

Abstracts presentados en congresos internacionales 2015

CIRUGÍA

OBESITY WEEK – LOS ÁNGELES, USA

SLEEVE GASTRECTOMY: STANDARDIZED SURGICAL TECHNIQUE

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Background: Sleeve gastrectomy represents more than 50% of the bariatric surgeries in the world. In Chile, the first experiences started around the year 2005. Since its original description, there have been several changes to the surgical technique, with no real unified or standard technique. Many reports present different incidence of complications or weight loss, but the techniques are commonly not standardized or can be difficult to replicate. Objective: The aim of this paper is to present a video and describe the standard surgical technique in 2500 consecutive patients who underwent laparoscopic sleeve gastrectomy, from January 1st 2006, to March 31st 2015. Procedure: This individual case corresponds to a 35 year old female, with a BMI of 35, dyslipidemia and insulin resistance. She had a normal upper endoscopy previous to the surgery, and no cholelithiasis was found on the ultrasound. The procedure starts with the surgeon in a French position, between the patients legs. There are two assistants, one on each side. We use 5 trocars total, 3 of them are 12mm, the other 2 are 5mm. Neumoperitoneum is created with a Veress needle, in the upper left quadrant of the abdomen. Once the trocars are in place, we start with the dissection of the greater curvature, freeing the greater omentum, from the angle of His to 5cm proximal to the pylorus. For this dissection we use the advanced hemostatic device Ergo 310 by BOWA inc. After we position a bougie in the lesser curvature, we start the creation of the sleeve by consecutive fires of a 60mm linear stapler. The first 2 charges are a 4.8mm thickness staplers, and then we use 3 to 5, 3.5 mm thickness staplers to finish the sleeve. This finally creates a gastric reservoir of about 100ml of capacity. The excised tissue is pulled out through the right incision, and sent to pathology study. The gastric sleeve is reinforced by a seromuscular invaginating suture, using reabsorbable polydioxanon (PDS) material. We always perform a methylene blue test, to check for hermeticity. Hemostasis is checked and no drains are used. Patients start a fluid diet at the first postoperative day and are usually discharged at the second day. Results: In the universe of 2500 patients, 21% correspond to males. All surgeries were performed by 3 surgeons. 5 patients presented with leaks, which correspond to a 0.2% incidence. There were no leaks in the first week. 4 leaks presented after 15 days. The last one was diagnosed at 2 months. There were 2 re-operations due to hemoperitoneum. 4 medical complications presented which corresponded to a pulmonary thromboembolism in one case, and 3 patients suffered with portal vein thrombosis. There was no early mortality. One patient died 1.5 year postop after a gastric obstruction from a feeding transgression. Mean EWL at 1 year was 75.1% and at 3 years was 70%. 900 patients have a follow-up of 5 years. 19.8% of this patients regained weight. Half of this patients that regained weight, went back to the original BMI previous to the surgery. Conclusions: Sleeve gastrectomy is a safe and useful bariatric procedure. The use of a standardized technique gives better results and lower operating times, thus making it safer for the patients. There is no technique that has demonstrated superiority over the others.

GASTRIC SLEEVE AND FUNDOPLICATION SURGERY IN PATIENTS WITH OBESITY AND GERD

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Background: Bariatric surgery in our country has suffered an explosive rise in the last decade. Nowadays most of the bariatric procedures are either sleeve gastrectomy or gastric by-pass. Sleeve gastrectomy has taken the advantage as the preferred surgical technique, but there is still discussion of its use in patients suffering from gastro esophageic reflux disease. The gastric

bypass and the other option, is also not exempt of short and long term complications. We present a cohort of patients with a novel surgical technique, which aspires to give both the benefits of the sleeve gastrectomy in weight control and antireflux surgery for the control of GERD. Objective: To report the short and long term results of this new surgical technique. Methods: We analyzed the clinical records and performed a telephonic interview on 15 patients that underwent this surgery in our hospital. The 15 patients span from year 2003 to 2012. All surgeries were performed by the same surgeon. Pre and post operative pH-metry and manometry were recorded. No statistical analysis was performed. Results: The patients correspond to 14 females and 1 male. The mean age was 46.2 years. The mean BMI previous to the surgery was of 33.9. All patients had altered pH-metry studies before the surgery. The mean acid exposure time was of 14%. The mean resting pressure of the LES was 8.4 mmHg. Mean surgical time was 157 minutes, and a hospital stay of 5 days. We had 1 minor complication, which corresponded to a wound seroma. There was no mortality. On the post operative follow up, the mean BMI at 6 months was 27.97, that represents a 66.71% EWL. The pH-metry and manometry at 3 months postop showed a mean resting pressure of the LES of 14 mmHg and an acid exposure time of 2.75%. During long term follow up with clinical records and a telephone interview, that spanned up to 9 years, 6 patients had needed a new surgery. Four of them corresponded to new weight gain, one for new symptomatic GERD, and one for both weight gain and GERD. One more patient had started developing weight gain, and another was in study for symptomatic reflux, but none of them had undergone a new surgery. Conclusions: We can observe good results on the long term, with studies showing improvement in pH-metry and manometry, as in weight loss in the first year. On the long term follow up, 6 patients required new surgeries, most of them for weight gain. At least two other patients are being studied for a new surgery. This would total a 50% of patients with a new surgery in almost 9 years. Although the evidence is not strong, we cannot recommend this surgery for patients who would undergo a sleeve, but present with GERD. We now perform gastric bypass to all of these patients.

GALLSTONES IN OBESE PATIENTS UNDERGOING BARIATRIC SURGERY: STUDY AND POSTOPERATIVE MONITORING

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Background: Chile is one of the countries with higher prevalence of gallstone disease in the world. Among the risk factors for gallstones are female sex, age and obesity. These factors, associated with rapid weight loss, are characteristic of obese patients undergoing bariatric surgery. It has been observed that patients undergoing these surgeries have a higher incidence of cholelithiasis in the 12 months postoperatively. Objectives: To characterize the prevalence of gallstone disease in obese patients undergoing bariatric surgery, and analyze the occurrence of this disease during the postoperative follow-up. Methods: Retrospective cohort study including 221 patients undergoing surgery in our center, with follow-up to 5 years. Review of clinical records and telephone survey was conducted. The statistical analyzes were performed using STATA 11. Significance was considered with $p < 0.05$. Results: The characteristics of the patients are shown in the graphics on the left. 18.09% of patients had a history of previous cholecystectomy. A 13.57% of patients had preoperative cholelithiasis. Monitoring was performed in 151 patients. In ultrasound at 1 year, 6.6% had cholelithiasis. At follow up three years later, 4.63% of the patients required a cholecystectomy. The EWL at 1 year was 83.84%, and 88.42% at 3 years. There were no significant differences in the occurrence of cholelithiasis with the type of surgery or weight loss. Conclusions: There is a high prevalence of cholelithiasis in the population undergoing bariatric surgery. The emergence of this disease in the first year was lower than that reported in the literature. There were no differences in incidence between the amount of weight loss or the surgery performed

16TH WORLD CONFERENCE ON LUNG CANCER - DENVER, COLORADO, USA

DETECTION OF MUTATIONS IN TUMOR AND BLOOD SAMPLES FROM LUNG ADENOCARCINOMA PATIENTS USING TWO DIFFERENT TECHNIQUES

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Background: Adenocarcinoma is currently the most common type of lung cancer in which genetic alterations with prognostic and predictive value have been identified. EGFR mutations are predictive of response to TKI and mutually exclusive with KRAS mutation. Molecular analyses from tissue biopsies are nowadays mandatory in initial pathology studies and recommended if TKI resistance develops. Molecular analysis in circulating cell-free DNA (cfDNA) appeared as an easier method to perform these studies. cfDNA analysis from plasma or serum in lung cancer have identified mutations in EGFR, KRAS, ALK and HER-2, that correlated with those observed in the primary tumor. This study compared two different techniques to determine KRAS and EGFR mutations in tissue and blood samples from patients with lung adenocarcinoma. Methods: Patients with suspected lung cancer admitted to Clinica Las Condes between October 2012 and March 2014, were offered to enter the Study. Previous to biopsy,

20ml of blood was drawn and samples of plasma and serum stored. When an adenocarcinoma was diagnosed EGFR and KRAS mutations of the biopsy were analyzed by COBAS[®] KRAS/EGFR Mutation Tests and by SSCP (Single Stranded Conformational Polymorphism) and confirmed by Sanger sequencing. Blind analysis of stored plasma and serum was performed, isolating cfDNA using QIAamp[®] Circulating Nucleic Acid kit, and tumor DNA by QIAamp[®] DNA FFPE Tissue kit. Clínica Las Condes Ethics Board approved the study, and informed consent obtained in all patients. Results: Twenty-one patients entered the study; two were excluded because final pathology showed Atypic Hyperplasia. Of the remaining 19 patients: 14 had invasive Adenocarcinoma, 3 in situ Adenocarcinoma and 2 Adenosquamous carcinoma. Tissue biopsies were obtained from the primary tumor in 14 cases, pleural metastases in 2, lymphnode metastases in 2 and brain metastases in one. Two patients had Adenocarcinoma in situ, 10 stage I, 1 stage II, 2 stage III and 4 stage IV. Seven patients have mutations detected by COBAS[®] and SSCP in tissue biopsies: 3 EGFR and 4 KRAS mutations. EGFR mutations were detected in 2 stage I, and one stage IV patients. KRAS in 1 ACAs, 2 stage I and one stage IV. In these patient's plasma only 1 mutation was detected in cfDNA (KRAS mutation in one stage IV patient), correlation between tissue biopsy and cfDNA 1 out of 7 (14%). No mutations were detected in cfDNA from serum samples. Conclusion: In our study EGFR and KRAS mutations rates were lower than expected for Chilean population, but it could be due to the small sample size. We had poor general correlation between mutations in tissue biopsies compared with those detected in cfDNA (14%). In stage IV correlation was better (50%). No EGFR mutations were detected in cfDNA, but again could be due to the sample size. COBAS[®] technique was useful to determine KRAS mutations in plasma cfDNA. Both SSCP and COBAS techniques allow determining mutations in tumor samples. cfDNA analysis could be used to determine KRAS mutations in patients with advanced disease. Its use to determine EGFR mutations need to be investigated in larger studies.

DERMATOLOGÍA

23TH WORLD CONGRESS OF DERMATOLOGY – VANCOUVER, CANADA

TOFACITINIB IN PATIENTS WITH MODERATE-TO-SEVERE CHRONIC PLAQUE PSORIASIS: 2-YEAR EFFICACY AND SAFETY IN AN OPEN-LABEL LONG-TERM EXTENSION STUDY

Augustin, Matthias; Paul, Carle; Valenzuela, Fernando; Azulay-Abulafia, Luna; Langley, Richard G; Leonardi, Craig; Cather, Jennifer; Gardner, Annie; Proulx, James; Rowinski, Carolyn; Tan, Huaming; Wolk, Robert; Kaur, Mandeep; Mallbris, Lotus; Rottinghaus, Scott.

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriasis treatment. Objective: To report safety, tolerability, and efficacy maintenance of tofacitinib from an ongoing (database not locked) Phase 3 openlabel long-term extension study (LTE) in patients with moderate-to-severe psoriasis (NCT01163253). Methods: Patients completing participation in randomized Phase 2 or 3 tofacitinib studies received tofacitinib 10mg twice daily (BID) until Month 3 (M3); investigators thereafter selected a 5 or 10mg BID dose, based on patient response. Pooled data from all patients are reported (data cutoff: 04 April 2014). Primary endpoints included adverse events (AEs) and laboratory safety data. Secondary endpoints included PGA response ("clear" or "almost clear") and PASI75. Efficacy endpoints are reported up to 2 years (full analysis set; observed cases); available safety data are reported to data cutoff. Results: Of 2847 patients treated (median [maximum] treatment duration: 395 [1259] days), 1912 were ongoing at analysis (1501 on tofacitinib 10mg BID \geq 80% study duration). Tofacitinib exposure in the qualifying study and duration between last qualifying study and first LTE visits varied. The most frequently reported AE terms among all patients receiving tofacitinib were nasopharyngitis (15.6%), blood creatine phosphokinase increased (9.8%), and upper respiratory tract infection (7.4%). Serious AEs were reported in 7.9% of patients; 9.2% discontinued due to AEs. Serious infections were reported in 1.8%; herpes zoster infections were reported in 3.5% (0.2% serious) of patients. Malignancies excluding non-melanoma skin cancer (NMSC) were reported in 1.2% and NMSC in 0.9% of patients. Increases in LDL-c, HDL-c, and total cholesterol were observed at M1 and stabilized thereafter. Initial increases in absolute lymphocytes subsequently decreased. Percentages of patients achieving PASI75 responses were 56% (1535/2732) at M1, 69% (1536/2221) at M12, and 64% (354/549) at M24. PGA responses ("clear" or "almost clear") were achieved in 56% (1551/2774) at M1, 60% (1329/2233) at M12, and 54% (300/557) at M24. Conclusions: A consistent safety profile and sustained (24-month) efficacy was observed in patients with psoriasis receiving tofacitinib. No new safety signals were observed compared with prior tofacitinib Phase 3 studies. Limitations: Only the open-label experience is included. Patients received up to 1 year of tofacitinib in qualifying studies. Longer and greater patient exposure will provide additional safety context.

DEPARTAMENTO DE MEDICINA

MEDICINA NUCLEAR

XXV CONGRESO ALASBIMN – PUNTA DEL ESTE, URUGUAY

PATRONES Y SEGURIDAD DE UTILIZACIÓN DE DIPIRIDAMOL EN ALTAS DOSIS EN SPECT MIOCÁRDICO: REVISIÓN RETROSPECTIVA
Enrique Hiplan, Luis Alarcón, Patricio González

Introducción: El test de perfusión miocárdica (TPM) realizado con Tecnecio 99 metaestable (Tc99m)- Sestamibi, es un estudio importante en cardiología nuclear para diagnóstico y evaluación de enfermedad coronaria (EC). El Dipiridamol se utiliza en pacientes incapaces de realizar test de esfuerzo o lograr la frecuencia cardíaca predicha durante el ejercicio, o como indicación de primera línea en pacientes con bloqueo completo de rama izquierda. Las dosis utilizadas son variables, usualmente se administra 0,56mg/kg, describiéndose baja incidencia de dolor torácico (10%; 362/3715) y efectos secundarios menores no-cardíacos (10%; 357/3715). Mientras que otros centros utilizan dosis altas (0,852mg/kg); sin una descripción clara de efectos secundarios (ES) relacionado a cantidad administrada, sugiriéndose dosis máxima de 60mg, independiente del peso. Objetivos: Describir los ES más frecuentes asociados al uso de Dipiridamol en TPM, así como la incidencia de éstos, según las dosis administradas. Metodología: Se realizó estudio descriptivo retrospectivo entre Octubre 2014 a Enero 2015. Se obtuvieron datos de las dosis administradas según peso (0,852mg/kg), edad, sexo, diagnósticos de referencia y antecedentes mórbidos de Hipertensión Arterial (HTA) y Diabetes Mellitus (DM); con los ES reportados. Se analizó estadísticamente con Odds Ratio con intervalo de confianza del 95% (OR IC 95%). Se considero estadísticamente significativo un valor $p < 0,05$. El TPM se realizó con protocolo de 2 días en Gamacámara Siemens E-CAM 180, año 2002, Software Syngo versión Esoft 3.5, con Tc99m-Sestamibi, marcado según instrucción de proveedor Nuclear CGM. Resultados: Se revisaron 123 fichas clínicas, excluyendo 3 por datos incompletos. El 23,3% (28/120), presentó algún ES, todos de carácter leve y transitorio; observándose más frecuentemente cefalea, cambios de presión arterial y dolor torácico clásico o atípico. El análisis de 28 pacientes con ES por dosis según OR IC 95% no mostró diferencias estadísticamente significativas; según edad, el grupo menor a 65 años muestra incidencia de 53,57% (15/28) con $p=0,058$; según sexo, las mujeres presentan 64,29% de los casos (18/28; $p=0,054$) y según peso, el subgrupo menor a 70kg un 39,29% (11/28), entre 70 a 79 kg un 25% (7/28) y mayor a 80kg un 35,71% (10/28); sin diferencias significativas ($p=0,739$). La incidencia de HTA fue 67,86% (19/28) con OR 0,43 (IC 0,15:1,33) con $p=0,094$ y de DM fue 35,71% (10/28) con $p=0,43$; según diagnóstico de referencia (1 sin datos), el 11,11% (3/27) eran EC conocidos, 48,15% (13/27) sospecha de EC y 40,74% (11/27) sin EC conocida; sin diferencias significativas entre ellos ($p=0,606$). Conclusión: El uso de Dipiridamol como estresor farmacológico es seguro en TPM, sin ES severos presenciados, con dosis altas de 0,852mg/kg e incluso sobre los 60mg; con ES similares a dosis convencional de 0,56mg/kg y menores de 60mg. Se observa cierta tendencia a mayor incidencia de ES en menores de 65 años y sexo femenino, con valor p límite. Sin otras correlaciones significativas identificables en este estudio.

PREVALENCIA DE DENSITOMETRÍA ÓSEA NORMAL EN MUJERES MAYORES DE 65 AÑOS REFERIDAS PARA ESTUDIO DE MASA ÓSEA Y ANÁLISIS DE IMC.

Eduardo Swett, Verónica Araya, René Fernández, Patricio González.

INTRODUCCIÓN: La esperanza de vida en Chile va en aumento; actualmente hay 1.019.479 mujeres sobre los 65 años (11,3% de población femenina), con esperanza de vida de 82 años. Son escasos los datos epidemiológicos de prevalencia de osteoporosis y osteopenia en Chile. En 1987, un estudio en mujeres de 50 años o más mostró un índice de prevalencia en fémur proximal de 46% para osteopenia y 22% para osteoporosis. OBJETIVO: Conocer la prevalencia de mujeres de 65 años o más con densidad mineral ósea (DMO) normal, referidas para estudio en un hospital universitario y análisis de índice de masa corporal (IMC). MATERIALES Y MÉTODOS: Estudio observacional retrospectivo de densitometrías óseas (DXA) realizadas desde Julio 2013 a Junio 2015 a mujeres mayores de 65 años en Hospital Clínico Universidad de Chile. Se utilizó equipo Lunar® Prodigy Advance, mediciones en columna lumbar, cuello femoral izquierdo, derecho y radio ultradistal no dominante, interpretadas según criterios OMS (T-score). Se calculó IMC previo a DXA. Se crearon 2 grupos de pacientes, uno con DXA normal y otro de igual número con DMO disminuida (T-score ≤ -1.1 en al menos una localización) creado mediante muestreo simple. Se compararon IMC, edad y DMO de cada segmento entre los grupos (t de Student y Wilcoxon). En el grupo normal se comparó DMO de cada segmento con IMC y edad (Pearson). RESULTADOS: De 2343 pacientes estudiados, 2169 (92.6%) correspondieron a mujeres de las cuales 32.5% (704 casos) eran ≥ 65 años. De éstas, 60 presentaron DXA completamente normal, correspondiendo a 8.5% de las mujeres ≥ 65 años y a 2.8% de

todas las mujeres estudiadas. De las 644 con DMO alterada, se creó un grupo aleatorio de 60 pacientes. El promedio de IMC en grupo normal fue 31 ± 4 (rango 22.4-41.6 kg/m²), con 50% de pacientes obesas (30/60), 45% sobrepeso (27/60), 5% normopeso (3/60) y sin pacientes con bajo peso; en el grupo con DMO disminuida el IMC fue significativamente menor ($p < 0.01$) con un promedio de 28.9 ± 5 , 35% obesidad (21/60), 45% sobrepeso (27/60) y 20% normopeso (12/60). Tanto DMO como T-score fueron significativamente menores ($p < 0.01$) en el grupo de anormales en todos los segmentos estudiados respecto al grupo normal. La edad en las normales fue menor que el grupo con DMO alterada (promedio 70 ± 4 v/s 72.7 ± 6). Entre las pacientes ≥ 65 normales, no hubo diferencias significativas de DMO respecto al IMC ni la edad. **CONCLUSIONES:** Un relevante número de mujeres mayor de 65 años presentó DXA normal (8.5%). Este grupo presentó IMC y exceso de peso significativamente mayores que el grupo con DMO disminuida, lo que apoyaría a factores nutricionales como protectores de la DMO en postmenopausia. Estaría plenamente justificado estudiar si existen otras razones por las cuales algunas mujeres postmenopáusicas conservan DMO normal.

EVALUACIÓN DE LA ADMINISTRACIÓN DEL RADIOTRAZADOR TC99M-MDP EN CINTIGRAMA ÓSEO.

Luis Alarcón, Enrique Hiplan, Patricio González, Sonia Otarola

Introducción. El Tecnecio99m-Metildifosfonato (Tc99m-MDP) es uno de los radiotrazadores más utilizados en medicina nuclear para cintigrafía ósea, del cual existe en la literatura escasa información sobre control de calidad de la administración, sin describirse reportes de su incidencia, sin embargo la cintigrafía ósea es un método mucho más sensible para éste propósito, por lo que obtener un reporte de su incidencia sería importante para posteriormente determinar las causales. **Objetivos:** Realizar un estudio descriptivo sobre administración del radiotrazador Tc99m-MDP en cintigramas óseos, realizados en nuestro centro. **Métodos:** Un total de 124 estudios fueron recolectados entre el 23 de abril al 5 de junio del 2015, categorizándose la presencia de actividad en el sitio de punción en forma subjetiva por equipo de Medicina Nuclear, de acuerdo a lo observado en las imágenes y objetiva en aquellos estudios procesados con región de interés para definir porcentaje de cuentas. Se obtuvieron los datos de los pacientes desde la ficha que se completa al realizarse el estudio. Se realizó cálculo de incidencia y comparación por edad, género, sitio de inyección y diagnóstico de referencia. Se analizó estadísticamente con Odds Ratio con intervalo de confianza del 95% (OR IC 95%). Se consideró estadísticamente significativo un valor $p < 0,05$. Previo al examen se firmó consentimiento informado. **Resultados:** De las 124 imágenes obtenidas, el promedio de edad fue 56.6 años, 40 hombres y 84 mujeres, objetivándose un total de 24 casos de extravasación apreciables cintigráficamente, sin efectos adversos reportados, lo que corresponde al 19.4% (24/124) del total de estudios de los cuales en la categorización subjetiva un 37% (9/24) son leves, 17% (4/24) moderada y 46% (11/24) marcada, mientras que para la cuantificación objetiva se obtuvieron 14 estudios, de los cuales un 42.9% (6/14) tienen un porcentaje de actividad extravasada, determinado como significativo sobre un 5%. Al comparar los resultados por sexo, edad, sitio de inyección y diagnóstico de referencia no se obtuvieron diferencias estadísticamente significativas. **Conclusión:** En el presente estudio, se determinó una incidencia de actividad en sitio de punción cintigráficas de un 19,3%, sin embargo las consideradas de carácter significativo fueron de un 10.5%, sin detectarse dentro de los grupos estudiados, factores de riesgo significativos para el radiotrazador en estudio. Estos datos son sugerentes de una mayor sensibilidad de la cintigrafía para detectar actividad peripunción, por lo que no se puede comparar este estudio con los reportes de incidencias para otros compuestos no isotópicos. Los valores obtenidos en nuestro estudio servirán de base para futuras comparaciones en la incidencia de este tipo de eventos, considerando las tareas docentes de nuestro centro, para así disminuir su ocurrencia.

CONFERENCE ON NUCLEAR CARDIOLOGY ICNC – MADRID, ESPAÑA

DIFFERENCES BETWEEN FULLY AUTOMATIC AND MANUAL PROCESSING FOR LEFT VENTRICULAR SYNCHRONY ASSESSMENT IN DILATED AND NON-DILATED HEARTS COMPARING REST AND POST-STRESS ACQUISITIONS.

Teresa Massardo, Eduardo Swett, René Fernández, Juan Pablo Zhindon, Víctor Manuel Vera.

The adequate assessment of left ventricular (LV) synchronism in dilated cardiomyopathy has increasing importance. Currently a new tool is available using myocardial perfusion imaging (MPI)-gated SPECT based on phase analysis. Our goal was to compare automatic and manual processing in different cardiac conditions in order to assess differences between dilated and non-dilated LV and also between rest and post-pharmacological stress. **Methods:** Patients underwent 99mTc sestamibi SPECT at rest and 1 hour post 0.84/mg/kg dipyridamole, mostly with 2 days protocol. SyncTool® Emory Toolbox was applied in both acquisitions with fully automatic and manual intervention by a single operator. Patients (mean age: 64 years; 67% males) were divided according to their left end-diastolic volume (EDV) at rest, calculated with Cedars QGS®. We included 58 patients referred to evaluate coronary artery disease, 28 of them with EDV < 120 ml and 30 > 120 ml; 4/28 and 17/30, presented prior myocardial infarction and also 9/29 and 16/30 some

ischemia, respectively. We compared phase peak, standard deviation (SD) and histogram bandwidth (BW) using paired and unpaired tests according to their parametric distribution and Spearman correlation for individual values. Results: It was clearly more difficult to process manually dilated LV with extended myocardial infarctions, cases with often inadequate automatic boundary detection. Phase analysis mean comparison in both groups is displayed in Table 1; peak phase was similar in all. Using manual technique, the correlations between rest and post-stress in non-dilated patients were: SD $r=0.731$ ($p<0.0001$); BW $r=0.763$ ($p<0.0001$) and in dilated: SD $r=0.298$ ($p=ns$) and BW $r=0.539$ ($p=ns$). Conclusions: Post-stress synchronism in dilated and non-dilated groups presented more differences between automatic and manual processing than rest studies. The best correlation between phase SD and BW using automatic and manual SyncTool® processing was obtained in non-dilated patients without significant differences in their mean values at rest. Careful manual apical and basal LV delimitation should be performed by the same operator, especially in those cases with big perfusion defects, in order to obtain accurate data and follow-up after eventual resynchronization therapy.

LEFT BUNDLE BRANCH BLOCK AND MYOCARDIAL INFARCTION INFLUENCE IN THE VENTRICULAR CONTRACTION SYNCHRONISM WITH MYOCARDIAL PERFUSION SPECT

R. Fernández, E. Swett, V. Vera, J.P. Zhindon, R. Alay, T. Massardo.

It is known that complete left bundle branch block (LBBB) and myocardial infarction (MI) may produce abnormalities in left ventricular (LV) contraction synchrony. The main goal was to evaluate the degree of influence of LBBB and MI in patients studied with myocardial gated SPECT using phase analysis comparing with patients with normal perfusion and contraction. Method: We studied 30 patients divided as: Group A) 7 without perfusion defect with LBBB; Group B) 14 with fixed SPECT perfusion defect (with Q wave, without LBBB); and Group C) 9 without perfusion or electrical abnormalities. Synchrony was analyzed using myocardial Tc-99m-sestamibi gated SPECT using 8 frames at rest, processed with Emory Cardiac Synctool®. We compared in the phase histograms: peak, bandwidth (BW), standard deviation (SD), and distribution shape (skewness and kurtosis) using t student (significant $p < 0.05$). Results: The mean BW and SD corresponded to 43.29 and 13.84 degrees; 98.5 and 27.32 °; and 30.56 and 11.07 °, in Groups A, B and C respectively. The differences between groups are shown in Table 1; peak, skewness and kurtosis were not different. Conclusion: Phase histogram was wider in MI than LBBB cases considering BW and SD. The synchrony method is simple to be implemented, is non-invasive and could be retrospectively performed with gated SPECT.

INMUNOLOGÍA

15TH EUROPEAN AIDS CONFERENCE – BARCELONA, ESPAÑA

APOBEC COULD EXPLAIN LOW VIRAL LOAD IN HIV PATIENT WITH HIGHLY ACTIVE THERAPY (HAART) WITH NUCLEOSIDE ANALOG REVERSE-TRANSCRIPTASE INHIBITORS (NRTIS) AND NON-NUCLEOSIDE REVERSE-TRANSCRIPTASE INHIBITORS (NNRTIS) RESISTANCE BUT WITHOUT CLINICAL CONSEQUENCES.

P. Ferrer, R. Tordecilla, A.M. Gallardo, M.A. Falconner.

Objectives: APOBEC are cellular antiviral proteins able to inhibit HIV replication and may protect from progression to AIDS. The aim of this study is characterize APOBEC activity in an asymptomatic HIV patient under HAART without viral suppression. Methods: A 29 years-old homosexual Chilean man with previous testicular cancer and surgical treatment (2009), receiving testosterone. HIV diagnosed in 2011 with CD4 cell-count: 427 (14%) cells/mm³; HIV-RNA load 33,000 copies/mL; no coinfections; and platelet count: 42,000. In March 2012 begun Abacavir (ABC) (negative HLA-B*5701), Lamivudine (3TC) and Efavirenz (EFV) because of persistent thrombocytopenia. Seven months later, HIV-RNA load < 20 copies/mL. Despite taking antiretroviral medication daily, CD4-cell count and HIV-RNA load were the following: 395 (21.8%) cells/mm³, 65 copies/mL (October 2013); 105 copies/mL (February 2014); 511 (27.6%) cells/mm³, 47 copies/mL (April 2014); 537 (28%) cells/mm³, 78 copies/mL (March 2015). Because of persistent low viral load, likely due to drug interaction between testosterone and efavirenz full HIV reverse transcriptase (RT) and protease genes were investigated by nested PCR and conventional sequencing using HIV proviral DNA. Only sequences approved by Recall® bioinformatics software were used in Stanford database for resistance report. Results: M184I and M230I mutations were found at HIV RT enzyme. Additionally we detected three stop codons (3/7, 42.9%), at W codon (TGG) positions, in codons 88, 153 and 212 (W88*, W153* and W212*) of the HIV RT gene. Conclusion: M184V caused high-level resistance to 3TC and low-level resistance to ABC. M230I was associated with low-level resistance to EFV. In our patient the three stop codons detected at W codon (TGG) positions of HIV RT gene may suggest an Apobec 3G/F Hypermutation activity and this could explain low level viremia and CD4 count up to 500 cells/mm³ for a year and a half without relevant clinical consequences.

HIV PROVIRAL DNA IS AN ADEQUATE GENETIC COMPARTMENT FOR DETECTION OF RESISTANCE MUTATIONS ASSOCIATED TO INTEGRASE INHIBITORS (INIS) THERAPY IN PATIENT WITH UNDETECTED OR LOW VIRAL LOAD.

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Objectives: Evaluate the use of proviral DNA as a source of viral genetic material for a genotyping resistance test for integrase inhibitors. **Methods:** We studied 47 patients with VF under ART that included RAL and viral load of >1,000 HIV-1 RNA copies/mL on simultaneously collected plasma RNA and proviral DNA. RNA genotyping used a RT-PCR nested assay. For proviral DNA, reverse transcription was omitted. PCR products were sequenced by Sanger's method. Sequences obtained were analyzed with Recall @ bioinformatics software. Only the sequences approved were interpreted in two databases: Stanford and Geno2pheno. The obtained mutations were compared for both nucleic acids and evaluate resistance to INIs. **Results:** Forty-one (87.2%) samples were concordant between RNA and proviral DNA for predictions of resistances to INIs. Six were discordant (12.8%). Five samples were RNA-Resistance/DNA-Susceptible and one was RNA-Susceptible/DNA-Resistance, in these cases mutations that could not be detected by proviral DNA were H155N (three samples), Q148H, and R263K and for RNA was Y143R. We found more amplification and sequencing errors in working with RNA (16 sequences failed) than with proviral DNA (8 sequences failed), and four samples (8.5%) could not be genotyped by or RNA or proviral DNA and were considered not reportable. For the samples concordant RNA and proviral DNA showed similar number and kind of mutations associated to INIs resistance. We can detected T97A, G140S, Y143R, Q148H, N155H which may explain the VF due to RAL exposure. **Conclusion:** proviral DNA offers a promising approach for resistances to INIs prediction in clinical practice, particularly for the assessment of treated patients with low or suppressed viraemia.

PEDIATRIC ALLERGY AND ASTHMA MEETING – BERLÍN, ALEMANIA

MOTHER'S PSYCHOLOGICAL STATE PREDICTS THE EXPRESSION OF SYMPTOMS IN FOOD ALLERGIC CHILDREN

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Background: It has been established that child allergies, such as asthma and rhinitis, have a direct impact on carers (usually the mother), increasing their likelihood of psychological disorders and social network deterioration. It is hypothesised a significant interaction between mother's psychological state and child's food allergy (FA) symptoms, however; there is very little information on FA regarding this topic. Therefore, this study compared the relative odds of the occurrence of gastric symptoms in the food allergic child given exposure to maternal psychosocial factors. **Methods:** Mother's psychological state was evaluated and analysed against the occurrence of FA gastric symptoms in their children in a cross-sectional study involving 206 participants (mothers and children). Logistic regressions were used to determine whether mother's psychological state is a risk factor for child's gastric symptoms and to compare the magnitude of different psychological variables as risk factors for a specific gastric symptom occurrence. **Results:** High levels of anxiety were found in 44% of the participants, depressive symptoms on the 21.4% and 68% had moderate or high psychosocial impact due to CFA. Low perceived social support was found in 21.4% of the mothers. Higher CFA-Related Impact (CFA-RI) and CFA-Related Social Impact (CFA-R SI) in the mother increase the possibility for abdominal pain (OR = 2.04; $p < .001$) and diarrhoea (OR = 1.32; $p = .05$) in the child. The possibility for abdominal bloating in the child increases when the mother suffer from higher anxiety (OR = 4.45; $p < .001$), lower perceived social support (PSS) (OR = 3.17; $p = .002$) and CFA-RI (OR = 1.32; $p < .05$). **Conclusions:** The psychological impact of caring a food allergic child and the perceived social support can predicts the occurrence of allergic symptoms in children. CFA is propounded as a process where biological, psychological and social variables have a relationship of mutual influence. Therefore, a comprehensive care strategy that considers the family perspective is proposed to achieve a more inclusive and integrative care of CFA focused on "families living with food allergy".

GERIATRÍA

INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY (SIOG) - PRAGA, REPÚBLICA CHECA

ESTIMATING HEMATOLOGIC CHEMOTHERAPY RISK OF TOXICITY IN ELDERLY TREATED PATIENTS IN CATHOLIC UNIVERSITY OF CHILE CANCER CENTER O.

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Introduction: Elderly have particularities that make therapeutic decisions difficult. They are a heterogeneous and complex population, with multiple comorbidities, geriatric syndromes and various states of functional decline. These characteristics affect life expectancy and determine a frailty phenotype, which heightens the risk of adverse events such as chemotherapy toxicity. Two different groups have developed scales to predict chemotherapy toxicity risk in elderly (CRASH and CARG). None of these have been validated in

Chile. Objectives: The purpose of this study was to check the predictive capacity of these instruments to determine the hematologic chemotherapy risk in elderly adults over 65 years of age in our country. Methods: Between April 2012 and April 2014, patients over 65 years of age with hematologic tumors were included in Catholic University of Chile Cancer Center. Before treatment was initiated patients were evaluated by a geriatrician who applied both instruments. After the end of the study, medical charts were reviewed looking for Grade 3, 4 or 5 hematologic toxicity during treatment. Results: Eighty five patients were included, 59% were women, age average was 75 years (65-91). Most prevalent diagnosis were digestive system neoplasms (GI) (54.2%), breast (14.3%), and urogyn (UG) (14.3%). Ninety four percent were ECOG 0-1. Twenty eight percent developed hematologic toxicity. When scales were checked, the predictors with higher correlations were: combined chemotherapy ($p=0.033$), GI or UG $p=0.036$, and anemia ($p=0.01$). Patients with higher CARG scores had more risk of toxicity than those with lower scores. CRASH scale did not show statistical significant correlations. Conclusion: CRASH score did not predicted hematologic toxicity risk in our sample. Higher CARG scores did related with higher risks of toxicity. It would be recommended to validate these data with other populations an bigger samples.

NEUROLOGÍA Y NEUROCIRUGÍA

ANNUAL MEETING AMERICAN ACADEMY OF NEUROLOGY - WASHINGTON DC, USA

CONGENITAL MYASTHENIC SYNDROME DUE TO DOK7 MUTATIONS IN A FAMILY FROM CHILE

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OBJECTIVE: To describe the clinical features, the genetic findings and the underlying pathophysiology of a congenital myasthenic syndrome (CMS) in a Chilean family. **BACKGROUND:** 53-year old female with slowly progressive bilateral ptosis, facial weakness, proximal limb weakness and scoliosis since early life. One female sibling has similar findings, and a second one milder symptoms, while her non-consanguineous parents, three additional siblings and her offspring are asymptomatic. **DESIGN/METHODS:** Repetitive nerve stimulation, single fiber EMG, deltoid muscle biopsy, muscle MRI and DNA testing for CMS. **RESULTS:** Repetitive nerve stimulation of facial nerve at 3 Hz showed 15% decrement of compound muscle action potential and single fiber EMG in the EDC muscle showed increased jitter and blocking. CK was slightly elevated and the muscle biopsy showed type-one fiber predominance without tubular aggregates. Sequencing of genes encoding the acetylcholine receptor (AChR) subunits and rapsyn was unrevealing, but sequencing of DOK7 showed that the three affected siblings were compound heterozygous for c.1457delC, which predicts p.Pro486Argfs*13; and c.473G>A, which predicts p.Arg158Gln. p.Pro486Argfs*13 truncates the protein at the C-terminal domain, while the previously reported p.Arg158Gln mutation disrupts the interaction of dok-7 with MuSK at the phosphotyrosine binding (PTB) domain. Unaffected family members carried only one or neither mutation. **CONCLUSIONS:** We report here that the combined effect of a PTB and a C-terminal domain mutation in dok-7 results in a recessively transmitted CMS in a large Chilean family. The phenotype of the affected patients was that of limb-girdle myasthenia with additional facial involvement, but there was high intrafamilial variability. Recognition of CMS due DOK7 mutations is important as patients with this condition often respond poorly to anticholinesterase drugs, but well to adrenergic drugs such as ephedrine and salbutamol.

OBSTETRICIA Y GINECOLOGÍA

ADVANCES IN OVARIAN CANCER RESEARCH: EXPLOITING VULNERABILITIES (AACR) – ORLANDO, FLORIDA, USA.

LEVELS OF PHOSPHO-CONNEXIN 43 AND PHOSPHO-TRKB IN EPITHELIAL OVARIAN CANCER.

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Cancer is the second cause of death in Chile, and one of the most aggressive and worse prognosis is ovarian cancer. Between 70 and 80% of ovarian cancer cases correspond to epithelial ovarian cancer (EOC). EOC has a poor treatment response, so that is necessary to study new targets in order to improve cancer therapy. In this context, the neurotrophin receptors (for instance TRK receptors) and cell adhesion and communication molecules such as connexins are very important. Researches undertaken by our group have found that Nerve Growth Factor and its high affinity receptor TRKA are involved in cell proliferation and angiogenesis in EOC. TRKB, another subtype of TRK receptor, by interacting with its high affinity ligand brain-derived neurotrophic factor or NGF has been strongly associated with metastatic processes and resistance to cancer therapies in many kinds of cancers. Specially, phosphorylation of TRKB on residue tyrosine 812 (pTRKB) is capable of activating FLCy-PKC pathway, which has an important role on proliferation, apoptosis and protein modifications, like connexins. On the other hand, cells are anchored and

connected into tissues through gap junctions, among others. These are channels that connect cytoplasmic contents of neighbor cells and also regulate many physiological processes such as cell cycle, permeability and migration. Connexins are proteins that form these channels. Connexin 43 (Cx43) has been widely studied in cell lines and tissues from cancer, being present in ovarian cancer. Phosphorylation of Cx43 on serine 368 (pCx43) disrupts gap junctions and intercellular junctional communication. This could be an advantage for malignant cells to survive in processes such as therapy resistance, proliferation and metastasis. This phosphorylation is induced by several tyrosine kinase receptors, for instance platelet-derived growth factor receptor. The main purpose of this study is to describe the presence and levels of pTRKB and pCx43 on women's ovary samples and to associate them with patients' survival through a retrospective study. Samples of female patients (age 26 -79, average 52 years) who underwent surgical procedures at University of Chile Clinical Hospital were used. Each participant signed an informed consent approved by the institutional ethics committee. Fresh tissue stored at -80°C and paraffin-fixed tissues were employed, jointly with retrospectively analysis of medical records. Biopsy and classification of samples were performed in the Pathology Department of the same Hospital, and the samples were classified in inactive or normal ovaries (N=17), ovarian tumor (N=18) and epithelial ovarian cancer (N=33). pCx43 and pTRKB levels were determined by immunohistochemistry (IHQ) and levels of Cx43 and pCx43 were measured by Western-blot. The semi-quantitative analysis was performed by ImageProPlus 6.0.250 and UnScan-It gel 6.1. These results were associated with patients' survival. Kruskal Wallis and Mann Whitney tests were performed. The results showed that pTRKB and pCx43 were found in epithelial cells of ovarian tissues which levels increased during the progression of EOC; in fact, pTRKB content was evaluated by IHQ being 1.7 times in tumors and 3,2 times in EOC ($p < 0.05$) compared to normal ovarian epithelium respectively. Levels of pCx43 were 3,6 times in tumor and 6,0 times in EOC respect to ovarian normal epithelium ($p < 0.01$). The pCx43/Cx43 ratio evaluated by western-blot, increased from 0,37 to 0,83 (2,3 times, $p < 0,05$) between inactive ovary and EOC. These results suggest that the studied molecules play a role in the progression of EOC and should be considered as potential targets to be evaluated in future research.

UROLOGÍA

INTERNATIONAL CONTINENCE SOCIETY ANNUAL MEETING – MONTREAL, CANADA

A VOIDING SYMPTOMS OBTAINED BY OPEN VERSUS DIRECTED ANAMNESIS AS PREDICTORS OF URODYNAMIC VOIDING DYSFUNCTION IN WOMEN WITH PREVIOUS ANTI-INCONTINENCE SURGERY

Valdevenito J P, Manriquez V, Wenzel C, Guzman Rojas R, Naser M, Diaz J P, Vega.

Hypothesis / Aims of the Study: The NICE clinical guideline for the management of urinary incontinence in women gives value to the presence of "symptoms suggestive of voiding dysfunction" and recommends multichannel urodynamics before surgery in patients who present them. However, there are few studies correlating voiding symptoms with the findings of pressure-flow studies in women, which focus on the diagnosis of bladder outlet obstruction, without considering the diagnosis of detrusor underactivity [1]. The aim of the study is to evaluate whether voiding symptoms obtained by open versus directed anamnesis are predictors of urodynamic voiding dysfunction in a group of women more likely to present it: women with previous anti-incontinence surgery. Study design, material and methods: One hundred and fourteen consecutive women with previous anti-incontinence surgery, undergoing conventional cystometry following "good urodynamic practices" by the same urologist, in a five year period, were included in a retrospective study. At the time of examination and in a standardized manner, patients were asked if they had "difficulty emptying the bladder" (question 5 of the short form of the "Urogenital Distress Inventory" questionnaire). If the answer was positive, they were asked to describe their symptoms, considering weak stream, strain to void and intermittent stream (voiding symptoms obtained by open anamnesis). If the patient responded negatively to the first question or did not present the three voiding symptoms, they were asked for the presence of each of these symptoms in a directed way (added to the above: voiding symptoms obtained by directed anamnesis). Symptoms were recorded as being either present or absent without any stratification for severity. Bladder outlet obstruction was defined as $Q_{max} \leq 12 \text{ mL/s} + p_{det} Q_{max} \geq 25 \text{ cm H}_2\text{O}$ [2], Detrusor underactivity was defined as $Q_{max} \leq 12 \text{ mL/s} + p_{det} Q_{max} \leq 10 \text{ cm H}_2\text{O}$ [3] and mixed voiding dysfunction as $Q_{max} \leq 12 \text{ mL/s} + p_{det} Q_{max}$ between 11 and 24 cm H₂O, with a concordant free uroflowmetry in all cases. Voiding symptoms and urodynamic diagnosis were tabulated independently. We sought statistical association between any urodynamic voiding dysfunction and the presence of any voiding symptom obtained by open and directed anamnesis using chisquare or Fisher's exact test. The same was done with each individual symptom. In case of obtaining a statistically significant result ($p < 0.05$) we calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, positive and negative likelihood ratios and strength of agreement using Cohen's kappa. The information was processed with Stata 11.2 program (Stata Corporation, 2009). Results: Of the 114 patients 23 were excluded (6 using

medication active on the lower urinary tract, 6 examinations done reducing pelvic organ prolapse, 5 with neurological diseases, 5 with urethrolisis done before the examination and 1 with bladder pain syndrome), leaving 91 patients for analysis. Table 1 shows the clinical history of the patients. Eighteen patients had urodynamic voiding dysfunction (19.8%; 13 bladder outlet obstruction, 3 detrusor underactivity and 2 mixed voiding dysfunction). Table 2 shows statistical association between voiding symptoms and urodynamic voiding dysfunction. There was a statistical association between urodynamic voiding dysfunction and a) presence of any voiding symptom obtained by open anamnesis and b) strain to void obtained by open anamnesis. There was no association with voiding symptoms obtained by directed anamnesis. Table 3 shows sensitivity, specificity, PPV, NPV, accuracy, positive and negative likelihood ratios and strength of agreement of the voiding symptoms with statistical association. Interpretation of results: In women with previous anti-incontinence surgery, there is a statistical association between urodynamic voiding dysfunction and a) presence of any voiding symptom obtained by open anamnesis and b) strain to void obtained by open anamnesis, being higher for strain to void. Nevertheless, the strength of agreement is low. There was no association with voiding symptoms obtained by directed anamnesis (that could be considered similar to those obtained by symptoms scores).