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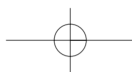

◆ INVESTIGACIÓN ARGENTINA

Publicamos los resúmenes de los trabajos realizados en la Argentina y aceptados para su presentación en la *Digestive Disease Week 2010* realizada en New Orleans (EE.UU.) del 1 al 5 de mayo.

APPROPRIATE INDICATION FOR UPPER ENDOSCOPY BASED ON ASGE GUIDELINES AND ITS RELATION WITH POSITIVE FINDINGS

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Introduction. Upper gastrointestinal endoscopy (UGE) is a safe and effective diagnostic procedure, but it is relatively costly and implies certain risk.Several guidelines have been published for its appropriate use, as the American Society for Gastrointestinal Endoscopy (ASGE). **Aims.** To assess if UGE is used appropriately according to ASGE guidelines.To assess the probability of detecting significant lesions by endoscopy in patients with appropriate indication and compared it with the endoscopic findings in patients with inappropriate indication. To assess the appropriateness of the indication according to referring phyisicians specialities. **Materials and methods.** We included data from 541 consecutive diagnostic UGE from January 2006 to December 2008 in outpatients referred to our center. We recorded age, sex,diagnosis,endoscopic findings and requesting doctor´s specialty. Endoscopic findings that had direct therapeutic or prognostic consequence were classified as "positive" or as "negative". Indications were classified as appropriate,inappropriate and doubtful according to ASGE guidelines.For statistical analysis we used X^2 test and multiple logistic regression with a confidence level of 95%. **Results.** We reviewed UGE reports of 364 (67%) women and 177 (33%) men.The mean age was 59,91 ± 16 years (range: 17-98). Patients referred by gastroenterologist were 350 (65%), 179 (33%) by generalists, 7 (1%) by surgeons, and by others 5 (1%). The most frequent referrals were upper abdominal pain in 195 (36%) patients, heartburn in 131 (24%),iron deficiency anemia in 27 (5%), dyspepsia in 13 (2%) and others in 175 (32%). Indications were classified as appropriate in 330 (61%) cases,inappropriate in 133 (25%) and doubtful in 78 (14%). Positive endoscopic findings were reported in 288 (53%) patients, in 182 (55%) with appropriate indication, in 64(48%) with inappropriate indication and 42 (54%) in doubtful (P = 0,38). The clinicians referrals showed the highest percentage of positive endoscopic findings. **Conclusions.** This study showed a significant frequency of inappropriate indications for UGE according to ASGE guidelines. The presence of positive endoscopic findings was not related to the appropriateness of the indication, but to the physician´s speciality. This study showed that current guidelines regarding the appropriateness of UGE are relatively inefficient in excluiding significant endoscopic findings.

APPROPRIATE INDICATION OF COLONOSCOPY BASED ON ASGE GUIDELINES AND ITS RELATION WITH POSITIVE FINDINGS

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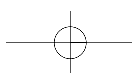
Introduction. The colonoscopy is a safe and effective diagnostic procedure,but it is relatively costly and implies certain risks-.Several guidelines have been published for the appropriate use of colonoscopy as the American Society for Gastrointestinal Endoscopy (ASGE). **Aims.** To assess: 1) The appropriate use of colonoscopy according to ASGE guidelines; 2) the probability of finding relevant endoscopic pathologies in the group of patients with appropriate indication and to compare them with endoscopic findings in patients with inappropriate indication and 3) the appropriateness of the indication according to the specialty of the referring doctors. **Materials and methods.** We included data from 466 consecutive diagnostic colonoscopy from January 2006 to December 2008 in outpatients referred to our center. We recorded the age, sex, diagnosis and endoscopic findings. Colonoscopy with endoscopic findings that had direct therapeutic or prognostic consequence were classified as "positive" or as"negative". Indications were classified as appropriate, inappropriate and doubtful according to ASGE guidelines.For statistical analysis we used X^2 test and multiple logistic regression with a confidence level of 95%. **Results.** We reviewed colonoscopy reports of 306 (66%) women and 160 (34%) men with a mean age of 63,46 ± 13 years(range: 23-91). Patients referred by gastroenterologists were 260 (56%), 156 (33%) by clinicians, 35 (8%) by surgeons, 14 (3%) by oncologists and others in 1 (0,21%). The most frequent indications were: low gastrointestinal bleeding 126 (27%), previous polypectomy 68 (15%), screening 65 (14%), constipation 59 (13%), surgery of previous colon cancer 40 (9%), iron deficiency anemia 32 (7%) and others in 76 (17%). Indications were classified as appropriate in 370 cases (79%), inappropriate in 10 (2%) and doubtful in 86 (19%). Positive endoscopic findings were reported in 172 (37%) patients,out of which 145 (84%) were with appropriate indication, 2 (1%) with inappropriate indication and 25 (14%) with doubtful indication (P = 0,11)There were no statistically significant differences among the different specialities of the referring doctors. **Conclusions.** This study showed a significant frequency of appropriate indication for colonoscopy according to ASGE guidelines regardless of the referring physician. There was a higher percentage of relevant findings in those with appropriate indication. The mean age of patients with significant findings were higher than those without findings.



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A PROSPECTIVE STUDY TO ASSESS COMORBID GASTROESOPHAGEAL REFLUX SYMPTOMS AT DIAGNOSIS OF CELIAC DISEASE AND EFFECT OF TREATMENT WITH THE GLUTEN-FREE DIET

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Introduction. A few studies have shown that patients with celiac disease (CD) often complain of gastroesophageal reflux (GER) symptoms. The characteristics of this association and the role of gluten consumption in the pathogenesis of symptoms remain to be elucidated. **Aims.** To assess the prevalence of GER comorbidity at the time of CD diagnosis and to determine the long-term effect of CD treatment on the reflux symptoms. **Subjects.** We followed and evaluated 130 adult CD patients (median age: 39 years; 98 females) from their diagnosis and 70 healthy controls of similar age and gender distribution for GER symptoms. While 95 patients had a classic clinical presentation of CD, 35 were categorized as presenting atypical or silent CD. Fifty-three patients completed questionnaires at different time points over a period of at least 4 years after diagnosis. **Methods.** We used the Gastrointestinal Symptoms Rating Scale, a validated, self-administered questionnaire for evaluating GER symptoms at baseline (ie, CD diagnosis) and after diagnosis. The reflux syndrome, which explores heartburn and regurgitation symptoms, was rated on a 7-point Likert scale. Patients were assessed at diagnosis, 3-month, 1-year, and more than 4-year time points (median: 53 months) after commencing CD treatment. The degree of compliance with the gluten-free diet was assessed during follow-up and categorized as strict or partial. **Results.** Cross-sectional analysis at diagnosis showed that patients with CD had a significantly higher reflux syndrome mean score than controls ($P < 0,001$). At baseline, 19,2% of CD patients had scores ≥3 compared with 4,7% of controls ($P < 0,01$). GER symptoms were significantly associated with having the classic type of CD compared with atypical/silent CD (24,2% vs. 5,7%; $P < 0,01$). Only 3,8% of the CD patients had endoscopic evidence of erosive GERD. During treatment follow-up, a rapid improvement was seen as early as 3 months after diagnosis ($P < 0,0001$) with the reflux syndrome scores comparable to that of healthy controls, and this improvement persisted thereafter. No significant difference was observed between patients strictly compliant with the gluten-free diet and those partially compliant at the 1-year and 4-year assessments. **Conclusion.** While GER symptoms were frequent in untreated, classically symptomatic CD patients, most cases are related to non-erosive GERD. Once treatment was initiated, patients demonstrated a rapid and long-term improvement and attained similar outcomes to healthy controls. Symptom improvement was not related to the degree of compliance with the gluten-free diet.

CELIAC DISEASE AND RISK OF COLORECTAL NEOPLASIA

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Introduction. although small bowel and esophagus neoplasia are recognized to occur more frequently in patients with celiac disease (CD), an association with colorectal cancer has not been described. **Aims:** To determine the risk of colorectal neoplasia among patients with celiac disease. **Materials and methods.** A nested case-control study was conducted using the Gastroenterology and Endoscopy electronic data base to identify patients that had performed colonoscopy. Patients with CD were regarded as "cases" and those without CD were regarded as "controls". For each case, two controls matched for age, sex, colonoscopy purpose and first and second grade family history of colorectal cancer, were randomly selected. A survey was carried out by telephone calls to assess patients on their risk factors and history disease. The main outcome evaluated was the risk of colorectal polyps, adenomas, advanced lesions and cancer. Risk was measured in odds ratio (OR) and its corresponding confidence intervals 95% (CI). **Results.** Out of 178 celiac disease patients analyzed, 44 had undergone a previous colonoscopy and were included in the study as cases and 88 as controls. In cases, the average age was 55 years old (range 34-82 years old), 86% women, the colonoscopy purpose was colorectal cancer screening in 63% and abdominal pain in 16% and strict adherence to the gluten- free diet occurred in 66%. Presence of polyps, adenomas and advanced colonic lesions was 9/44 (20%), 7/44 (16%) and 2/44 (4,5%) respectively. In controls, the average age was 55 years old (range 33-82 years old), women 86%, and the colonoscopy purpose was colorectal cancer screening in 55% and abdominal pain in 15%. Presence of polyps, adenomas and advanced colonic lesions was 13/88 (15%), 8/88 (9%) and 3/88 (3,4%) respectively. The risk of polyps, adenomas and advanced colonic lesions was similar in both groups (OR 1, 48, IC 0, 59-3,73 $P = 0,40$, OR 1,89, CI 0,66-5,42 $P = 0,24$, and OR 1,34 CI 0,26-7,05 $P = 0, 74$, respectively). No colorectal cancer was identified. **Conclusion.** It has been shown that the risk of colorectal neoplasia within a cohort of patients with celiac disease who presented a strict adherence to the gluten- free diet, was similar to the general population.

DIAGNOSTIC YIELD OF ENDOSCOPIC STUDIES IN PATIENTS WITH CANCER OF UNKNOWN PRIMARY

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Background. Cancer of unknown primary accounts for 10% of cancer diagnosis. Most of them arise from lung or pancreas. The initial diagnostic strategy does not include endoscopic studies for upper and lower digestive tract. However, gastroenterologists are commonly asked to perform endoscopic studies in patients with cancer of unknown primary without digestive symptoms, and the yield of endoscopic studies in this group of patients is not well established. **Aim.** To assess whether endoscopic studies in patients with cancer of unknown primary without digestive symptoms have clinical benefits. **Patients and methods.** Cross sectional survey of consecutive patients referred to our endoscopic center to perform upper endoscopy, colonoscopy or both because of cancer of unknown primary. Patients with dysphagia, hematochezia, melena, anemia, positive fecal occult blood test, personal or family history of gastrointestinal cancer and imaging study suggesting gastrointestinal abnormality were excluded. A positive finding was defined as digestive cancer confirmed by histopathological analysis. **Results.** Eighty one studies (45 upper endoscopies and 36 colonoscopies) were performed in the 60 patients included (29 males and 31 females, mean age 63,9 ± 16 yrs). In 21 patients both studies were performed, whereas upper endoscopy alone was realized in 24 and colonoscopy alone in 15 patients. Positive findings were evidenced in 8/45 (17%) upper endoscopies and 3/36 (8%) colonoscopies. In the group of patients with upper gastrointestinal malignancy 6 had gastric and 2 duodenal cancer (2M/6F, mean age 63 yrs.), while the 3 patients with lower gastrointestinal malignancy had colorectal cancer (1M/2F, mean age 62 yrs.). It is important to note that 4 of the 8 upper gastrointestinal malignancies occurred in patients under 55 years old, and 3 of them were women. **Conclusion.** In this study, the diagnostic yield of endoscopic studies in patients with cancer of unknown primary without digestive symptoms is low. These results are consistent with the initial diagnostic strategy suggested in this group of patients. However, the finding of upper gastrointestinal cancers in patients under 55 years old with female predominance might be evaluated in larger studies.

ENDOSCOPIC AND/ OR SEROLOGICAL AND HISTOLOGICAL CONCORDANCE IN PATIENTS WITH SUSPICION OF CELIAC DISEASE

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Introduction. Celiac Disease (CD) is a chronic autoimmune enteropathy triggered by gluten ingestion. It affects 0,7 to 1,5% of general population. However its real prevalence is unknown because of the varied clinical presentations and the lack of an absolute diagnostic method. Positive histological and serological concordance lead to unequivocal diagnosis, but its absence does not rule the disorder out. Considering that untreated CD is associated with high morbidity and mortality, its early detection is mandatory. **Objectives.** Estimate sensitivity, specificity, likelihood-ratio (positive and negative) of endoscopy, serology and combination of methods for CD diagnosis. **Methods.** This prospective, observational and cross sectional study included adults with clinical suspicion or family history of CD. Clinical suspicion was based on gastrointestinal, non gastrointestinal symptoms or associated autoimmune diseases. The protocol was conducted in gastroenterological outpatients' clinics in Buenos Aires city, from June 2006 to June 2009. All included patients had endoscopic, serologic (EMA Ig A, tTG Ig A and total Ig A) and histological tests performed. Histology was considered the gold standard method for diagnosis and histological findings were classified according to Marsh criteria modified by Oberhuber. CD was established in patients with positive serology and concordant histology, irrespective of endoscopic findings. Statistical Analysis: EPIDAT 3,1 y VCCstat 2,0. **Results.** 119 patients were included (92 females, 27 males, average age: 32,5 years). CD was diagnosed in 44/119 patients (37% IC95 28.2- 46.3%). Chronic diarrhea and iron deficiency anemia were the most prevalent modes of presentation. Sensitivity, specificity, likelihood-ratio positive and negative of endoscopy were 60,5% (IC95 48,6-71,6%), 89,1% (IC95 77,7-95,9%), 5,54 (IC95 2,55-12,06) and 0,443 (IC95 0,33-0.594) respectively. Sensitivity, specificity, likelihood-ratio positive and negative of serology were 62,9% (IC95 50,4-74.1%), 93,9% (IC95 83,1-98,8%), 10,26 (IC95 3,38-31,18) and 0,396 (IC95 0,289-0,541) respectively. Sensitivity, specificity, likelihood-ratio positive and negative of combination of methods were 63,5% (IC95 50,4-75,3%), 97,6% (IC95 87.4-100%), 26,6 (IC95 3,81 to infinite) and 0,374 (IC95 0,269-0,52) respectively. **Conclusions.** 1) Our results revealed that endoscopy and serology separately or in combination have the same usefulness for CD diagnosis. 2) Considering both, the substantial evidence for the benefit of the combination of methods for the diagnosis and the results of this study, it is required to enlarge the number of patients to obtain conclusive data.

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ENDOSCOPY IN THE ELDERLY. FINDINGS JUSTIFY RISKS?

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Background. As demographics shifts towards an aging population, the use of endoscopy in the elderly is increasing every year. However, the risk of the procedures ant the discomfort produced for bowel preparation in this group of patients must be considered. Furthermore, the clinical benefits of performing endoscopic studies in patients over 80 years of age remain unclear. **Aim.** To assess whether endoscopic studies in patients over 80 years old have clinical benefits. **Patients and methods.** Cross sectional survey of consecutive patients over 80 years of age referred to our endoscopic center to perform upper gastrointestinal endoscopy (EGD), colonoscopy or ERCP in a two-year period. Positive findings were defined as those entities in which medical, endoscopic and/or surgical treatment potentially modify the therapeutic behavior and eventually the prognosis and/or quality of life of the patient. Findings were classified as negative when treatment and prognosis do not change (normal studies, hiatal hernia < 5 cm, gastric and colonic polyps under 0,5 cm and non-complicated colonic diverticular disease). Immediate procedure-related complications were measured in all cases. **Results.** Of a total of 5,598 endoscopies, 375 (6,7%) were performed in patients over 80 years. Upper gastrointestinal endoscopy were performed in 162 patients (71 M/91 F, mean age 84 ± 3,9 yrs), colonoscopy in 171 (66 M/105 F, mean age 83,6 ± 3 yrs) and CPRE in 42 (15 M/27 F, mean age 85,8 ± 5 yrs). Positive findings were evidenced in 90/162 (55,5%) EGD, 54/171 (31,5%) colonoscopies and 32/42 (76%) ERCP. Procedure-related complications did not occur. **Conclusion.** In this study the clinical benefits of performing endoscopic studies in patients over 80 years old is high. Endoscopic treatment was performed in more than 60% of these patients. The low rate of complications and the high diagnostic and therapeutic yield of endoscopic studies justified the use of advanced endoscopic procedures in patients over 80 years old.

IMPROVED PERFORMANCE OF CELIAC DISEASE-RELATED SEROLOGY TESTS IN PREDICTING THE DEGREE OF PATIENTS' COMPLIANCE WITH LONG-TERM GLUTEN-FREE DIET. NEW CUT-OFFS ARE NECESSARY

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Introduction. The usefulness of celiac disease (CD)-related antibody tests in monitoring clinical outcome of patients being treated with a gluten-free diet (GFD) has not been well studied. **Aims.** To assess the performance of serology changes in a cohort of CD patients and to determine whether antibody assays can identify partial adherence to the GFD in long-term follow-up. **Methods.** Serum samples from 53 adult CD patients, obtained at baseline, 1-year, and beyond 4-year time points after treatment initiation, were assayed for: 1) IgA anti-tissue transglutaminase (a-tTG), 2) IgA endomysial (EmA), 3) IgA and 4) IgG anti-deamidated gliadin peptide (a-DGP), 5) a-DGP Dual, and 6) DGP/tTG Screen. The degree of adherence to the GFD was assessed by expert nutritionists at the 1- and 4-year visits, and patients were categorized as strictly or partially compliant. **Results.** Based on the cut-off values provided by the manufacturers (20U/mL), the serologic tests had very high sensitivities (>92%) at diagnosis with the exception of IgA AAA (70%). Follow-up assessments indicated that new cut-off values for these tests were required to define the best predictive performance. At the 1-year assessment, the test performance for detecting partial adherence, measured by the area under ROC curve (AU ROC), ranged from 0.60 (95% CI 0,45 to 0,73) for IgG a-DGP to 0,69 (0,55 to 0,81) for a-tTG and IgA a-DGP. At the 4-year assessment, the performance for detecting partial adherence ranged from 0.70 (0,56 to 0,82) for DGP/tTG Screen and IgG a-DGP to 0,78 (0,64 to 0,88) for IgA a-DGP. At this time point, the IgA a-tTG test showed an increased AU ROC to 0,75 (0,61 to 0,85) at a cut-off value of 12U/mL. The best cut-off for IgA a-DGP was 15U/mL. Although the IgA EmA test could only be assessed as positive or negative at 1:5 dilution, its positive predictive value for detecting partial adherence to the GFD beyond 4 years was 100% with a negative predictive value of 62%. **Conclusion.** GFD treatment produced rapid and significant qualitative and quantitative changes in CD-related antibody assay results in adult patients. The long-term assessments suggested that the cut-off values used for CD diagnosis were not useful for determining patients' adherence to the GFD. With statistical analyses, however, the serologic tests with new cut-off values may be effective in monitoring patient adherence to treatment increasing their performance in the long-term. IgA a-DGP and IgA a-tTG had similar performance, which was better than the other tests, at the 1-year and 4-year assessments.

INCREASED INTESTINAL PERMEABILITY (IP) IN CIRRHOSIS IS ASSOCIATED TO THE SEVERITY OF THE LIVER DISEASE AND A HIGHER MORTALITY

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Background. Few studies on the assessment of IP in cirrhotic patients are available and their results are controversial. Moreover, it is not clear if these changes could be related to the degree of the functional liver compromise or to long-term survival. **Aim.** Our aim was to determine whether IP is altered in cirrhotic patients and the relationship between IP changes, the stage of liver disease and survival. Patients/methods: We prospectively enrolled a cohort of 63 patients with liver cirrhosis (19 females; mean age: 55 yr; range: 18-75). The severity of the liver disease was assessed according to the Child-Pugh classification. Cases with an associated disease, impaired renal function, continuing alcohol consumption and drug intake which is known to have an effect on IP were excluded. At entry the study, patients underwent a sugar permeability test ingesting lactulose (Lac) and mannitol (Man) (2g). The urinary excretion of sugars was measured by HPLC. A prospective database of clinical variables was kept for all patients. We analysed mortality rate and causes two years after being enrolled in the study. Survival was assessed using Kaplan-Meier curves. Multivariate analysis of factors at presentation was also performed. **Results.** (median±SEM). At baseline, patients had increased Lac/Man ratio (0,031± 0,03);. Thus, 26 of 63 cirrothic patients (41,2%) had Lac/Man ratio values over the normal upper limit Normal value: < 0,025). A significant correlation was found between clinical severity scores for liver disease and IP. Thus, impairment of small intestinal permeability was statistically greater in patients Child C (n=10) (0,054±0,01) compared with those Child A (n=21) (0,022±0,002) and Child B (n=32) (0,031±0,006) (P < 0,03). The median follow-up was 19,5 months (range 1 to 41). Abnormal IP was associated with greater mortality (Relative risk [RR] and log-rank test: 0,04; P < 0,02). Multivariate analysis also showed that hepatorenal syndrome and variceal bleeding independently predicted higher mortality (RR and log rank test: 8,75; P < 0,0005 and 7,7; P < 0,002, respectively). **Conclusions.** Impaired IP, a frequent finding in patients with cirrhosis, is associated to the severity of the disease and could predict a higher mortality.

NONALCOHOLIC FATTY LIVER DISEASE: "ACUTE HEPATITIS LIKE" ANOTHER CLINICAL PRESENTATION FORM?

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Background and aim. Nonalcoholic fatty liver disease (NAFLD) is the main cause of chronic liver disease in developed countries. It is strongly associated with the metabolic syndrome (MS) and today recognized as a cause of cryptogenic cirrhosis. Usually it is asymptomatic or presents unspecific symptoms. However, in this study we observed and report other cases where acute hepatitis like syndrome was the clinical presentation form. **Methods.** In prospective form between September 1995 to September 2009 in all the patients (pts) we suspected NAFLD and appropriate exclusion of other causes of liver disease such as alcohol intake, hepatitis A, B, C, autoimmune disease and drug induced hepatitis. A liver biopsy was indicated if the alanine aminotranferase (ALT) was elevated more than 1.5 times the normal levels in three consecutives determinations. When the NAFLD was confirmed the pts were divided in two groups according to symptoms and level of the ALT. Group 1 (classic NALFD) was integrated by asymptomatic pts or with unspecific symptoms (vague abdominal discomfort) and ALT< 7 times the normal values (2-41 IU/ml).While the pts in group 2 presented intense fatigue, abdominal pain on the rigth side and the ALT> 7 times the normal values. The last group was defined as "acute hepatits like" (AHL). In both groups: age, gender, body mass index(BMI: Kg/m2) and MS prevalence were determined. The Matteoni's histological classification was used to defined the following subgroups: type 1 fatty liver alone, type 2 fatty and lobular inflammation, type 3 fatty, inflammation and ballooning degeneration and type 4 the previous signs plus fibrosis. Student Test and Mann-Whitney were used for continuous variables and Fisher test for discontinuous variables. **Results.** 139 pts presented NAFLD confirmed by biopsy: 130 (94%) belonged to group 1 (classic NAFLD) and 9 (6%) to group 2 (AHL): no differences were observed between both groups in gender, BMI, MS and histological diagnosis (69% and 78% of type 3 and 4 prevalence of Matteoni's classification in groups 1 and 2 respectively). However, there were differences in: mean age 29 ± 9 (range 20-45) in group 2 vs 50 ± 9 (range 27-65) in group 1 (P < 0,01) the mean of ALT: 410 IU/ml (range 328-682) in group 2 vs 84 IU/ml (range 62-240) in group 1 (P < 0,01) and the group 2 was symptomatic in the 100% (9/9) of the cases vs 30% (39/130) in group 1 (P < 0,01). **Conclusions.** of all the NAFLD 6% presented acute hepatitis like features: younger pts, intense symptoms and high level of ALT were clinical characteristics. Further and prolonged studies are necessary to confirm this data and to investigate the prognostic significance.

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P-GLYCOPROTEIN (P-GP) FUNCTIONAL ACTIVITY IN PERIPHERAL BLOOD LYMPHOCYTES (PBL) AND COLONIC BIOPSIES OF ULCERATIVE COLITIS (UC)

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Background. The multidrug resistant gene (MDR1) encodes the P-gp, a transmembrane efflux pump, over-expressed in resistant cancer-cells, decreasing intracellular drug concentration. Regarding IBD, MDR maps in a susceptibility genome site and P-gp is expressed in apical intestinal epithelial cells (EC) and immune cells (PBL, mucosal lymphocytes). P-gp hyperfunction was a factor proposed for IBD refractoriness, but a deficient function to pump-out harmful toxins was postulated for pathogenesis. AIM: to study P-gp activity in UC from PBL and colonic biopsies. **Material and methods.** P-gp functional activity was evaluated in PBL (with cell-populations immunomarcation) of UC (n 49) and healthy controls (HC, n 78) with simultaneous assessment in intraepithelial lymphocytes (IEL) and epithelial cells (EC), isolated from colonoscopic biopsies (UC 18, HC 11). Rhodamine123 (a fluorescent P-gp substrate) efflux was studied by flow cytometry, in absence and presence of P-gp modulators Verapamil 100 μM, Valspodar 1_M. Data were expressed by the behaviour of two markers defined by % of cells with different fluorescence levels: M1 (high fluorescence, low P-gp pump activity) and M2 (low fluorescence, high activity). Patients were categorized in responders (RESP: n 26) or refractory (REFR: n 23) to current treatment (mesalazine, steroids, 6-MP) and activity was scored (DAI). **Results (mean±SD).** Irrespective of kind of current treatment, significant differences were observed in PBL, showing increased P-gp functional activity in REFR vs RESP (M2: 60,0±15,9 vs 47,4±10,7 $P < 0,002$, Median test) and HC (47,9±12,3 $P = 0,009$), but not between RESP vs HC. Reassessment in responders showed P-gp reduction. Interestingly, an UC subset assessed before any treatment (n 10) showed increased activity vs HC (M2: 54,2±5,8 $P < 0,04$) and RESP ($P < 0,02$). In the inhibition assay mean M2 was higher in REFR (26,6±22,6) vs RESP (9,1±5,6 $P < 0,002$) and HC (12,6±8,0 $P < 0,001$). In spite of mild global DAI correlation, in severe pts (DAI 9-12, n12) surgery was required in 3/4 cases showing M2>M1 in the inhibition assay. Results for biopsies were: IEL T cells showed decreased P-gp activity vs HC (only basal M2: 30,3±22.4 vs 53,6±22,4, $P < 0,02$). PBL and IEC (T cells) did not showed correlation in UC or HC. P-gp in EC was higher than HC (basal: 1096±35 vs 1515±51 $P < 0,01$, inhibition: 1015±37 vs 1794±50 $P < 0,002$). **Conclusions.** We found significant P-gp activity differences between UC and HC. PBL and IEC did not show correlation. Because of P-gp is able for modulation, its research in UC, could improve disease management and pathogenesis knowledge, either if the behaviour is cause or consequence of the disease.

POST-ERCP HYPERAMYLASEMIA AND PANCREATITIS. THERAPEUTICS MANEUVERS AS ASSOCCIATED RISK FACTORS

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Background. Hyperamylasemia and pancreatitis rate after ERCP plus sphynterotomy are well documented. In the almost exclusively therapeutic-ERCP era, different maneuvers for the management of the biliary pathology may increase the post ERCP related complications including hyperamylasemia and pancreatitis. **Aim.** To identify the therapeutic maneuvers more frequently associated to post ERCP-related hyperamylasemia and pancreatitis. Patients and Methods: 895 ERCPs were performed in 674 patients from July 2004 to October 2009. 863 (96,5%) were therapeutics procedures and were included in the analysis. 386 procedures were excluded from analysis because patients had elevated serum amylase at least three months before or at the procedure time, acute pancreatitis or previous history of chronic pancreatitis. Serum amylase levels were determined prospectively at 6, 16 and 24 hours after procedure, as well as physical and clinical patient evaluation. Post ERCP hyperamylasemia was defined as any amylasemia level increase without abdominal pain, nausea and/or ileo. Post ERCP pancreatitis was defined as mild, moderate or severe using the Atlanta or Cotton criteria. All endoscopic therapeutics maneuvers indicated for cholecolithiasis (mechanical litotripsy, basket and baloon stone retrieval), benign and malignant strictures (biopsy, brushing, baloon dilation and stenting) at the procedure time, were collected retrospectively from patients electronically clinical records. Multivariable logistic regressions was used to identify assocciated risk factors. **Results.** 477 procedures were eligible for analysis. Median age was 66 (SD 17,28), 55% female. The indication for ERCP was Choledocolithiasis 232 (48,64%), benign strictures 93 (19,5%), malignant strictures 136 (28,51%) and post surgical leakeage 16 (3,35%). 323 (67,7%) procedures had uneventful outcome and patients were discharged from the unit 24 hours after. Hyperamylasemia occurred after 143 (29,97%) procedures. Median amylasa value was 234 (IQ25 155-IQ75 635) upper baseline values. Most frecuent assocciated therapeutics maneuvers were basket stone retrieval (32,17% CI95 24,09-42,95) in the lithiasis group, brushing (71,43% CI95 29,73-171,61) in the bening strictures group and metalic stent (40,54% CI95 24,44-67,25) in the malignat stricture group. Post ERCP pancreatitis occurred after 16 (1,85%) procedures, 12 (75%) were mild and 4 (25%) severe. **Conclusions.** Hyperamylasemia occurs after 143 (29,97%) therapeutics ERCPs procedures, and the most frequent assocciated maneuvers were basket stone retrieval, brushing and metalic stent. Pancreatitis rate was 1,85% (mild 75% and severe 25%)

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PREVALENCE OF PELVIC FLOOR DYSFUNCTION SYNDROMES. A COMMUNITY SURVEY IN AN ARGENTINE POPULATION

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Background. the pelvic floor dysfunction is a common disorder. Epidemiological studies related to this syndrome are lacking in Latin America. **Aim:** to assess the prevalence of fecal incontinence(FI), urinary incontinence(UI) and outlet constipation(OC) in Argentine. **Methods.** FICA self-report questionnaires validated at Mayo Clinic, USA, were submitted to a sample of 1000 residents (aged 18–70 years) from 17 representative geographical areas of Argentina. The samples were selected and stratified according to age, gender, geographical areas and size of town of residence provided by the Argentine Bureau of Statistics and Census. **Results.** 831 subjects returned valid questionnaires (445 F, mean age 40,2 ± 13,8 y)Prevalence of FI was 11,4% (95% CI: 9,2% - 13,7%). 10,7% in males, and 12,1% in females; 17,1% in olders than 55y. And 10.3%. in youngers than 55. FI of solids and liquids was 1.3% and gas FI 10,6%. Severity score for FI was Slight 19,6%, moderate 62,4 and severe 18%. UI global prevalence 17,1% (95% IC: 14,7% - 19,5%). 7,4% in males and 26,2% in females 14,8% in youngers than 55 and 28,8% in olders than 55y. Effort UI (EUI) subtype prevalence was 11,1%. 2,1% EUI in males and 19,6% in females, 9,7% in youngers than 55 and 18,6% in olders than 55. Urgency urinary incontinence (UUI) prevalence was present in 6,1%, 2,8% in male, 9,3% in females, 4,3% in youngers than 55 y. and 15,3% in olders than 55y. Global OC prevalence was 5,1% (95% CI: 3,6% - 6,7%). 0,7% in males and, 9,3% in females, 5,2% in youngers than 55 y. and 5,0% in olders than 55y. Combined FI and UI prevalence was 2,7%, FI and OC 1,1%, UI and OC 1,4%. FI+UI+OC, 0,3%. **Conclusions.** Pelvic floor syndromes are very prevalent in Argentina particularly in older people.

REMOVABLE AUTOEXPANDABLE (AE) STENTS AS TREATMENT OF COMPLETE POST SURGICAL COLONIC STENOSIS

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Introduction. Colonic Anastomotic stenosis ar quite frequent (2 to 7%), specially after using mechanic stapling devices and or in very distal resections. Proliferation of fibroblasts and cross linking of collagen fibers is the suspected mechanism.The usual endoscopic technique consists of perforating the newly formed membrane and dilate it with balloons, and or injecting steroids. Our strategy was to perforate the closed anastomosis by means of a Rendez-vous technique and inserting a removable autoexpandable stent to mantain the dilation. **Material and methods.** Two male patients (50 & 55 yrs old) presented with a complete stenosis after a recto sigmoideal cancer surgery (termino-terminal colorectal anastomosis 8 cms proximal to the anal margin). No orificial lumen was seen. Radio therapy had not been indicated. One patient was sent to us 3 months after surgery. The other one year after.An Olympus 145 Videocolonoscope was inserted through the left colostomy. From the anus we inserted a GIF XQ fiber gastroscope. Radiological control and transilumination confirmed the opposition of the scopes. By means of a needle knife (Boston Scientific) a perforation was done,a guide wire passed and hold from the anus, and in a direct way an auto expandable removable stent inserted through the orifice with proximal scope control (Polyflex Esophageal Stent -21-25 mm length 90 mm Boston Scientific). Expansion of the stent was radiologically controlled.10 days later the stent was removed, a diameter of 20 mm confirmed and the colostomy surgically closed 24 hs after the removal. **Discussion.** Total obstruction of colorectal anastomosis is a huge problem for both patients and surgeons. Dilation complications include leaks, bleeding and perforation in up to 5% of the cases. Metal AE stents have been described as a treatment method. We decided to change from AE metal to removable polyurethane stents. The first step was creating a new orifice and inserting the stent. It was removed 10 days later and the colostomy closed 24 hours later. 6 months control shows patency of the lumen. **Conclusions.** AE removable stents allows a safe and quick one step dilation. In a 2nd. step the stent is removed and the colostomy closed. And thus the complete colorectal stenosis is treated. This method could reduce the complication rate. Costs and long term evolution should be evaluated.

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RISK OF FRACTURE AFTER DIAGNOSIS OF CELIAC DISEASE IS COMPARABLE TO THAT OF CONTROL POPULATION

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Background. Several studies have shown that celiac disease (CD) is associated with increased risk of fractures. Although diagnosis and treatment of CD may improve patients' bone density and nutritional status, thus reducing the risk factors for fractures, data are limited on fracture risk in diagnosed and treated CD patients. **Aims.**The objective of this study was to determine whether the diagnosis and treatment of CD had an impact on patients' risk of fractures in the peripheral skeleton. **Methods.** We collected the history of fractures in a cohort of 265 patients with a diagnosis of CD that was established at least 5 years prior and a control cohort of 530 age- and sex-matched individuals with functional gastrointestinal (GI) disorders (Rome III) during in-person interviews at four hospital centers in Buenos Aires, Argentina. Overall follow-up time for patients was 11,286 yr (3,536 yr after diagnosis). All cases and controls responded to a questionnaire which included demographic data, age at CD diagnosis, fracture history, type of trauma producing the fracture, site of damage, and degree of compliance with the gluten-free diet (GFD). Subjects with co-morbidities that potentially affected their risk of fractures were excluded. We compared the incidence rate (IR) of the first event of any type of fractures before and after the CD diagnosis (index date) between cases and controls. **Results.** Overall, CD patients had a significantly higher IR of fractures (6.2 fractures /100 subjects/yr) than controls (3.9 fractures) (Hazard ratio [HR] 1,53; 95% confidence interval [CI]: 1,09-2,13; $P < 0{,}02$). Compared with their respective controls, the IR of fractures in CD males (6.1 vs. 17.7, respectively; HR 2,90; 95% CI 1,49-5,65; $P < 0{,}002$) was higher than those shown in females (3,7 vs. 4,8; HR 1,27; 95% CI 0,86-1,88; pNS). Before the CD diagnosis, IR was significantly higher in the overall population (HR: 1,90; 95% CI: 1,23-2.98; $P < 0{,}004$) and in males (HR 3,93; 95% CI 1,52-10,17; $P < 0{,}005$), but borderline for females (HR 1,62; 95% CI 0,98-2,68; $P < 0{,}06$). After diagnosis, patients (IR 5,9) and controls (IR 6.1) had comparable risk of fractures (HR 0,97; 95% CI 0,54-1,74; pNS). Patients who strictly adhered to the GFD had a lower incidence of fractures than those partially compliant, but the difference was not significant. **Conclusions.** The CD patients had an increased incidence of fractures in the peripheral skeleton. This increased risk is mainly associated to the male gender. After diagnosis and treatment, however, the fracture risk became comparable to the control cohort.

RISK OF GASTRIC LESIONS BETWEEN CAUCASIAN AND ASIATIC PATIENTS WITH EPIGASTRALGIA IN A PRIVATE COMMUNITY HOSPITAL IN ARGENTINA

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Introduction. The widely accepted model leading to intestinal-type gastric cancer begins with premalignant lesions of gastric mucosa. The risk of these gastric lesions seems to be higher in Asiatic than Caucasians patients. **AIM.** To assess the risk of gastric lesions (ulcers, active gastritis, atrophic gastritis, intestinal metaplasia, dysplasia and cancer) and Helicobacter pylori infection between Caucasian patients born in Argentina and Asiatic patients (mostly from Korea) who live in Argentina that presented with epigastralgia. **Materials and methods.** The clinical records of patients with epigastralgia who had performed an upper digestive endoscopy between January 2008 and December 2008 were retrospectively analyzed. Those with previous upper digestive endoscopies and gastric surgeries were excluded. A case-control study was carried out, defining Asiatic patients as "cases", and Caucasian patients as "controls". The risk, measured in odds ratio (OR) and its corresponding confidence intervals 95% (CI), of presenting the mentioned above gastric lesions was assessed. **Results.** 399 patients were analyzed: 132 Asiatic (cases) and 267 Caucasian (controls) patients. In the cases, the media age was 50 ± 12 years old, 57% women; the most frequent endoscopic findings were erytematous mucosa (77%), erosions (39%), and ulcers (9%) and normal mucosa (4%); 50% had active or severe gastritis, 51% had Helicobacter pylori infection, and 24% had intestinal metaplasia. In the controls, the media age was 49 ± 15 years old, 61% women; the most frequent endoscopic findings were erytematous mucosa (67%), erosions (35%), normal mucosa (10%) and ulcers (3%); 28% had active or severe gastritis, 31% had Helicobacter pylori infection, and 7% had intestinal metaplasia. The presence of a normal stomach was more frequent in Caucasians (OR 2,56, CI 1,06-6.2). Asiatic patients had higher risk to have erythematous mucosa (OR 1,71, CI 1,06-2,75), gastric ulcers (mostly benign, OR 3,24, CI 1,32-7,9), Helicobacter pylori infection (OR 2,43, CI 1,48-3,72), active gastritis (OR 2,5, CI 1,62-3,85), and intestinal metaplasia (OR 4,7, CI 2,51-8,76). The risk of atrophic gastritis, dysplasia and cancer was similar in both groups ($P = 0{,}17$, $P = 0{,}45$ and $P = 0{,}33$, respectively). **Conclusion.** The results of this study showed a higher risk of the initial premalignant stages of gastric cancer (Helicobacter pylori, active gastritis and intestinal metaplasia) in Asiatic patients that live in Argentina. On the contrary, data did not provide convincing evidence of an increase in the risk of dysplasia or gastric cancer. However, screening should be considered in this high risk group.

SERRATED ADENOMAS OF THE COLON: PREVALENCE AND ASSOCIATION WITH NEOPLASTIC LESIONS

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Background. Serrated adenomas (SA) of the colon are thought to be precursor lesions of colorectal cancer through a different pathway than the classical sequence of adenoma-carcinoma. Their prevalence and malignant potential is not well defined. **Aim:** To determine the prevalence of SA in patients who underwent colonoscopy in a private community hospital, and the frequency of high grade dysplasia (HGD) and adenocarcinoma in these polyps. Moreover, to establish the association with synchronic and metachronic neoplastic lesions. **Methods.** Reports from patients undergoing colonoscopy and polypectomy from January 2003 to June 2008, were obtained from the electronic database of a private community hospital. SA were reanalyzed by a pathologist and classified based on the diagnostic criteria described by Snover. The prevalence of these polyps and the clinical and endoscopic features of the patients were determined. Synchronic lesions were defined by the presence of cancer and/or adenomas with or without advanced histologic features (AHF) (>1cm, HGD and/or >75% of villous component) in the same colonoscopy. Metachronic lesions were identified in patients who underwent surveillance colonoscopies, describing the time interval between studies. An univariate analysis was performed, looking for independent predictors for HGD and synchronic and metachronic neoplastic lesions in patients with SA. **Results.** 12693 colonoscopies were carried out in the analyzed period, identifying 116 patients with a total of 158 SA and a prevalence of 1,24%. 92,4% were sessile, 5,7% traditional and 1,9% non-classified SA. The mean age was 60; 56% were men. Most of the polyps were less than 1cm (81%) and sessile (80%), with predominant distribution in the rectosigmoid colon (52%). HGD was found in 8.2% of the SA, all of them in sessile serrated adenomas. No adenocarcinomas were identified. Synchronic lesions were found in 26% of the patients: 75% adenomas, 16% adenomas with AHF and 9% adenocarcinoma. 11% of the patients carried out surveillance colonoscopies within the first three years, 31% had metachronic lesions: SA (40%), adenomas (40%) and adenomas with AHF (20%). HGD and cancer were not found. We did not identify independent predictors for HGD and synchronic and metachronic neoplastic lesions in patients with SA. **Conclusion.** In the present study, the prevalence of SA was low, similar to that reported in the literature. We found a relevant association with neoplastic lesions; therefore, it is important to establish specific guidelines for the management of these kind of polyps.

STEROID-DEPENDENT UC. COLECTOMY RISK AT 5 YEARS FOLLOW-UP WITH THIOPURINE THERAPY

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Background. Mercaptopurine (6-MP) and its parent drug azathioprine (AZA) are purine analogues widely in the management of steroid dependent Crohn's disease. In UC, the alternative of the IPAA has been a factor for reluctance to immunossuppresion. However, short and long term IPAA complications, and poor predictive markers, validates such a research. Bibliographic information is limited, providing small size samples to report surgical risk and safety beyond 2 years follow-up, remaining controversial if thiopurines are a delay of colectomy or a long-term option. **Aim.** Our aim in this study was to evaluate the long term efficacy and safety of 6-MP in the treatment of steroid-dependent ulcerative colitis. **Material and methods.** We investigate the evolution at 5 year follow up of a cohort steroid-dependent of UC patients attending a single centre, treated with 6-MP as alternative to a colectomy, by a protocol starting from Jan 2000, where 80 patients (40 males) were included, mean age at inclusion 31 yrs (range 13-68), extensive UC: 39 patients, left-sided: 36, distal: 5, mean time from UC onset until 6-mp treatment was 6,8 yrs (6mo-28 yrs). Indication was steroid-dependent UC defined as difficulty to withdraw steroids during previous 6 mo. with two discontinuation attempts. Tentative 6-mp dose was 1 mg/kg. An 8 wk course of oral mepred-nisone started at 40 mg/d with or intravenous steroids according needed was used as a bridge. Kaplan Meier table analysis was used. **Results.** Surgical requirement at 6 mo, 1, 2, 3, 4 an 5 yrs were 8% (n 69), 12% (n 66), 15% (n 61), 16% (n 54), 23 % (n 46), 25% (n 41)- 1/3 of colectomized were 6-mp intolerant. Steroids were discontinued in 4.7±0.4 mo, 29% of cases needed sporadic steroid courses (£2 in five years) and 4% of patients required ≥ 3 courses but did not fulfilled the steroid dependence criteria at follow-up. Mean 6-MP dose for achieving efficacy was 0,94±0,03 mg/kg. Side effects, observed in 31 patients (38,7%) of patients, were: raised liver enzymes (10%) normalized by stopping 6-mp, 3 of them continued with lower dose), leucopenia (10%, 5 of them reverted by decreasing dose), fever (2,5%), pancreatitis (2,5%), nauseas (3,7%) and infections 7,5%: pneumonia (2), varicella (2) herpes zoster (1), urinary infection (1), neoplasias 2,5%: ovarian cancer: (1), colonic adenoma with displasia (1). Thirteen (16%) patients discontinued 6-MP. Hospitalization was only required in non-responders. **Conclusion.** 6-MP has shown to be effective in steroid dependent UC treatment, exhibiting a suitable low rate of colectomy in long-term 5 follow up. Benefits of 6-mp seem to outweigh potential risks of surgical procedures.

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VACUOLE-MEMBRANE-PROTEIN-1 (VMP1) AND P21 EXPRESSION REGULATE CROSSTALK BETWEEN AUTOPHAGY AND APOPTOSIS IN HUMAN PANCREATIC CANCER.

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Abstract. Pancreatic ductal adenocarcinoma is one of the most aggressive human malignancies with 2-3% five-year survival rate. Autophagy is a degradation process of cytoplasm constituents. In cancer, autophagy can either be a form of programmed cell death or play a cytoprotective role. VMP1 is a pancreatitisinduced protein whose expression triggers autophagy. We previously showed that VMP1-autophagy pathway promotes apoptotic cell death in PANC-1 and MIAPaCa-2 pancreatic cancer cells. Here, we evaluate the expression of VMP1 and its relationship with p21 and p53 in human pancreatic ductal adenocarcinoma. We also investigated autophagy evaluating LC3 expression, a classic marker of the autophagic process. Two different tissue microarrays were performed from tumor stage advanced; 50-pancreatic ductal adenocarcinomas and seven control samples were included. Immunohistochemistry assays revealed positive expression of VMP1 in glandular cells in 10 (20%) of the tumor samples and none of the controls. The same expression pattern was observed for LC3, suggesting VMP1-mediated autophagy in tumor samples. Tumor samples also showed loss expression of p21, and VMP1 expression in tumor tissue significantly correlated with p21 loss expression ($P < 0{,}001$). In addition, significant correlation between p21 loss expression and p53 expression ($P < 0{,}03$) were observed. Interestingly, patient's survival was higher in VMP1-expressing pancreatic cancer samples. In order to analyze the relationship between VMP1 and p21 expression we used HCT116 and HCT116 p21-/- cells. Real time RT-PCR assay showed a significant increase of VMP1 expression in HCT116 p21-/- cells compared to HCT116 cells. Moreover, starvation-induced autophagy promoted higher activation of VMP1 expression in p21 deficient cells. Also, HCT116 p21-/- cells showed activation of autophagy evidenced by the recruitment of LC3. Finally we study apoptosis development by flow cytometry of anexin V. We found significant reduction of apoptosis levels in HCT116 p21-/- cells compared to HCT116 cells after starvation-induced autophagy. On the contrary, over expression of VMP1 in HCT116 cells showed significant increase of apoptosis after autophagy induction. Our results demonstrate a relationship between VMP1 and p21 expression in human pancreatic cancer and show that the expression of p21 allows apoptosis in VMP1-expressing cells under autophagic stimuli. On the contrary, loss of p21 reduces apoptosis and favors autophagy, disassembling VMP1-mediated autophagy from apoptosis. We conclude that VMP1 and p21 expression are involved in the crosstalk between autophagy and apoptosis in human pancreatic cancer.