. Routine use of subcutaneous drain and abdominal elastic belt 100% patients. Mean hospital stay: 3 days. **Conclusion:** Elective surgery, limited to BMI below 32, drastically reduced post operatory morbidity. Onlay technic, showed excellent results.

FITZ HUGH CURTIS SYNDROME AS AN INCIDENTAL FINDING DURING A CHOLECYSTECTOMY

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Introduction: Fitz-Hugh-Curtis Syndrome (FHCS) is a perihepatitis produced by peritonitis secondary to the ascending of bacteria, this result of a pelvic inflammatory disease, being the most frequent etiologic agent Chlamydia trachomatis; it presents clinically with right upper quadrant pain (1). The FHCS has an incidence of 4.7 % in laparoscopy due to benign gynecological pathology (2). **Objetive:** To describe a clinical case of Fitz-Hugh-Curtis Syndrome **Materials & Methods:** A patient undergoing cholecystectomy is included and the presentation of the FHCS is described. **Results:** Clinical Case. A 65-year-old woman with a history of sporadic abdominal distension, without abdominal pain and without a history of gynecological organ infections. The blood tests were normal, no abdominal computed tomography (CT) was performed and the abdominal ecotomography showed cholelithiasis, so laparoscopic cholecystectomy was performed, and multiple adhesions from the liver to the abdominal wall were found as an intraoperative finding (Figure 1). Chronic phase evidences adhesions between hepatic surface and abdominal wall, characterized by the resemblance to "violin strings", this image is considered diagnostic criteria. In the acute episode, CT shows hepatic capsular enhancement in arterial phase that reflects blood flow in inflamed hepatic capsule and in chronic stage shows delayed phase that may reflect a capsular fibrosis (3). **Conclusion:** Fitz-Hugh-Curtis syndrome in the chronic stage may be asymptomatic and therefore may be present as an incidental surgical finding in abdominal surgery.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

XXIV WORLD CONGRESS OF NEUROLOGY - EMIRATOS ARABE, DUBAI

AUTONOMIC NERVOUS SYSTEM DISORDERS/HISTORY OF NEUROLOGY/MOTOR NEURON DISEASE/MOVEMENT DISORDERS/MS & DEMYELINATING DISEASES/NEUROMUSCULAR DISORDERS/VESTIBULAR DISORDERS AND NUTRITIONAL DISORDERS OR INTOXICATIONS. SERIAL DECLINE OF NO EVIDENCE OF DISEASE ACTIVITY-4 STATUS IN EARLY DISEASE STAGES OF MULTIPLE SCLEROSIS

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Background. In relapsing-remitting multiple sclerosis (RRMS), no evidence of disease activity-3 (NEDA-3) is defined as no relapses, no disability progression and no MRI activity. NEDA-4 status is defined as meeting all NEDA-3 criteria plus having an annualized brain volume loss (aBVL) of $\leq 0.4\%$. **Objective.** To determine the impact of adding a-BVL to NEDA-3 (NEDA-4). **Methods.** Forty-five patients were prospectively followed at baseline, months 12 and 24, at the University of Chile Hospital. SIENA software was used to assess a-BVL. **Results.** The patients had a mean age of 33.0 years (18-57), disease duration of 1.9 years (0.4-4), EDSS score of 1.3 (0-4) and 67% were female. 73% were on first-line DMT (interferons (53%), glatiramer acetate (11%), teriflunomide (9.0%)) and 18% were on second-line DMT (fingolimod). At 12 months, 58% (26/45) of patients achieved NEDA-3. An aBVL of $\leq 0.4\%$ was observed in 52.0% (21/45) (mean: 0.45%). Adding a-BVL (threshold of 0.4%) the proportion of patients achieving NEDA4 was 36% (16/45). At 24 months, 48% (22/45) of patients achieved NEDA-3. An a-BVL of $\leq 0.4\%$ was observed in 49 % (22/45) (mean: 0.53%). 28% (13/45) achieved NEDA-4. 51% (23/45) were now on second-line DMT (fingolimod 47%; alemtuzumab 2% and natalizumab 2%). **Conclusion.** NEDA-4 has the potential to capture the impact of DMT therapies in RRMS. a-BVL may be a key domain to consider when assessing the effectiveness of the first line DMT. Considering NEDA-4 status, clinicians may select a second-line DMT earlier in the disease course to control subclinical disease activity of RRMS.