

Oral Abstracts

Bacteriology/Virology

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Is levofloxacin a feasible option for *Helicobacter pylori* rescue therapy in Singapore?YT WANG,¹ LUI SY,² LING KL¹¹Department of Gastroenterology and Hepatology, Singapore General Hospital, ²Department of Pathology, Singapore General Hospital

Background Increased *Helicobacter pylori* (HP) treatment failure to triple therapy consisting of a proton pump inhibitor, clarithromycin and amoxicillin has been reported worldwide. Levofloxacin based regimens have been proposed as possible 'rescue' treatments. However, levofloxacin resistant HP strains have been reported recently which may diminish its efficacy.

Aim To study the prevalence of HP resistance to metronidazole, clarithromycin, amoxicillin, tetracycline and levofloxacin in treatment naive patients in Singapore.

Methods 122 HP isolates were examined from 2 periods: May 1997 to July 2001 (54 isolates) and December 2005 to March 2010 (68 isolates). Antibiotic sensitivity of these isolates to the 5 antibiotics was determined using E-test.

Results There was no HP resistance to amoxicillin and tetracycline. The prevalence of metronidazole resistance remained similar in the 2 time periods, 44.4% (24/54) (1997–2001) vs 55.9% (38/68) (2005–2010) ($p = 0.209$). Clarithromycin resistance doubled, 13% (7/54) (1997–2001) to 30.9% (21/68) (2005–2010), this was statistically significant, $p = 0.019$. There was a greater than 10 fold increase of levofloxacin resistance from 1.9% (1/54) (1997–2001) to 19.1% (13/68) (2005–2010) ($p = 0.003$). Of the isolates with clarithromycin resistance, concomitant levofloxacin resistance was found in 0% (1997–2001) vs 42.9% (2005–2010).

Conclusions An increase in HP resistance to clarithromycin and levofloxacin was observed from 1997 to 2010. The high prevalence of levofloxacin resistant HP isolates, particularly in those with clarithromycin resistance as well, suggests that empirical levofloxacin based rescue therapies may not be effective in Singapore.

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Ademetionine in chronic hepatitis C treatment

BUEVEROV ALEXEY

Moscow Medical Academy

Aim To estimate the role of ademetionine (Heptral®) in increase of efficacy and improvement of tolerability of combined antiviral therapy of patients with chronic hepatitis C (CHC).

Methods 80 patients were included in original investigation. The basic group received IFN- α 2b 3 IU 3 times per week, ribavirin 800–1200 mg per day and ademetionine (Heptral®) 400 mg 3 times per day orally. Patients of comparison group received similar antiviral therapy without ademetionine. The patients infected by HCV of genotype 1, received treatment for 48 weeks, those infected by genotypes 2 HCV and 3 HCV—for 24 weeks. The period of monitoring of all patients after the termination of treatment was 24 weeks. Questioning by the Hospital Anxiety and Depression scale (HADS) was carried out additionally.

Results In patients, infected by HCV genotype 1, rapid virologic response (RVR) was obtained at 50% of patients within 4 weeks of treatment, in both basic and comparison groups. Early virologic response

(EVR) within 12 weeks was revealed in 80 and 90% of patients of these groups respectively. At HCV-infection with non-1-st genotype RVR was observed at 80% in the group, receiving ademetionine and at 65% in comparison group, EVR—at 100 and 90% respectively (differences were statistically insignificant). At 76% of patients receiving ademetionine, by the 12th week of treatment depression was not found (in the group of comparison it was absent at 42% of the cases). Clinically significant depression by the 12th week was diagnosed only at 3% of patients while in group of comparison its frequency made 24% ($p < 0.05$).

Conclusions Addition of oral ademetionine (Heptral®) in daily dose of 1200 mg to complex treatment by IFN- α 2b and ribavirin in patients with CHC causes high frequency of RVR and EVR achievement. Despite lacking of significant differences with comparison group, it is necessary to consider, that in group of the patients receiving ademetionine, it was characterized by a panel of factors complicating antiviral therapy. Depression on a background of ademetionine application in combination to antiviral agents developed significantly less often and was mild in comparison to patients received no ademetionine.

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Metformin pretreatment and the efficacy of antiviral therapy in chronic hepatitis C (genotype 3) patients

PO BOGOMOLOV, AO BUEVEROV, OS KUZMINA, MV MACIEVICH, ON UVAROVA, NA BARSUKOVA, TV PAVLOVA, EN KUDRYAVTSEVA

Moscow Regional Center of Hepatology, Moscow, Russia

Objective To evaluate the influence of preceding metformin administration (pretreatment) on the efficacy of antiviral therapy in chronic hepatitis C (genotype 3) (CHC G3) patients.

Methods 76 CHC G3 patients were included into the study. Patients were stratified according to presence or absence of hepatic steatosis (liver biopsy results). Patients in each group were randomly assigned to undergo treatment with one of two regimens: metformin (20 mg/kg/day) preceding antiviral therapy or only antiviral therapy with conventional interferon and ribavirin.

Baseline patients characteristics were balanced and comparable among the groups and included sex, age, body mass index, degree of activity of hepatitis, fibrosis stage and prescribed antiviral therapy (interferon alfa-2b 3 million IU 3 times a week in combination with ribavirin 13 mg/kg/day). The patients with metabolic syndrome were not included in the study. Metformin pretreatment was assigned for 3 months before the antiviral therapy, and then patients continued with metformin combined with antiviral therapy. Viral load level (PCR level of detection—50 UI/ml), rate of rapid virologic response (RVR) and early virologic response (EVR) achieving were assessed before pretreatment and at the start of antiviral therapy.

Results Patients ($n = 25$) with CHC G3 and hepatic steatosis assigned to metformin achieved 80% rate of RVR and 96.5% rate of EVR.

In the patients with hepatic steatosis ($n = 16$) prescribed antiviral therapy without metformin pretreatment resulted in 62.5% RVR rate and 85% EVR rate. When treated with metformin the patients with CHC G3 and without hepatic steatosis ($n = 24$) showed RVR in 83.3%, and EVR was registered in 100% of the patients. Patients without hepatic steatosis and without metformin pretreatment ($n = 11$) achieved RVR in 72.2% and EVR in 85.7%.

Conclusion Metformin pretreatment favors the increase in the efficacy of the antiviral therapy with conventional interferon and ribavirin in chronic hepatitis C (genotype 3) patients regardless of hepatic steatosis presence or absence.

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The effect of *Helicobacter pylori* on p53 and PUMA in human normal gastric epithelial cell line GES-1

Z YANG, L CHEN, X SHU, ZH L, Y XIE, NH LV
 Department of Gastroenterology, The First Affiliated Hospital of Nanchang University, Nanchang, China

Object To investigate the effect of *Helicobacter pylori* (Hp) on p53 and PUMA in human gastric epithelial cells, elucidate the effect and pathogenic mechanisms of Hp in vitro.

Materials and methods GES-1 were co-incubated with the culture supernatants of Hp strains (NCTC11637 (CagA+, VacA+) or NCTC11639 (CagA+, VacA-) at 48 h, the control treated with Hp medium at the same time. The level of p53 and PUMA protein was determined by Western blot.

Results The expression of p53 protein in GES-1 was significantly higher than that of control group when treated with NCTC11637 Hp culture supernatants (2.775 mg/ml) for 48 h ($P < 0.01$), but there were not significant difference with NCTC11639 Hp culture supernatants (3.75 mg/ml) for 48 h. The expression of PUMA protein in GES-1 was significantly lower than that of control group when treated with NCTC11639 Hp culture supernatants (3.75 mg/ml) for 48 h ($P < 0.05$), but there were not significant difference with NCTC11637 Hp culture supernatants (2.775 mg/ml) for 48 h ($P > 0.05$).

Conclusion The effects of Hp strains on p53 and PUMA are some different, which warrants further study to clarify the exact mechanism.

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The effect of *Helicobacter pylori* on the biologic behavior of gastric epithelial cell line GES-1

Z YANG, X SHU, L CHEN, ZH L, Y XIE, NH LV
 Department of Gastroenterology, The First Affiliated Hospital of Nanchang University, Nanchang, China

Objective To research the effect of *Helicobacter pylori* (*H. pylori*) culture supernatants on the biologic behavior of human normal gastric epithelial cell line GES-1.

Materials and methods GES-1 were co-incubated with different diluted culture supernatants of NCTC11637 (CagA+, VacA+) Hp strain, the control only treated with *H. pylori* medium, and cells were collected and detected at different time points. The cell viability, cycle and apoptosis were detected by MTT assay or flow cytometry.

Results At the 24th hour survival rates of 1:8, 1:4, 1:2 (dilution ratio) groups were found significantly lower compared to control ($p < 0.05$); at the 48th hour survival rates of 1:4 and 1:2 groups were found significantly lower than those of control ($p < 0.05$) in a concentration-dependent way; at 72nd hour survival rates of all concentrations were found significantly lower compared to control ($p < 0.05$) in a concentration-dependent way, among them significant differences were found ($p < 0.05$); at the 80th day after introduction of 1:8 culture supernatants, compared to control (Parallel Passage) survival rate increased ($p < 0.05$). 48 h after introduction of 1:4 culture supernatants, G0/G1 cell cycle arrest was found and apoptosis rate increased ($p < 0.05$).

Conclusions In short-term effect, *H. pylori* culture supernatants caused apoptosis and decay of activity of human gastric epithelial cell, and this

effect was related to concentration and action time; with a long-term introduction of low concentration of culture supernatants, *H. pylori* could induce the increase of cytoactive of gastric epithelial cell.

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The diagnostic value of the cytomegalovirus (CMV) antigenemia assay for CMV gastrointestinal disease in immunocompromised patients

N NAGATA, S NISHIMURA, T YADA, M KOBAYAKAWA, T GOTODA
 National Center for Global health and Medicine, Department of Gastroenterology

Introduction Cytomegalovirus (CMV) gastrointestinal disease (GID) is a major cause of morbidity and mortality in immunocompromised patients. It is essential to make a diagnosis at an early stage.

Aim To evaluate the utility of CMV antigenemia assay for diagnosis of CMV-GID.

Materials and methods Immunocompromised patients who had endoscopic findings and underwent both histological examination and CMV antigenemia assay were collected for this study from medical records in our hospital. Patients with a history of treatment of anti-CMV therapy were excluded. CMV-GID was defined as the detection of CMV by endoscopic biopsy specimens. We evaluated the association between CMV-GID and patient characteristics (symptoms, underlying disease, medication, leukocyte counts, and CMV antigenemia).

Results A total of 99 patients (45 patients were HIV infected, 19 had malignancy, 18 had autoimmune disease, 3 were post-transplantation) were analyzed. Fifty patients used immunosuppressive drugs. Fifty-five patients were diagnosed CMV-GID. By univariate analysis, HIV infection, leukopenia, and CMV antigenemia were found to be associated with the CMV-GID ($p < 0.05$). The sensitivity, specificity, PPV, and NPV of CMV antigenemia for CMV-GID were 65.4%, 93.6%, 91.9%, and 71.0%, respectively. Multivariate analysis using logistic regression revealed that HIV infection and CMV antigenemia were the only independent factors that related to CMV-GID ($p < 0.01$).

Conclusions If CMV antigenemia is positive in immunocompromised patients, endoscopic lesion is probably CMV-GID. But negative CMV antigenemia does not always exclude CMV-GID, especially for HIV patients.

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Mutations of *Helicobacter pylori* in fluoroquinolone resistance and the effect of point mutation of *gyrA* on 2nd line eradication therapy in Korea

JW LEE, N KIM, PJ SEO, JH PARK, MK LEE, RH NAM, JA CHA, DH LEE
 Departments of Internal Medicine, Seoul National University Bundang Hospital, Seoungnam, Gyeonggi-do, Korea

Background Fluoroquinolone resistance of *H. pylori* is mostly depend on mutations in QRDR of *gyrA*.

Study *H. pylori* strains were isolated from gastric mucosal biopsy specimens obtained from 121 Korean patients. The susceptibilities of the isolates to antibiotics including fluoroquinolone were examined using agar dilution method. DNA sequencing was performed to detect mutations in QRDR of *gyrA*.

Results 94 fluoroquinolone resistant strains and 27 susceptible strains were examined. In fluoroquinolone resistant group, 19 patients had received *H. pylori* eradication therapy before this study. In primary fluoroquinolone resistant strains, the occurrence of *gyrA* mutations was 54 of 75 strains (72.0%). In secondary resistant strains, the occurrence of *gyrA* mutations was 19 of 19 strains (100.0%). Regardless of primary and secondary resistance, most common mutation is Asp-91 (37.2%) and Asn-87 (33.0%). Moxifloxacin-based eradication therapy was performed in eight patients with fluoroquinolone resistant isolates. In three patients with Asn-87 mutated strains, there were two failures. In contrast, only one case failed among five patients with Asp-91 mutated strains. *H. pylori* transformation experiments for resistance isolates are undergoing.

Conclusions Point mutation of Asn-87 could be considered to be the most important determinant in failure of fluoroquinolone based eradication. However, Asp-91 point mutation could be possible mechanism.

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Increased osteopontin expression correlates with chronic *H. pylori*-related gastric inflammation and the presence of gastric precancerous lesions

WL CHANG,¹ HB YANG,² HC CHENG,¹ CH CHUANG,¹ BS SHEU¹

Departments of ¹Internal Medicine and ²Pathology, National Cheng Kung University Hospital, Tainan, Taiwan

Introduction This study investigated whether OPN is involved in *H. pylori*-related chronic gastric inflammation and precancerous changes as intestinal metaplasia (IM).

Methods 105 dyspeptic patients were enrolled, including 29 without and 76 with *H. pylori* infection (46 without and 30 with IM). Patients' gastric OPN expressions were immunohistochemically stained for antrum and body, respectively (range: 0–4 for both epithelium and lamina propria). In each specimen, the intensity of OPN was the sum of epithelium and lamina propria (range 0–8). Gastric inflammation and IM were assessed by the updated Sydney System. *In vitro* cell line assay validated OPN expression by *H. pylori* co-culture.

Results *H. pylori*-infected patients had higher gastric OPN expression than the non-infected patients (7.4 vs. 5.3, $p < 0.001$). Among the *H. pylori*-infected patients, an increase OPN expression correlated with more severe chronic gastric inflammation and the presence of IM ($p < 0.001$). After *H. pylori* eradication, both OPN expression and gastric inflammations decreased (OPN: 6.6 to 4.6, $p < 0.001$; chronic inflammation score: 5.5 to 3.4, $p < 0.001$). Within the same gastric bits, lamina propria expressed OPN stronger than epithelium, suggesting OPN may originate from inflammatory cells. The *in vitro* assay confirmed *H. pylori* could stimulate OPN expression in the monocyte (U937), but not gastric epithelial cells.

Conclusion *H. pylori* infection can stimulate OPN expression in the inflammatory cells and may thus facilitate the development of the gastric precancerous lesion.

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Hepatitis B Virus surface antigen level in e antigen negative chronic Hepatitis B infection

RM MUKHERJEE,¹ A JYOTHI,¹ PN RAO,² RP BALKUMAR,¹ M SASIKALA,¹ R GUPTA,² RD NAGESHWAR²

¹Asian Health Care Foundation, ²Asian Institute of Gastroenterology, Somajiguda, Hyderabad, India

Background Hepatitis B surface antigen (HBsAg) is routinely detected qualitatively in Hepatitis B Virus (HBV) infection. The persistence of HBsAg beyond 6 months defines chronic hepatitis B (CHB) infection. Hepatitis Be antigen (HBeAg) usually indicates active HBV replication and risk of transmission of infection. In spite of the emerging importance of chemiluminescence based quantitative measurement of HBsAg for therapeutic monitoring of the patients, we tried to measure HBsAg concentration by sandwich ELISA in treatment naïve subjects of CHB infection.

Methods Sixty two subjects were evaluated for serum HBeAg, anti HBe and ALT status by standard ELISA and biochemical procedures. The amount of serum HBV DNA determined by real time TaqMan PCR assay (Roche Diagnostics, USA). Serum HBsAg level was ascertained by a third generation sandwich ELISA kit (Alpha Diagnostics International, USA).

Results The median age of the subjects was 40.5 years (IQR = 18; 90% male) of which 92% were HBeAg negative and anti-HBe positive. Median ALT value was 35.5 IU/ml (IQR = 37). Median viral load (Log copies/ml) and HBsAg (ng/ml) were 4.57 (IQR = 2.84) and 16.31 (IQR = 10.18) respectively. When grouped on the basis of viral load (<2000 IU/ml >), the median HBsAg concentration seen is 15.2 (IQR = 18.4) and 19.1 (IQR = 10.7) while median ALT values were 29 (IQR = 21.2) and 47 (IQR = 73.2) in lower (<2000 IU/ml) and higher (>2000 IU/ml) viral load groups respectively.

Conclusion Serum HBsAg concentration showed no correlation with serum HBV DNA level in our study subjects which is at par with other studies on CHB patients. Based on the reported correlation between serum HBsAg level and intrahepatic ccc DNA, higher amount of HBsAg in subjects having lower viral load is indicative of the presence of higher amount of intrahepatic HBV DNA in these subjects warrant further study.

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Relationship between the expressions of Akt, Mdm2, mutant p53 protein and the infection of *H. pylori* in different gastric mucosal lesions

X SHU, N-H LU, Z YANG, L CHEN, J CHEN, Y XIE
Department of Gastroenterology, First Affiliated Hospital, Nanchang

Introduction Many studies have found an association between *Helicobacter pylori* infection and the development of chronic non-atrophic gastritis (CNAG), metaplastic atrophy (MA), dysplasia (Dys) to gastric cancer (GC), but this relation with Akt-Mdm2-p53 signaling pathway remains uncertain.

Materials and Methods Pathologic specimens of gastric mucosa (*H. pylori* related or not) with CNAG, MA, Dys or GC were collected and detect Akt, pAkt, Mdm2, mutant p53, PCNA protein with immunohistochemical method. *H. pylori* infections were detected with Giemsa's staining in pathologic specimens.

Results (1) In gastric mucosal lesions with CNAG or MA, DYS or GC, pAkt expression in Group CNAG was much higher in *H. pylori*-positive specimens compared to *H. pylori*-negative specimens ($P < 0.05$); Akt expression showed no significant difference among all the groups ($P > 0.05$); Mdm2 expression in Group Dys was also significantly higher in *H.*

pylori-positive specimens compared to *H. pylori*-negative specimens ($P < 0.05$); Mutant p53 of Group MA was much higher in *H. pylori*-positive specimens compared to *H. pylori*-negative specimens ($P < 0.05$); PCNA of Group Dys was significantly higher in *H. pylori*-positive specimens compared to *H. pylori*-negative specimens ($P < 0.05$). (2) In *H. pylori* related gastric mucosal lesions with CNAG or MA, DYS or GC, Akt, pAkt and mutant p53 expression showed no significant difference among all the groups ($P > 0.05$). Mdm2 and PCNA protein expressions in Group GC and Dys were significantly higher than in Group CNAG and MA ($P < 0.05$).

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Akt-Mdm2-p53 signaling pathway of gastric epithelial cells is activated by *Helicobacter pylori* culture filtrate

X SHU, NH LV, Z YANG, L CHEN, J CHEN, Y XIE
Department of Gastroenterology, First Affiliated Hospital, Nanchang

Introduction The balance of human gastric epithelial cell proliferation and apoptosis will be broken by the infection of *H. pylori*, and the Akt-Mdm2-p53 signaling pathway plays an important role in the regulation of proliferation and apoptosis.

Materials and methods Prepare the culture filtrates of type culture strain (NCTC11637 *H. pylori*), concentration is set to be 11 mg/ml, and then dilute it to different concentrations, co-cultured with GES-1 cells. In control group only *H. pylori* culture medium is added, cells are collected and detected at different points to detect the protein level with western blotting.

Results (1) Akt-Mdm2-p53 signaling pathway related protein after the introduction of culture filtrate of *H. pylori* to GES-1 cells: After the introduction of 1:4 dilution of culture filtrate of *H. pylori*, Akt changed little ($p > 0.05$). pAkt increased 1 h after the introduction, reached the peak at 3rd hour and kept increasing during 48 h after the introduction. Mdm2 showed similar changes. p53 did not change during 12 h but increased at 24th and 48th hour. Bax increased 1 h after the introduction and kept increasing during 48 h. (2) After the treatment with Akt inhibitor, LY294002, introduce 1:4 dilution of culture filtrate of *H. pylori* to GES-1 cells at 24th hour the phosphorylated-Akt and Mdm2 expressions decreased significantly ($p < 0.05$), but p53 protein increased significantly. ($p < 0.05$)

Biliary Tract

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Risk factors for early dysfunction of biliary covered metallic stents in patients with unresectable pancreatic cancer

T HAMADA, Y NAKAI, H ISAYAMA, O TOGAWA,
H KOGURE, K KAWAKUBO, T SASAKI, Y ITO,
N YAMAMOTO, K HIRANO, N SASAHIRA, M TADA,
M OMATA, K KOIKE

Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo

Background & Aim Covered metallic stents (CMS) have longer patency period and lower occlusion rate than plastic stents or uncovered metallic stents for distal malignant biliary obstruction. However, one of the problems of CMS is early dysfunction after placement, and it may be caused by impaction of food scraps, migration and sludge formation.

Patients & methods Between 1997 and 2009, CMS were placed consecutively in 269 unresectable pancreatic cancer with distal biliary obstruction for initial placement, and 246 patients who were followed more than 3 months were studied. We analyzed the incidence, causes and risk factors of early dysfunction (<3 months).

Results Median survival and time to dysfunction were 217 and 188 days, and early dysfunction occurred in 80 cases (33%). Causes of early dysfunction were stent occlusion in 36, non-occlusion cholangitis in 16, migration in 16 and others in 12. Multivariate analysis showed that duodenal invasion was the only significant risk factor (OR 2.20, 95%CI 1.24–3.96, $p = 0.007$). The rate of early dysfunction in cases with duodenal invasion was higher than that in cases without duodenal invasion (41.9% vs 27.2%; $p = 0.019$).

Conclusion Duodenal invasion is the risk factor for early dysfunction of CMS.

Cell/Molecular biology

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Analysis of 6 circulating cytokines and colonic STAT3 activation pattern in patients with inflammatory bowel disease of different disease activity and duration

RA RAJA ALI,¹ L HARTNETT,¹ LJ EGAN^{1,2}

¹Clinical Pharmacology and Therapeutics, ²Clinical Research Facility, National University of Ireland Galway, Ireland

Introduction A broad array of cytokines which act by the signal transducers and activators of transcription 3 (STAT3), may link inflammatory bowel disease (IBD) and colorectal cancer (CRC). Although many cytokines and STAT3 activity are known to be elevated in IBD, whether disease activity or duration influences them is unknown.

Aims To measure the level of serum Interleukin- (IL-1 β , IL-2, IL-6, IL-8, IL-17), tumour necrosis factor α (TNF- α) and colonic STAT3 activity in IBD and control patients.

Methods Three groups of IBD patients were stratified based on disease activity and durations: active/short, inactive/short, inactive/long and controls. Cytokines levels and colonic activity of total/phospho (t/p-STAT3) were measured by Bioplex assay and immunohistochemistry respectively.

Results 72 patients (60 IBD/12 controls, mean age 53.5/50.1 years) were studied. All cytokines level and t/p-STAT3 positive intestinal epithelial cells (IECs⁺) were significantly elevated in IBD patients as compared to controls. Respective means of 6 cytokines levels and t/p-STAT3 IECs⁺ are shown in table A.

Conclusions Colonic STAT3 is activated in IBD patients. Elevated levels of serum IL-1 β , IL-2, IL-6, IL-8, and IL-17 are found in long standing IBD patients, potentially contributing to CRC risk.

Table A

| Mean values | Control | Active/ Short | Inactive/ Short | Inactive/ Long | p value |
|---------------------------------|---------|------------------|--------------------|-------------------|---------|
| t-STAT3, % IECs ⁺ | 23.4 | 79.3 | 35.2 | 61.3 | 0.001 |
| p-STAT3, % IECs ⁺ | 0 | 59.4 | 15.4 | 32.5 | 0.001 |
| IL-1 β (pg/ml) | 0 | 0.6 | 0.1 | 14.3 | 0.01 |
| IL-2 | 0 | 9.3 | 4.8 | 383.5 | 0.001 |
| IL-6 | 1.1 | 12.1 | 6.6 | 43.8 | 0.001 |
| IL-8 | 10 | 53.5 | 16.7 | 132.1 | 0.001 |
| IL-17 | 0 | 2.9 | 1.1 | 101.1 | 0.001 |
| TNF- α | 0.2 | 45.7 | 9.4 | 3.7 | 0.001 |

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Genetic polymorphism of inflammation response genes TNF- α -308G > A and TL-8 -251 T > A and their influence on colorectal cancer predisposition risk in Malaysian population
MM AMINUDIN,¹ MS SITINURFATIMAH,¹ AA AHMADAIZAT,¹ RN VENKATESH,³ BM BISWAL,² Z ZAIDI,⁴ AMS SHANWANI,⁴ AH MOHAMMAD RADZI,⁵ R ANKATHIL¹

¹Human Genome Centre, ²Department of Nuclear Medicine, Radiotherapy & Oncology, School of Medical Sciences, ³Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia, ⁴Surgical Department, Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan, Malaysia, ⁵Internal Medicine Department, Hospital Sultanah Bahiyah, Alor Setar, Kedah, Malaysia

Introduction Several lines of evidence including animal models and epidemiological observations suggest that a continuous inflammatory condition predisposes to CRC. Study was designed to investigate the association of IL-8T251A and TNF- α -308G > A with CRC susceptibility risk.

Method In this case control study, peripheral blood samples of 118 normal controls and 116 CRC patients were collected, genomic DNA was extracted and genotyped employing allele specific PCR.

Results Investigation on the association of the variant genotypes with CRC susceptibility risk, IL-8T251A showed significantly increased risk with OR 3.524 (CI 1.318–9.424, P = 0.012) and TNF- α -308G > A showed significantly increased risk with OR 2.622 (CI 0.985–6.942, P = 0.050). The risk was pronouncedly higher when the homozygous variant genotypes were combined. (OR 9.000 CI 1.087–66.914, P = 0.041).

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Genetic polymorphisms of xenobiotic metabolizing enzymes cytochrome P450 1A2 in Malaysian population and colorectal cancer susceptibility risk

MS SITINURFATIMAH,¹ MM AMINUDIN,¹ AA AHMADAIZAT,¹ RN VENKATESH,³ BM BISWAL,² Z ZAIDI,⁴ AMS SHANWANI,⁴ AH MOHAMMAD RADZI,⁵ R ANKATHIL¹

¹Human Genome Centre, ²Department of Nuclear Medicine, Radiotherapy & Oncology, ³Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia, ⁴Surgical Department, Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan, Malaysia, ⁵Internal Medicine Department, Hospital Sultanah Bahiyah, Alor Setar, Kedah.

Introduction Genes encoding xenobiotic metabolizing enzymes especially CYP1A2 play an important role in determining the outcome of carcinogen exposure and Colorectal Cancer susceptibility risk. Functional polymorphisms of G3860A, T739G and C729T of CYP1A2 gene have been identified.

Aims A case control study was designed to genotype the Malaysian normal controls and CRC patients to determine the variant allele frequencies of three polymorphisms of CYP1A2 and to evaluate whether variant genotype has any association either singly or in combination with CRC susceptibility risk.

Material & method Genotyping of the 3 polymorphisms (G3860A, T739A & C729T) CYP1A2 genes was performed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) on 111 sporadic histopathologically confirmed CRC patients and 123 normal healthy controls.

Result When the 3 polymorphisms G3860A, T739G and C729T were analyzed singly, there was no significant association. When the risk association was evaluated using combination genotypes, the combination of G3860A / T739T genotype showed statistically significant risk with OR 1.75.

Endoscopy**63**

Quantitative perfusion analysis with contrast-enhanced harmonic EUS facilitate distinguishing autoimmune pancreatitis (AIP) from pancreatic cancer

H IMAZU, K IKEDA, H KAKUTANI, H TAJIRI

Department of Endoscopy, The Jikei University School of Medicine, Tokyo, Japan

Background AIP may present as mass lesion and be misdiagnosed as pancreatic cancer (PC). Recently, contrast-enhanced harmonic EUS (CH-EUS) with second generation ultrasonographic contrast (Sonazoid) was shown to be useful for diagnosis of pancreaticobiliary malignancies.

Study aims To evaluate if the quantitative perfusion analysis with CH-EUS facilitate differentiation of AIP from PC.

Methods Consecutive patients with PC or AIP who underwent CH-EUS from January 2009 to March 2010 were analyzed. An electronic radial echoendoscope, ALOKA ProSound alpha10 processor and Sonazoid were used. CH-EUS was performed with intravenous administration of 0.015 ml/

kg of Sonazoid, and the graph of "Time Intensity Curve (TIC)" from software installed in the alpha10 was generated to depict the changes in signal intensity over time within the region of interest (ROI). ROI was placed to cover an area with a pancreatic mass.

Results 6 patients with AIP and 18 patients with PC were evaluated by TIC. Peak intensity and maximum intensity gain of mass lesion in patients with AIP were significantly higher than that of PC (15.9 dB vs 9.4 dB, $p < 0.05$, 14.2 vs 6.2, $p < 0.01$).

Conclusion Mass lesions of AIP and PC showed marked different perfusion patterns with TIC. This novel diagnostic modality using TIC generated by CH-EUS might offer an opportunity to improve accuracy in differential diagnosis between AIP and PC.

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Chemically assisted ESD vs. traditional ESD in the resection of early stage gastric cancers

H NAGANO,¹ K SUMIYAMA,² H TAJIRI^{1,2}

¹Division of Gastroenterology and Hepatology, Department of Internal Medicine, The Jikei University School of Medicine, Tokyo, Japan, ²Department of Endoscopy, The Jikei University School of Medicine, Tokyo, Japan

Introduction Endoscopic submucosal dissection (ESD) enables a large diseased mucosa to be radically excised with en bloc fashion. However, ESD is technically more challenging and time-consuming. We previously reported that the injection of a chemical (mesna) could facilitate submucosal dissection process, the most error-prone procedural process in ESD^{1,2}.

Materials and Methods Results of thirty consecutive early-stage gastric cancer cases who underwent chemically assisted ESD (CA-ESD) and 30 consecutive cases who underwent traditional ESD (ESD) were retrospectively compared.

Results Technical success rate and en bloc resection rate of the lesion were 100% in the both groups. Difference in treated lesion size was not significant. Overall procedural time (PT) and time for submucosal dissection (SD) were significantly shorter in CA-ESD group (PT: 20.13 + 11.39, SD: 13.93 + 9.02) than ESD group (PT: 56.2 + 59.59, SD: 38.73 + 44.38) ($p = 0.004$ in PT, 0.007 in SD)

Conclusions Results of this study demonstrated that the topical application of mesna could expedite ESD for gastric cancers.

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The influences on blood gas analysis and intestinal gas volume under the new technique: duodenal balloon occlusion method for gastric endoscopic submucosal dissection

H MORI, A MURAMATSU, M KOBAYASHI, H INOUE, T MASAKI

Department of Gastroenterology and Neurology, Kagawa Medical University School of Medicine, Japan

Introduction The procedure of endoscopic submucosal dissection (ESD) may take a long time and cause abdominal distension from excessive intestinal insufflations. Nowadays we use CO2 insufflation for ESD, which is more absorbed from digestive tract walls. To overcome these side effects, we developed new ESD technique called the duodenal balloon occlusion method (D-BOM) that not insufflate air beyond the duodenum.

Materials and methods We performed ESD to 20 patients suffered from esophageal or gastric cancer. We divided them into two group at random. With D-BOM (Group A) and without D-BOM (Group B). Before we performed ESD, we put the balloon commonly used to esophageal varix sclerotherapy at the duodenal bulb. Then the balloon was inflated with 60 ml of air. Under the CO2 insufflation, before and after the ESD with or without D-BOM, computed tomography was carried out, and the volume of intestinal gas was calculated. Also blood gas analysis was examined.

Results The volume of intestinal gas in the patient before ESD with D-BOM was the same as that after the procedures. However without D-BOM resulted in a marked intestinal distension, nausea and vomiting. The blood gas analysis (pH and PaCO₂) is the same between two 2 groups.

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A prospective study of narrow band imaging for detection and differentiation of premalignant and malignant gastric lesions

TL ANG, KM FOCK, EK TEO, JYL TAN, JPL ONG, DSW ANG, ABE KWEK

Department of Gastroenterology, Changi General Hospital, Singapore

Introduction This study compared narrow band imaging (NBI) against white light endoscopy (WLE) in the detection and differentiation of premalignant and malignant gastric lesions in a Chinese population.

Methods A gastroscope with WLE, NBI and optical magnification functions (GIF FQ260Z, Olympus, Tokyo, Japan) and a high definition monitor were used. WLE was performed first followed by NBI. The incremental diagnostic yield of NBI over WLE, and ability of NBI with magnification to differentiate gastric mucosal pathology, was analysed. The reference standard was histology obtained from targeted biopsies of focal lesions and random biopsies of the antrum, incisura, corpus and cardia.

Results Over a 20-month period, 374 patients (mean age 51.8 years, 54% male) were recruited. WLE detected a focal gastric lesion in 44.7% (167/374); a definitive diagnosis could be made endoscopically by WLE in 101/167 (100 benign lesions and 1 gastric cancer). NBI detected an additional 31 cases of intestinal metaplasia (8.3%) missed by WLE. Among the 66 focal lesions detected by WLE without a definitive endoscopic diagnosis, NBI with magnification correctly predicted benign pathology in 65/66 and early gastric cancer in 1/66.

Conclusion NBI was useful in detecting intestinal metaplasia missed by WLE. NBI with optical magnification was able to differentiate the pathology of gastric mucosal lesions.

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A pilot study of contrast harmonic endosonography using DEFINITY™ in the evaluation of suspected pancreatic tumors
TL ANG, EK TEO, KM FOCK

Department of Gastroenterology, Changi General Hospital, Singapore

Introduction Endosonography (EUS) is used for diagnosis and T-staging of pancreaticobiliary malignancies. The assessment of tumor extent and vascular invasion remains challenging. Contrast harmonic EUS (CHEUS) with DEFINITY™, a second generation microbubble agent used in contrast echocardiography, may improve visualization of pancreatic tumors but currently there are no published data. This pilot study assessed the utility of CHEUS using DEFINITY™ in the evaluation of suspected pancreatic tumors.

Methods Patients with suspected pancreatic tumors underwent EUS followed by CHEUS which was performed with intravenous injection of 10 µl/kg of DEFINITY™. The incremental yield of CHEUS was compared with EUS. A positive diagnosis of malignancy was based on cytology or histology; a negative diagnosis for malignancy was based on negative cytology and benign clinical course.

Results Eighteen patients underwent CHEUS. The final diagnoses were: pancreatic adenocarcinoma (10), metastasis to pancreas (2), chronic pancreatitis (2) and one each of endocrine neoplasm, periampulla adenocarcinoma serous cystadenoma and normal pancreas. CHEUS enhanced the margins of the lesion in 94% and changed T-stage in 13% with detection of vascular invasion. CHEUS demonstrated fine abnormal vessels in all cases of cancer not seen in benign lesions ($p < 0.001$).

Conclusion CHEUS using DEFINITY™ was useful for evaluation of suspected pancreatic tumors. It improved visualization of tumor margins and vascular invasion, and demonstrated fine abnormal vessels in malignant masses.

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Narrow band imaging with optical magnification: high accuracies with high confidence in predicting histology in colorectal lesions

R SINGH,^{1,2} S CHEN YI MEI,¹ W TAM^{1,2}

¹Lyell McEwin Hospital, ²University of Adelaide, Australia

Introduction Narrow Band Imaging with optical magnification (NBI-Z) enables mucosal morphology to be assessed in real time with magnification of upto 115X.

Methods Colorectal lesions detected were assessed with NBI-Z. Histology was predicted using the modified Sano's classification based on capillary network patterns (cn); Type I: absent cn (hyperplastic), Type II: cn present, surrounding mucosal glands (adenoma), Type IIIa: high density cn with tortuosity and lack of uniformity (intramucosal cancer) and Type IIIb: nearly avascular cn (invasive cancer). Each lesion was also graded with a confidence level (low/high). High definition videos of each lesion assessed with NBI-Z were taken. This was followed by polypectomy, endoscopic or surgical resection. NBI-Z diagnosis was compared to the final histopathology. To test for interobserver agreement, an endoscopist blinded to the video acquisition process and histology then graded the videos.

Results 50 lesions (2 assessors: 100 studies) (average size: 8.4 mm) (20 hyperplastic, 25 adenomas, 2 intramucosal cancers, 3 invasive cancers) in 32 patients were assessed. The overall accuracy of NBI-Z in predicting

histology was 90% which increased to 95% (88/93) when lesions were predicted with high confidence. The Sensitivity (Sn) and Specificity (Sp) in differentiating neoplastic from non neoplastic lesions with high confidence were 98% and 89% respectively whilst the Sn and Sp in predicting endoscopic resectability [Type II, IIIa vs. Type I, IIIb] was 100% and 90% respectively. The interobserver agreement (kappa) was substantial at 0.89. **Conclusions** Using confidence levels, NBI-Z permits prediction of colorectal neoplasia with high accuracies and may allow prompt decisions to be made if a lesion should be left in situ, resected and discarded or biopsied.

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Cost-effectiveness analysis of endoscopic ultrasound as a first-line staging tool for patients with non-small-cell lung cancer
LH LAI,¹ MK HSIN,² YK TSE,¹ FKL CHAN¹

¹Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong S.A.R., China, ²Department of Surgery, Prince of Wales Hospital, Hong Kong S.A.R., China

Introduction There was little data on the cost-effectiveness of endoscopic ultrasonography with fine-needle-aspiration (EUS-FNA) as the first-line staging tool for non-small-cell-lung-cancer (NSCLC), especially when compared with the gold standard mediastinoscopy.

Methods We reviewed consecutive cases referred for NSCLC staging between February 2008 and February 2009. Patient with enlarged mediastinal lymphadenopathy (more than 1 cm based on computer tomography [CT]) were included. A decision analysis model that represented staging pathways for patients with newly diagnosed NSCLC was constructed and structuralized by treatment decision. Direct costs of mediastinoscopy and EUS-FNA were analyzed.

Results Totally 52 patients were identified (mean age: 66 years, male: 79%). The probability of lymph node metastasis was 0.73 (95%CI 0.59–0.84), and the sensitivity and specificity of EUS-FNA to detect lymph node metastasis were 0.66 (95%CI 0.49–0.80) and 1.00 (95%CI 0.73–1.00) respectively. The direct cost for EUS-FNA and mediastinoscopy were US\$600 (range: US\$400–1000) and US\$2000 (range: US\$1300–2500) per examination respectively. Decision analysis revealed that the cost per correct nodal staging was US\$1800 for EUS-FNA and US\$2300 for mediastinoscopy. The outcome was sensitive to the prevalence of nodal metastasis and sensitivity of EUS-FNA using one-way sensitivity analysis. The model predicted that EUS-FNA was more cost-effective than mediastinoscopy even if the probability of nodal positivity was only 0.43 or the sensitivity of EUS-FNA was as low as 0.39.

Conclusions This study shows that EUS-FNA is more cost-effective than mediastinoscopy as a first-line staging tool for patients with NSCLC and enlarged lymph node on CT.

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Discrepancy between endoscopic and histologic measurement of colonic polyp size

SC NG,¹ AWH CHAN,² KF TO,² JCY WU,¹ FKL CHAN,¹ JJY SUNG,¹ JYW LAU³

¹Department of Medicine and Therapeutics, ²Department of Pathology, ³Department of Surgery, Chinese University of Hong Kong

Background The American and British Society of Gastroenterology guidelines recommend polyp size as one of the key factors in determining

polyp surveillance. Accurate assessment of polyp size is important as larger polyps are associated with increased risk of colorectal cancer. Tissue fixation has not been shown to affect polyp size.

Aim To compare polyp size assessment by endoscopists and pathologists in consecutive symptomatic patients undergoing colonoscopy in one single centre.

Methods Polyps removed at colonoscopy were measured to the nearest 1 mm by endoscopists and the values were compared with pathologists' measurement after fixation.

Results Two-hundred and twenty consecutive patients (60% male; mean age \pm SD, 65 \pm 11.2, range, 24–94 years) had 461 colonic polyps removed by 12 endoscopists at colonoscopy. 72% of the polyps were adenomas and 28% were hyperplastic. 42% of polyps were located in the right colon. The size of polyps measured by endoscopists [median (interquartile range): 3.00 mm (3.00–5.00)] was significantly greater compared with the measurement of polyps by pathologists [2.00 mm (2.00–3.00) ($p < 0.001$)], with an interclass correlation coefficient of 0.899. Polyp size was overestimated by endoscopists in 64% of polyps. Results were not dependent on the polyp histology (eg. dysplasia) or location. Mean differences between endoscopic and histology measurements according to the grade of endoscopist were: 1.00 mm (0–2.00), 2.00 mm (0–3.00), 1.00 mm (0–3.00) for experienced, independent and trainee endoscopists, respectively. Twenty-three polyps (5%) were ≥ 10 mm on histology. In four cases (17.4%), endoscopic measurement was < 10 mm in polyps that were found to be ≥ 10 mm (range difference, 2–7 mm) on pathological measurement.

Conclusions Endoscopists consistently over-estimate polyp size (by more than 1 mm) in polyps < 5 mm when compared with pathologists' measurement. However, 17% of polyp ≥ 10 mm on pathological assessment were underestimated by endoscopists. This has implications on risk stratification and future polyp follow-up.

Reference

Schoen et al. GIE 1996

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Validity of narrow band imaging in detecting colonic polyps based on sano classification of capillary pattern

SR TRECERO, WCR ACUESTA, R DE GUZMAN, J KHOW, A UY, R LOPEZ, E ONG, CP LIM
Metropolitan Medical Center, Manila, Philippines

Significance Narrow-band imaging (NBI) enhances visualization of superficial vascular structures and is useful in detecting small polyps and flat adenomas that are easily missed in conventional white-light colonoscopy.

Objective To determine sensitivity, specificity, positive predictive value, negative predictive value and accuracy of NBI in distinguishing neoplastic from non-neoplastic polyps and adenoma from hyperplastic polyps.

Method A prospective study involving 50 patients who underwent colonoscopy and proctosigmoidoscopy using Olympus CF-H180AL with narrow band capability. Each video was reviewed and targeted polyps seen under NBI were photographed before biopsy. A total of 60 images were included, 20 each for hyperplastic, adenomatous and carcinomatous polyps. Histopathology reports were collected and reviewed as the criterion standard. Three endoscopists were blinded on history and other data. They were given explanation and sample images of colonic polyps based on capillary pattern of Sano. Consensus interpretation were noted on each image whether hyperplastic, adenomatous or carcinoma.

Result The overall sensitivity of NBI in detecting carcinoma was 73.68%, specificity of 97.5%, positive predictive value of 93.75%, negative predictive value of 88.63% and diagnostic accuracy of 90%. While in

differentiating adenoma from hyperplastic polyps, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were the same at 75%.

Conclusion Based on Sano Classification, NBI can differentiate neoplastic from non-neoplastic lesions but have a low accuracy rate in differentiating adenomatous from hyperplastic polyps. Our initial experience with NBI is encouraging and holds promise for future use.

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Autolytic changes of resected gastric specimen in rat model—a pilot study

JONG JIN HYUN, HOON JAI CHUN, HYUK SOON CHOI, HYE JIN CHO, JUHYUNG KIM, BORA KEUM, YEON SEOK SEO, YONG SIK KIM, YOON-TAE JEEN, HONG SIK LEE, SOON HO UM, CHANG DUCK KIM, HO SANG RYU

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Korea University Anam Hospital, Seoul, Korea

Introduction Endoscopic submucosal dissection (ESD) is increasingly practiced in countries with a high incidence of early gastric cancer and its indication has recently expanded to include larger and/or ulcerative lesions. However, expansion of ESD indication results in complications and longer procedure times, which could lead to autolytic changes from the periphery of the specimens. We tried to evaluate the autolytic process and histomorphological changes over time after gastric resection.

Materials and methods Fresh rat stomach was resected, and cut out in a size of 1.0 \times 1.0 cm, and fixed on a cork board. Tissues were put into pH4 solution which is same intragastric environment and then immersed into formalin solution at interval of 10 minutes up to 120 minutes. 12 pieces were then processed for light microscopic examination, staining with ordinary hematoxylin and eosin, and PAS stain. This experiment was repeated five times. We evaluated histomorphological changes occurring during 2 hours after resection.

Results The loss of PAS positive granules was observed in 20 minutes after resection. Pericellular edema, decreased cellular density, vacuolation and pyknosis occurred in 80 minutes after resection. Decreased cellular components and vacuolation was prominent in 80 minutes after resection. Epithelial desquamation was focally observed in 120 minutes after resection.

Conclusions Initial autolytic changes after gastric resection in rat model occurred at an early stage. Autolytic changes showed tendency to progress over time. Increasingly expansion of ESD indication is associated with a long procedure time and consequently, may lead to autolytic changes especially in peripheral margin of the resected specimen. Therefore, we think that there is the possibility of inadequate pathologic diagnosis for margin by autolysis in a longer procedure time.

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Carbon dioxide insufflation during routine esophagogastroduodenoscopy examination decreases patient postprocedural abdominal pain

YASUKO HOSHIMIYA,¹ TOSHIKI HIRASAWA,² SAYUKI MICHIHARA,¹ YUMI KURIHARA,¹ YORIMASA YAMAMOTO,² TOMOHIRO TSUCHIDA,² JUNKO FUJISAKI,² IGARASHI MASAHIRO,² RIKIYA FUJITA²
¹Division of nursing, Cancer Institute Hospital, Tokyo, Japan, ²Department of Gastroenterology, Cancer Institute Hospital, Tokyo, Japan

Background Carbon dioxide (CO₂) is rapidly absorbed in gastrointestinal tract and excreted through lungs. Several previous studies reported that CO₂ insufflation during various endoscopic examination and treatment including colonoscopy, endoscopic retrograde cholangiopancreatography and endoscopic resection is safe and effective, but no study on its use in routine esophagogastroduodenoscopy (EGD) examinations has been published yet. Our aim was to assess effect of CO₂ insufflation on postprocedural abdominal pain following routine EGD examinations.

Methods During four-week period, patients undergoing routine EGD examinations received air insufflation (Air Group) first two weeks and CO₂ insufflation (CO₂ Group) last two weeks. Patients with chronic obstructive pulmonary disease or suboptimal mental status based on pain score assessments were excluded. Blood pressure (BP) and heart rate (HR) were recorded before and during examinations and 10-point visual analogue scale was used to evaluate abdominal pain five minutes after each examination.

Results Total of 458 patients were enrolled in this study with Air Group and CO₂ Group consisting of 204 and 254 patients, respectively. While two groups were similar in terms of patient age, procedure duration, sedative (midazolam) dose and rate of use, BP and HR before and during examinations, patient postprocedural abdominal pain was significantly lower in CO₂ Group ($p < 0.001$).

Conclusion CO₂ insufflation during routine EGD examinations significantly reduced patient postprocedural abdominal pain.

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Metoclopramide combined with right lateral position can increase the rate of complete small bowel examination in capsule endoscopy

ZQ SONG, LY ZHOU
 Department of Gastroenterology, Peking University Third Hospital, Beijing, China

Introduction Approximately 20%–30% capsule endoscopy (CE) failed to reach cecum within 8 hours of battery life, which limited its diagnostic yield. The aims of this prospective, randomized, blinded and controlled study were to determine whether the rate of complete small bowel examination (CSBE) and diagnostic yield in CE were affected by metoclopramide combined with right lateral position (RLP).

Methods Seventy patients were randomized to either the intervention group (10 mg metoclopramide administered intramuscularly 15 min before capsule ingestion and staying 30 min in RLP after) or the control group (receiving nothing and being discharged immediately after capsule ingestion). CE was performed with the SB PillCam system and interpreted with RAPID software.

Results In the intervention group, the rate of CSBE was significantly higher and the gastric emptying time (GET) was shorter. No statistical differences were found at the rate of gastric retention (GR), small bowel

transit time (SBTT) or diagnostic yield between the two groups ($P > 0.05$). See Table below.

| | Intervention group (<i>n</i> = 35) | Control group (<i>n</i> = 35) | <i>P</i> value |
|-------------------|--|-----------------------------------|----------------|
| GR <i>n</i> | 0 | 1 | 0.314 |
| CSBE <i>n</i> (%) | 33 (94.3%) | 26 (74.3%) | 0.022 |
| GET (min) | 15 (1–136) | 35 (2–465) | 0.007 |
| SBTT (min) | 236.1 ± 82.1 | 274.9 ± 106.3 | 0.094 |

Conclusions Metoclopramide combined with right lateral position increased the rate of complete small bowel examination in capsule endoscopy without influence on the diagnostic yield.

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EUS based changes in management plan of cystic neoplasms of pancreas in a tertiary referral center

M RAMCHANDANI, K RAKESH, S LAKHTAKIA, R GUPTA, GV RAO, DN REDDY

Department of Gastroenterology, Asian Institute of Gastroenterology, Hyderabad, India

Introduction Cystic neoplasms of pancreas are increasingly recognized due to improved sensitivity of cross sectional abdominal imaging. Endoscopic ultrasound (EUS) is the most sensitive imaging modality for the detection of pancreatic cystic lesions. EUS with or without Fine needle aspiration (FNA) helps in management of these lesions by categorizing them as benign or malignant lesions.

Aim To assess the change in management plan of cystic neoplasms of pancreas after EUS with or without EUS-FNA.

Methods All patients with cystic lesions of pancreas referred for EUS from March 2008 to 2009 have been evaluated retrospectively. All of them underwent radial EUS followed by linear array EUS-FNAC as required. The cystic lesions were classified based on the morphology, cyst fluid analysis, histopathology and cytology.

Results 32 patients with mean age—43.8, range (24–66), median—44 and S.D—12.28. M:F ratio—18:14. Mean diameter of the cyst was 3.54, range (0.7–17), median—3 and S.D—3.04. The site of location of cysts were: head & uncinate: 5, neck & body: 17, tail: 4, and neck, body & tail: 6 respectively. Morphological types included: IPMN—17 (4 main branch, 13 side branch), Mucinous cystic neoplasms—2, Serous cystadenomas—8 and others (solid & cystic -1, hydatid cyst & TB-3) EUS-FNAC was done in 8/32 (25%). Surgical intervention (central pancreatectomy) was done in 2 patients, 4 were inoperable after exploration, 1 underwent laproscopic pancreatic jejunostomy and hydatid cyst excision respectively.

Conclusion Endoscopic ultrasound (EUS) is a good modality for the detection of pancreatic cystic lesions. EUS-FNA is valuable in preoperative diagnostic assessment as seen in 25% of our patients. It helped in categorizing the patients into surgical, endoscopic or percutaneous management. Hence, EUS helps in change of management strategies in these patients with cystic neoplasm of pancreas.

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A randomized controlled trial of Rebamipide plus Rabeprazole for artificial ulcer healing after endoscopic submucosal dissection

S FUJIWARA,¹ Y MORITA,¹ T TOYONAGA,²
M YOSHIDA,¹ H KUTSUMI,¹ T AZUMA¹

¹Department of Gastroenterology, Kobe University, School of Medicine, Kobe, Japan, ²Department of Endoscopy, Kobe University, School of Medicine, Kobe, Japan

Introduction Endoscopic submucosal dissection (ESD) is an increasingly common technique to resect early gastric cancer. Eight weeks proton pump inhibitor (PPI) treatment is reported to heal patients with post ESD ulcer; however, not all patients are healed, particularly those with atrophic gastritis. We aimed to examine whether addition of a mucosal healing agent, rebamipide, might improve healing rates, particularly in those with atrophic gastritis, after ESD.

Methods Patients were randomly assigned to two treatment groups following ESD: Rabeprazole 20 mg once daily (PPI group) or rebamipide 300 mg daily and rabeprazole 20 mg daily (combination group). All patients were treated for 8 weeks. The primary endpoint was to evaluate the proportion of patients with ulcer healing to scar-stage at 56 days after ESD. A pre-specified sub-group analysis examined ulcer healing in patients with atrophic gastritis.

Results Progression to S-stage was 54.8% (17/31) in the PPI group, 86.7% (26/30) in the combination group (Odds ratio: 5.3, 95% CI: 1.50–19.02, $p = 0.006$). Patients with atrophic gastritis were healed 22.2% (2/9) in the PPI group, and 92.9% (13/14) in the combination group (Odds ratio; 45.5, 3.48–594.67, $p < 0.001$)

Conclusion Treatment with PPI plus rebamipide improved healing rates at eight weeks for patients with post ESD ulcer, and appeared particularly effective for patients with severe atrophic gastritis.

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A Taiwan grading system for iatrogenic nasal bleeding after transnasal esophagogastroduodenoscopy can reduce this complication

C-T HU

Transnasal Endoscopy Unit, Division of Gastroenterology, Department of Internal Medicine, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

Introduction Transnasal endoscopists need to have a grading system to score nasal bleeding in the sinonasal tract after unsedated ultrathin transnasal esophagogastroduodenoscopy (UT-EGD). The Japanese grading system proposed by Dr Moris et al [1] demonstrated only the severity of nasal bleeding from grade 0 to grade 3, but it does not show bleeding mechanisms (B), location (L), and grading (G) together.

Materials and methods We performed UT-EGD for 2661 consecutive patients at Buddhist Tzu Chi Hospital, between September 2005 and November 2008, by transnasal endoscopes. As of 2007, we subdivided the locations (L) of bleeding into the inferior or middle turbinate (Lit or Lmt), anterior or posterior septum (Las or Lps) and the anterior or posterior lateral wall (Law or Lpw). Also, bleeding (B) was denoted during anesthesia (Ba), insertion (Bin) or exertion (Bex).

Results The majority of patients (172/203, 85%) with contact nasal bleeding ($n = 203$) were just after withdrawal through the middle nasal turbinate (142/203, 69.9%) and inferior nasal turbinate (61/203, 30.1%).

There were a total of 51 cases who received UT-EGD in 2005 and repeated UT-EGD in 2006. However, a total of 45 cases had repeated bleeding in 2006 (88.2%). With the use of our new "BLG" reporting system, there were a total of 36 cases who had UT-EGD in 2007 and repeated the same exam in 2008. Only 7 out of these repeated 36 cases (19.4%) had bleeding in 2008. The dramatic drop of bleeding rate (88.2% vs 19.4%, $p < 0.0001$) was statistically significant.

Conclusion Our "BLG" grading method is more informative on the locations and mechanisms of hemorrhage so that epistaxis can be avoided in the next UT-EGD.

Reference

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Epidemiology

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Prevalence and characteristics of chronic constipation in an Asian community

KEWIN TIEN HO SIAH,¹ KOK ANN GWEE,¹
REUBEN WONG KONG MIN,¹ WONG MEE LIAN²

¹Department of Medicine, National University Hospital, ²Department of Community, Occupational & Family Medicine, National University Singapore, Singapore

Aims To investigate the prevalence and characteristics of chronic constipation in Singapore.

Methods A proportional stratified random sample of 3000 household was selected. From each household, one individual aged 20 was selected randomly for interview with a validated questionnaire.

Results One-third of the population had some form of bowel disturbance. Chronic constipation (CC) was the most common bowel disturbance affecting 571 of 2276 (25.1%) of the total population, while only 10.0% had chronic diarrhoea and 0.6% had an alternating bowel pattern. Among all the subjects, 50.8% had hard stool form, 30.0% had straining and 6.0% had bowel movements of less than 3 times a week. Although overall CC was more common in women than men (27.0% vs. 23.2%; $p < 0.05$), when the different age groups were analysed, the highest prevalence of CC was observed in men > 70 (35.8%), with women in the 20–29 years having the second highest prevalence (30.5%). Better educated women (>6 years formal education) had significantly higher prevalence of CC than their lesser educated counterparts (34% vs. 25%, $p = 0.04$). No statistically significant differences were found for race and marital status. A high proportion (21.8%) of chronic constipators thought they had normal bowel habits. Self-reported constipation prevalence was 5.0%.

Conclusion This study presents further evidence that bowel disturbances are more prevalent among Asian men than appreciated. A high percentage of chronic constipators thought they had normal bowel habits.

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Correlation between MELD score and occurrence of SBP

A DEEPAK,¹ M JAIN²

¹Bombay Hospital & Medical Research Centre, ²Gastroenterology Centre, Western Railway Hospital

Aim To determine whether a greater MELD score is associated with a greater risk of development of spontaneous bacterial peritonitis.

Methods This prospective study enrolled 148 consecutive patients with cirrhosis and ascites admitted between May 2008 to March 2010. After excluding patients who were immunosuppressed, had history of prior antibiotic use, had previous episodes of SBP and had other confounding etiological factors for ascites, sixty seven patients were included in the study. SBP was defined as ascitic fluid PMN count >250 /cu.mm. The odds ratio for development of SBP associated with MELD score and grouped MELD score was calculated (<15, 16–24, >25). Variables like albumin, INR, creatinine, creatinine clearance and ascitic fluid analysis measurements were compared in the two groups.

Results The prevalence of SBP was 20.9%. The mean MELD score in SBP group was 23.14 9.87 and in the non SBP group was 18.46 7.43. The odds ratio for development of SBP was 1.23 for each point rise in MELD score. ($p = 0.0032$). Patients with MELD > 25 had an odds ratio of 9.52 ($p = 0.001$) for SBP as compared to patients with MELD < 15. Ascitic fluid PMN count and creatinine clearance were significantly altered in the SBP group.

Conclusions Increasing MELD score is independently associated with a greater risk of SBP. For every point increase in MELD score, the risk of developing SBP increases by 12.3%. Prophylactic antibiotics should be considered in patients with MELD score > 25.

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Population-based epidemiology of primary sclerosing cholangitis in Canterbury, New Zealand

JH NGU,^{1,2} A WRIGHT,² RB GEARRY,^{1,2} BA CHAPMAN,¹ MJ BURT,¹ ML BARCLAY,^{1,2} CAM STEDMAN^{1,2}

¹Department of Gastroenterology, Christchurch Hospital, New Zealand, ²University of Otago, Christchurch, New Zealand

Background/Aim The precise etiology of primary sclerosing cholangitis (PSC) remains unknown and epidemiological data are very limited worldwide. Our aim was to perform a population based epidemiological study of PSC in Canterbury, New Zealand.

Method Multiple case finding methods were employed. All public and private, adult and pediatric outpatient clinics, hospital discharge summaries, radiology and pathology reports were searched to identify all cases of PSC in the region. Cases were included if they have ERCP, MRCP or liver biopsy proven PSC.

Results 79 cases of PSC were identified. Incidence in 2008 was 1.4/100,000 (95% CI 0.4–2.5/100,000). Point prevalence on 31 December 2008 was 10.3/100,000 (95% CI 7.5–13.2/100,000). Age-standardized (WHO standard population) incidence and prevalence were 1.6 and 10.3 per 100,000 respectively. Mean and median ages at diagnosis were 51 and 50 years respectively. Gender-specific prevalence confirmed a male predominance. 76% have co-existing inflammatory bowel disease (IBD) while 8% overlap with autoimmune hepatitis. 22% developed malignancy, of which cholangiocarcinoma and colorectal cancer make up 50% and 20% respectively.

Conclusion This is the first population based epidemiological study of PSC in Asia Pacific region to be reported. It shows that PSC is most prevalent in elderly male with a strong association with IBD. Nearly a quarter of this cohort develops malignancy.

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Primary biliary cirrhosis in Canterbury, New Zealand: a population-based study

JH NGU,^{1,2} A WRIGHT,² RB GEARRY,^{1,2} BA CHAPMAN,¹ MJ BURT,¹ ML BARCLAY,^{1,2} CAM STEDMAN^{1,2}

¹Department of Gastroenterology, Christchurch Hospital, New Zealand, ²University of Otago, Christchurch, New Zealand

Background/Aim Primary biliary cirrhosis (PBC) is a cholestatic liver disease of unknown aetiology. Its epidemiology has not been studied systematically in New Zealand. Our aim was to perform a population based epidemiological study of PBC in Canterbury, New Zealand.

Method To identify all known PBC cases in this region, computer records of all public and private, adult and pediatric outpatient clinics and hospital discharge summaries were searched. Cases were included if at least two of the following criteria were fulfilled: positive antimitochondrial antibodies, elevated alkaline phosphatase for greater than 6 months, and compatible liver histology.

Results 70 cases of PBC were identified. Incidence of PBC in 2007 was 1.3/100,000 (95% CI 0.3–2.2/100,000). Point prevalence on 30 November 2007 was 9.3/100,000 (95% CI 6.9–12.1/100,000). There is a female predominance (93%). AMA, ANA and SMA were positive in 84%, 27% and 22% respectively. Immunoglobulin M and G were elevated in 78% and 53% respectively. 17% overlap with autoimmune hepatitis. Age at diagnosis peaked at the seventh decade with mean age of 61.

Conclusion This is the first population based epidemiology study of PBC in New Zealand to be reported. The observed rates almost doubled those reported in Victoria, Australia which has similar population composition. This suggests an environmental factor(s) contributes to the development of PBC.

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Knowledge and attitude on colorectal cancer screening among moderate risk patients in West Malaysia

MY HARMY,¹ D NORWATI,¹ MN NORHAYATI,¹ AR AMRY²

¹Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia, ²Department of Internal Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction Colorectal cancer is the commonest cancer among men and the third among women in Malaysia. However, almost 80% sought treatment for cancer only when they were already in late stage due to lack of awareness. Hence, the objectives of this study were to determine the knowledge and attitude of colorectal cancer screening among moderate risk patients.

Methods A cross-sectional study was conducted between August 2009 and April 2010 in 44 selected health clinics with Family Medicine Specialist in West Malaysia using stratified multistage random sampling. A validated Malay version of the questionnaire with Cronbach's alpha of 0.65 to 0.82 was used. Data was entered using SPSS 12.0 and analysed using STATA 8.0.

Results A total of 1905 (93.8%) patients responded. The mean (SD) knowledge and attitude score among moderate risk patients were 69.5% (6.1) and 66.5% (7.1), whereas, the percentage of good knowledge and attitude was 4.1% and 3.3% respectively. Less than 1% had undergone

colorectal cancer screening and the main reasons for not undergoing screening were not bothered, busy and embarrassment.

Conclusion Majority of patients who had moderate risk for colorectal cancer had extremely low knowledge and attitude towards colorectal cancer screening. As a result, majority did not undergo any form of colorectal cancer screening.

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A systematic review of inflammatory bowel disease genetic variants in Asia

SC NG,¹ KKF TSOI,¹ MA KAMM,² B XIA,³ J WU,¹ FKL CHAN,¹ JJY SUNG¹

¹Department of Medicine & Therapeutics, Chinese University of Hong Kong, ²St Vincent's Hospital, Melbourne, Australia, ³Zhongnan Hospital, Wuhan University, China

Background The incidence of inflammatory bowel disease (IBD) is rising in Asia. Preliminary findings suggest genetic susceptibility of IBD in Asia differ from the West. We performed a systematic review of case-control studies to evaluate susceptibility genes in Asian IBD patients.

Methods Two investigators independently identified eligible studies from 1950 to 2010 in MEDLINE, EMBASE, EBM Reviews and BIOSIS Previews.

Results 477 abstracts were identified, and 103 eligible studies with 19,171 IBD patients and 27,350 controls, were included. Common NOD2 variants associated with CD in the Caucasian population, were detected in Turkish and Iranian CD patients, but were absent in CD patients of Japanese, Korean, Han Chinese, Indian and Malaysian descent. Novel mutations of NOD 2, JW1 and SNP5, were found in Malaysian and North Indian patients with CD, respectively. ATG16L1 was not associated with CD in Japanese, South Korean and Han Chinese population. IL-23R was weakly associated with CD in South Koreans and novel Gly149Arg on IL-23R was identified in Chinese with CD. In East Asians, polymorphisms of TNF-SF15 and HLA-DR were associated with CD whereas CTLA-4, MICA allele and HLA-B*52 were associated with UC.

Conclusion IBD in Asians is associated with genetic mutations different from that of Caucasians. Novel genes in Asian IBD patients allow exploration of new disease-associated mechanisms.

Table 1 Major Findings of IBD Genes in Asia

| | NOD2 | ATG-16L1 | IL-23R | TNF-SF15 | TLR-4 | HLA-B*52 | HLA-DR | CTLA-4 | MICA |
|--------------|------|----------|---------|----------|-------|----------|---------|----------|---------|
| | CD | CD | CD | CD | CD | UC | UC | UC | UC |
| Han | - | - | + | | - | | + | + | + |
| Chinese | | | (OR0.3) | | | | | (OR14.6) | (OR3.8) |
| Japanese | - | - | - | + | | + | + | + | + |
| | | | | (OR1.9) | | (OR5.1) | (OR3.7) | (OR0.3) | (OR2.6) |
| South Korean | - | - | + | + | - | | | | |
| | | | (OR1.8) | (OR2.8) | | | | | |
| Indian | - | | | | | | | | |
| Malaysian | - | | | | | | | | |
| Turkish | + | | | | | | | | |
| Iranian | + | | | | | | | - | |
| Israel | + | | + | | | | | | |

Empty box: not studied; +, Associated; -, Not associated

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Prevalence of celiac disease: a community based study from North India

AK VERMA,¹ GK MAKHARIA,¹ R AMARCHAND,² P DAS,³ V BHATIA,⁴ A GOSWAMI,² S BHATNAGAR,⁴ S DATTA GUPTA,³ V AHUJA,¹ K ANAND²

Department of ¹Gastroenterology and Human Nutrition, Centres for ²Community Medicine, ³Pathology and ⁴Pediatrics, All India Institute of Medical Sciences, New Delhi, India

Background While celiac disease affects about 1% of world's population, it is thought to be uncommon in Asia. There is a lack of data on the community prevalence of celiac disease from Asian region.

Methods We estimated the prevalence of celiac disease in an Indian community in National Capital Territory, Delhi. A structured questionnaire was used to collect sociodemographic data and symptoms and signs related to celiac disease from all the participants (home to home) for symptoms of celiac disease such as chronic or recurrent diarrhea, anemia, short stature (linear height below 5th percentile for age) and failure to thrive/gain weight. All patients with screen positive (any one of the above) and 10% of screen negative were called for serological testing (anti-tissue transglutaminase antibody). All serologically positive were invited to undergo further evaluation. Celiac disease was diagnosed on the basis of ESPGHAN criteria.

Result Amongst 12,573 contacted, 10,488 (83.4%) (50.6% male) agreed to participate. Based on screening, 5622 (56.6%) participants were screen positive. 2167 (38.5%) screen positive and 712 (14%) screen negative returned for serological testing. The overall seroprevalence of celiac disease was 1.4% (95% CI 1.18–1.64). The overall prevalence of celiac disease was 0.89 (95% CI 0.72–1.08). The prevalence of celiac disease in adults and children was 0.7% (95% CI 0.52–0.93) and 1.32% (95% CI 0.97–1.74), respectively.

Conclusion The prevalence of celiac disease in an Indian community 1 in 123. Celiac disease appears to be more common but neglected disorder than has generally been recognized in India.

Large Intestine

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Expression of tight junction proteins in Crohn's disease, ulcerative colitis and intestinal tuberculosis

P DAS, GK MAKHARIA, P GOSWAMI, V SREENIVAS, V AHUJA, SD GUPTA

Department of Pathology, Department of Gastroenterology and Human Nutrition and Biostatistics, All India Institute of Medical Sciences, New Delhi, India

Background Intestinal barrier function is largely regulated by tight junction (TJ) proteins, which is impaired in various autoimmune and inflammatory diseases of intestine. The direct relationship of changes in colonic permeability and the TJ alterations is largely speculative. There is paucity of data on direct structural analysis of tight junction proteins in these conditions.

Patients and methods Multiple colonic biopsies were obtained from eleven patients with active Crohn's disease (CD) as well as 10 each with ulcerative colitis and intestinal tuberculosis (ITB). Both clinically and histologically normal 8 control intestinal biopsies were taken. The immunohistochemical expression patterns of ZO-1, claudin-2, claudin-4 and

occludin were evaluated semi quantitatively and compared between these disease groups and control biopsies.

Results Claudin-2 expression was limited to the upper most part of intercellular junction (ICJ) in control biopsies and colonic biopsies of ITB patients; while full membranous positivity was noted both in CD and UC. There was a significant under-expression of claudin-4 in all the disease groups, in comparison to control biopsies. While claudin-4 expression was seen in full ICJ in controls; in CD, ITB as well as in UC the distribution was focal and restricted to the lower most part of ICJ. In CD there was an under-expression of ZO-1 both in the mucosal and glandular surface. There was no significant difference in the expression of occludin in disease groups as compared with controls.

Conclusions There are noticeable alterations of TJ key proteins in ITB, CD and UC. Apart from the occludin; the other tested TJ markers as ZO-1, Claudin-2 and 4 showed marked alteration in disease groups in comparison to controls. The changes of claudin-2 expression were distinctly different in ITB, in comparison to the IBD group; indicating different pathophysiological changes in these two groups.

Liver

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Primary prophylaxis of hepatic encephalopathy in patients with cirrhosis: a open labeled randomized controlled trial of lactulose versus no lactulose

SB CHANDER, S PRAVEEN, A AMIT, SS KUMAR
Department of Gastroenterology, G. B. Pant Hospital, New Delhi, India

Background and aims Development of hepatic encephalopathy (HE) is associated with poor prognosis. There is no study on the prevention of HE in patients who never had HE using lactulose.

Patients and methods Consecutive cirrhotic patients who never had HE were randomized to receive lactulose (Gp-L group) or no lactulose (Gp-NL). All patients assessed by psychometry [(number connection test (NCT-A/NCT-B), figure connection test if illiterate (FCT-A/B), digit symbol test (DST), serial dot test (SDT), line tracing test (LTT)] and critical flicker frequency test (CFF) and at inclusion and after 3 months. These patients were followed monthly for development of overt HE (primary end point).

Results Of 250 patients screened, 120 (48%) included. Minimal hepatic encephalopathy (MHE) present in (10/22, 45%) in Child A, (37/68, 54%) in Child B and (21/30, 70%) in Child C patients. Number of patients with MHE comparable in two groups at baseline (Gp-NL vs Gp-L, 36:32, $p = 0.29$). Lactulose improved MHE in 66% of patients. Patients diagnosed to have MHE had CFF significantly lower than those who did not had MHE in Gp-NL (38.3 ± 2.8 vs 41.7 ± 3.2 Hz, $p = 0.001$) and in Gp-L (38.5 ± 3.2 vs 40.5 ± 2.4 Hz, $p = 0.001$). Twenty one (20%) of 105 patients followed developed an episode of HE. Six (11%) of 55 in Gp-L group and 15 (30%) of 50 in Gp-NL group, $p = 0.02$. Ten (20%) in Gp-NL and 5 (9%) in Gp-L group died, $p = 0.16$. On multivariate analysis CPT score and MHE is significantly associated with development of HE.

Conclusions Lactulose is effective for primary prevention of hepatic encephalopathy in patients with cirrhosis.

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Asian criteria should be adopted to predict unreliable and failed Liver Stiffness Measurement (LSM) in the Chinese population GLH WONG, SHT CHU, VWS WONG, HLY CHAN Institute of Digestive Disease, The Chinese University of Hong Kong

Background Body mass index (BMI) > 30 kg/m² was associated with unreliable and failed LSM in the West but uncertain in Chinese.

Methods We prospectively recruited patients with liver diseases from primary care and hospital clinics for LSM. Unreliable LSM was defined as < 10 valid shots, an interquartile range/LSM $> 30\%$, or a success rate $< 60\%$. Failed LSM failure was defined as zero valid shot.

Results Among 3,205 patients with LSM, 371 (11.6%) and 88 (2.7%) had unreliable and failed LSM, respectively. The rates of unreliable and failed LSM started to increase when BMI was ≥ 28.0 kg/m². Comparing patients with BMI 28.0–29.9 kg/m² versus those with BMI ≥ 30.0 kg/m², the rates of unreliable (16.4% vs. 18.9%; $P = 0.62$) and failed (11.8% vs. 17.8%; $P = 0.16$) LSM were similar. BMI ≥ 28.0 kg/m² was the most important factor associated with unreliable (OR = 2.9, 95% CI = 2.1–3.9, $P < 0.0001$) and failed (OR = 10.1, 95% CI = 6.4–14.2, $P < 0.0001$) LSM. Central obesity, defined as waist circumference > 80 cm in women and > 90 cm in men, was another independent risk factor of unreliable (OR = 1.3, 95% CI = 1.0–1.6, $P = 0.04$) and failed (OR = 5.8, 95% CI = 2.9–11.5, $P < 0.0001$) LSM.

Conclusion The BMI and waist circumference associated with unreliable and failed LSM in Chinese was lower than those in the West.

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Impact of microvascular invasion on the survival of HCC resection patients

KC LIM,¹ JC ALLEN, GS CHIA,¹ MS LIM,¹ PC CHEOW,² AY CHUNG,² LL OOI,^{2,3} SB TAN,¹ PK CHOW^{2,3}

¹Duke-NUS Graduate Medical School, Singapore,

²Singapore General Hospital, ³National Cancer Centre, Singapore

Background The Milan Criteria (tumor size, tumor number, macrovascular invasion) allows judicious selection of patients who would benefit from liver transplantation (LTR) in hepatocellular carcinoma (HCC) and is also believed to similarly impact outcomes with surgical resection (SR). Microvascular invasion (McVI) is a known independent factor for poor survival in HCC but its relative significance on overall survival (OS) in comparison with Milan Criteria is unclear.

Method Patients undergoing SR from Jan 2000 to Mar 2009 at the Singapore General Hospital were followed up for long term outcomes till 1 Jan 2010. They were stratified first by Milan Criteria and then by presence of McVI and compared for OS.

Result 384 of 454 patients resected for cure were stratified into Group 1 (Milan+, McVI-), Group 2 (Milan+, McVI+), Group 3 (Milan-, McVI-) and Group 4 (Milan-, McVI+). 5 year OS were 60%, 38%, 60.5% and 17.6% respectively. Pair-wise comparison of OS showed significant difference except between Group 1 and 3. The 1, 3, 5 year overall survival of Group 1 and 3 were 90%, 73%, 60% and 86%, 71%, 61% respectively (See Figure 1).

Conclusion McVI is a significantly stronger predictor of overall survival than Milan Criteria after SR for HCC and would contribute to patient selection for LTR after SR. This should be evaluated in a prospective study.

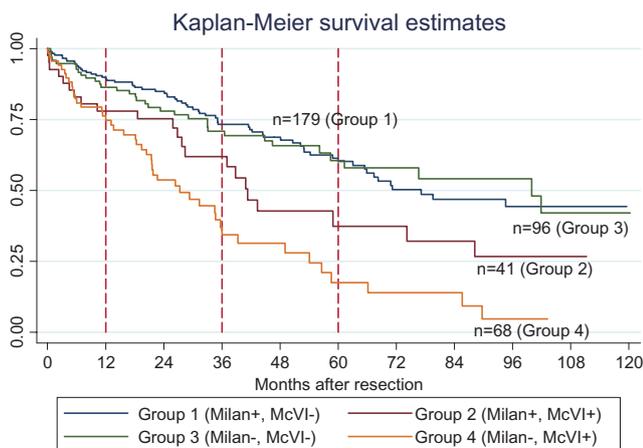


Fig. 1. Overall survival of n = 384 patients.

Motility

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Chili induces epigastric burning symptom in non-erosive reflux disease (NERD) with no effect on gastric accommodation (GA)

C KRIENGGIRAKUL,¹ P VASAVID,² S GONLACHANVIT¹
¹Dpt of Internal Medicine, ²Dpt of Radiology
 Chulalongkorn University, Bangkok, Thailand

To investigate the effects of chili on upper GI symptoms and GA in NERD patients compare to healthy volunteers (HV).

Methods After an overnight fast, 10 HV (7 M, age 32 ± 2.5 years) (mean \pm SEM) and 9 NERD patients (4 M, age 48 ± 3.0 years) underwent single photon emission computed tomography for gastric volume in supine position after ingestion of 2 gm red chili (capsaicin = 1.46 mg) or placebo in capsules, in a randomized double blind cross-over fashion with a one-week washout period. A standard 250 ml-liquid meal was ingested at 15 min after chili or placebo ingestion. Images for gastric volume were taken before ingestion of chili or placebo, before the meal, and then every 10 min after the meal ingestion for 50 min. The GA volume was the maximal postprandial gastric volume minus the fasting gastric volume. Upper gastrointestinal symptoms were evaluated using 10 cm long visual analog scales.

Results In NERD patients, abdominal burning score was significantly increased after chili (4.04 ± 1.10) compared to placebo (2.50 ± 1.03) ($p < 0.05$) and to that of after chili in HV (0.51 ± 0.16) ($p < 0.05$). Heartburn and other symptoms were not significantly different between chili and placebo ($p > 0.05$) in both groups. GA was not significantly different between after chili and placebo ingestion in both NERD (418 ± 24 vs 424 ± 37 ; $p > 0.05$) and HV (381 ± 24 vs 373 ± 15) ($p > 0.05$). The gastric volume at any time were not significantly different between chili and placebo in both groups ($p > 0.05$).

Conclusions Chili ingestion induces abdominal burning in NERD patients more than HV. GA in patients and HV were not significantly affected by chili. This suggests that NERD patients are hypersensitive to chili and capsaicin sensitive pathways may not involve in GA of the stomach in both NERD and HV.

New Technology

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Image-guided Raman endoscopy for in vivo differentiation between malignant and benign ulcers in the gastric

MS BERGHOLT,¹ W ZHENG,¹ L KAN,¹ KY HO,² M TEH,²
 KG YEOH,³ J SO BOK YAN,⁴ Z HUANG^{1*}

¹Optical Bioimaging Laboratory, Division of Bioengineering, Faculty of Engineering, National University of Singapore, Singapore 117576,

²Department of Medicine, Yoo Loo Lin School of Medicine, National University of Singapore and National University Hospital, Singapore 119260,

³Department of Pathology, Yoo Loo Lin School of Medicine, National University of Singapore and National University Hospital, Singapore 119074,

⁴Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore and National University Hospital, Singapore 119074

Introduction Raman spectroscopy is a vibrational analytic technique sensitive to the changes in biomolecular composition and conformations occurring in tissue. With our most recent development of integrated near-infrared (NIR) Raman spectroscopy with multimodal wide-field imaging modalities, *in vivo* Raman measurements during clinical gastroscopy have been realized.

Material and methods A total of 177 *in vivo* Raman spectra from 16 gastric patients have been measured in which 110 spectra were from benign peptic ulcers and 67 spectra were from malignant peptic ulcers as confirmed by histopathology. Multivariate statistical analysis including partial least squares discriminant analysis (PLS-DA) was employed to generate diagnostic algorithms.

Results We demonstrate for the first time that the Raman endoscopic technique developed can identify malignant ulcers *in vivo* with a sensitivity of 92.7% and specificity of 89.6%. This work illustrates that Raman endoscopy technique has promising potential to become a powerful tool for *in vivo* diagnosis of malignancies in the stomach at the molecular level.

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EUS-guided Ethanol Lavage with Paclitaxel Injection (EUS-EP) for Pancreatic Cystic Tumor (PCT)

DONG WAN SEO

Department of Internal Medicine, University of Ulsan
 College of Medicine, Asan Medical Center

Background EUS-guided intervention has been recently used for the treatment of PCT. The present study analyzed the treatment response of EUS-EP over longer period among a larger study population, and factors which may influence the treatment response.

Methods Fifty-one patients were enrolled for EUS-EP. Under EUS-guidance, cyst fluid aspiration, ethanol lavage and injection of paclitaxel were performed. The safety of EUS-EP was analyzed by monitoring the patients during the first 30 days. The treatment response and its predictors were analyzed. Using CT images, the volume PCT was calculated by computer estimations of the areas on each axial image and slice thickness.

Results Mean diameter and estimated volume were 31.8 mm (17–68 mm) and 14.09 mL (1.16–68.74 mL), respectively. Twenty PCT were oligolocular. Mean CEA level was 463 ng/mL (1–8190). Mean volume of PCT decreased from 14.09 mL to 3.31 mL. CR was observed in 28 patients, PR in 6 patients, and a cyst persisted in 12 patients. CR was achieved by 6 months in 10 patients and after 6 months in 17 patients. Of 12 patients with persistent cyst, 4 patients underwent surgical resection. Histopathologic findings demonstrated focal remnant mucinous epithelium in 2 patients, full epithelial ablation in 1 patient, and neuroendocrine tumor in 1 patient. In univariate analysis, EUS diameter (<35 mm) and original volume (<16 mL) were predictive of cyst resolution. In multivariate analysis, original volume and type of PCT were predictive. Splenic vein thrombosis as procedure-related complication occurred in 1 patient.

Conclusions EUS-EP appears to be a safe method for treating PCT. Complete resolution of PCT was achieved in 60%. Smaller cystic lesion and nonmucinous cyst were predictive of complete resolution.

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Is a pure NOTES feasible and safe? A single center experience in a porcine model

TAE JUN SONG, DONG WAN SEO, HONG JUN KIM, CHOONG HEON RYU, DO HYUN PARK, SANG SOO LEE, SUNG KOO LEE, MYUNG-HWAN KIM

Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea

Introduction Natural orifice transluminal endoscopic surgery (NOTES) may represent a paradigm shift in the area of therapeutic endoscopy and minimally invasive surgery. We conducted this study to find out technical feasibility and safety of pure NOTES with transgastric approach in a porcine model.

Method From August 2009 to February 2010, we performed peritoneoscopy, liver biopsy, salphingo-oophorectomy and fallopian tubal ligation in 10 healthy female minipigs weighing about 40 Kg. All procedures were performed with transgastric approach by using a 2-channel therapeutic endoscope.

Results Technical success rate was 100% in peritoneoscopy (8/8), liver biopsy (5/5), salphingo-oophorectomy (10/10), and fallopian tubal ligation (10/10). Nine cases of complication including one case of spleen injury during entry into peritoneal cavity, three cases of peritonitis, one case of liver biopsy site bleeding, two cases of small bowel adhesion, and two cases of bleeding after salphingo-oophorectomy occurred. Gastric puncture site was repaired with multiple hemoclips in three cases and detachable snare in five cases. Gastric closure was technically successful in 80% (8/10). Among them, complete closure could be achieved in 75% (6/8).

Conclusion Pure NOTES procedure for peritoneoscopy, liver biopsy, salphingo-oophorectomy, and fallopian tubal ligation may be technically feasible, but considerable complications can occur. Further studies with dedicated methods and accessories to decrease the possible complications are thus necessary.

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Characterization of a reproducible gastric pain model using oral capsaicin titration: a placebo-controlled, double-blind study

C YANG,¹ L XINHUA,¹ RWONG,¹ H KHEK YU,¹ CH WILDER-SMITH¹²

¹Dept. Medicine, National University, Singapore, Singapore, ²Brain-Gut Research Group, Berne, Switzerland

Introduction A fixed dose of capsaicin has recently been studied to distinguish FD from controls, but shows highly variable sensory responses and most subjects not reporting pain. We aimed to develop a reproducible gastric pain model to achieve at least moderate pain.

Methods 43 controls swallowed one capsule containing capsaicin 0.5 mg or placebo double-blindly every 15 minutes until the pain reached an intensity > VAS 30 (0 = none, 100 = max) for at least 5 minutes. Abdominal pain was rated on the 100 mm VAS scale every minute. A maximum of 8 capsules was allowed. The capsaicin test was performed three times with an interval of at least 2 days.

Results The mean gastric pain during 5 minutes after onset of moderate pain was 41.6 (95%CI: 37.4–45.9). The mean dosage to induce stable moderate pain was 2 capsules (1.8–2.3). The mean duration of moderate pain was 8.6 minutes (7.2–10.0). There were no significant differences between the repeated measurements in time to onset of moderate pain ($p = 0.52$) and the titrated capsaicin dosage ($p = 0.49$). Only one male reported moderate pain after ingestion of placebo.

Conclusions Standardised gastric pain can be conveniently achieved in a majority of healthy subjects using oral capsaicin capsule titration. The between-test reproducibility is high and placebo responses negligible. The technique is currently under investigation for sensory testing in patients with FD.

Oesophagus

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The roles of gas refluxes and saliva swallows on the development of acid and non-acid refluxes in non-erosive gastroesophageal reflux disease (NERD) evaluated by 24 h esophageal impedance pH monitoring

T PATCHARATRAKUL, C KRIENGKIRAU, S GONLACHANVIT

GI Motility Research Unit, Chulalongkorn University, Bangkok, Thailand

To investigate the role of saliva swallows and gas refluxes on the development of acid (AR) or non-acid refluxes (nARs), 39 NERD patients (29F, age 46 ± 13 years) underwent 24 h pH-impedance monitoring following esophageal manometry during off therapy. Complete liquid and mixed liquid/gas swallows defined as the impedance changes that move downward and reach the most distal impedance sensor. Each AR or nAR event was analyzed visually for temporal relationship with swallows or meal ingestions, liquid/gas composition of the refluxates, and bolus contact time. Reflux events during meal ingestions were excluded. ARs and nARs were defined as typical impedance changes associated with pH fell below 4 and remaining > 4, respectively.

Results Eleven patients (28.2%) had % time pH < 4 at lower esophagus > 4.5%. 628 ARs and 238 nARs were developed during the impedance testings. 80% of reflux events occurred during 0–3 h after meal ingestion. The proportion of nAR/total reflux number was similar between reflux

events occurring during fasting and the first 3 h-postprandial periods (0.33 vs 0.26, $p > 0.05$). Mixed liquid-gas refluxates developed more often in ARs (62.4%) compared to nARs (43.3%, $p < 0.005$). nAR had shorter reflux bolus contact time compared to AR (13.8 ± 9.6 vs 27.5 ± 21 seconds, $p < 0.005$). 55% of nAR events developed within 30 seconds after swallowing, whereas 40.8% of acid reflux events developed during this period ($p < 0.05$). 33.3% of reflux events that developed within 30 seconds after complete swallows were nARs, which was significantly more often compared to those developed after 30 seconds (11.8%, $p < 0.001$).

Conclusions Non-acid refluxes often develop short after complete swallows in NERD patients. Mixed liquid-gas reflux and prolonged bolus contact time were associated with acid refluxes.

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In patients with GERD, electrical stimulation therapy (est) significantly and consistently increases lower esophageal sphincter (LES) pressure

R BANERJEE, N PRATAP, R KALAPALA, DN REDDY
Department of Gastroenterology, Asian Institute of Gastroenterology, Hyderabad, India

Background EST has shown to raise LES pressures in animals, however data on effect of EST on LES in patients with GERD is lacking.

Aim To study the effect of EST on LES pressures and esophageal function in patients with GERD.

Methods Patients with diagnosis of GERD responsive to PPI, increase esophageal acid on 24 h pH monitoring off GERD medications and esophagitis <LA Grade B were included in the study. Temporary pacemaker lead (Medtronic 6416, 200 cm) was placed endoscopically in the LES by creating a 3 cm submucosal tunnel. The lead was secured to the esophagus using endoclips and exteriorized nasally. EST was delivered 6–12 h post-implant: 1) Short-pulse (SP) 200 usec, 20 Hz, 10mAmp; if no response, increase to 15mAmp and 2) Intermediate-pulse (IP) 3 msec, 20 Hz, 5mAmp for 20 minutes; if no response, increase to 10mAmp. Each session of EST lasted 20 minutes and was followed by a washout period of 20 minutes or time needed for LES pressure to return to baseline, whichever was longer. Manometry was performed using standard protocol pre-, during and post-stimulation. Continuous cardiac monitoring was performed during and after the stimulation.

Results 6 patients underwent successful lead implantation; first patient had premature lead dislodgement. 5 patients underwent successful EST. All patients had a significant increase in the LES pressure with all sessions of EST (Table 1). There was no effect on swallow induced LES relaxation and improvement in esophageal body pressures and post-swallow LES pressure augmentation with EST. There were no EST related adverse symptoms or any cardiac rhythm abnormalities.

Conclusions In patients with GERD, EST results in a significant increase in LES pressure without effecting patients' swallow function. EST delivered via a wired or wireless electrical stimulator may offer a novel therapy to patients with GERD.

Oncology

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Enhanced cytotoxicity and activation of ROS-dependent c-Jun NH2-terminal kinase and caspase-3 by low doses of tetrandrine loaded nanoparticles in lovo cells—a possible trojan strategy against cancer

WH SUN,¹ XL LI,^{1,2*} BR LIU²

¹Department of Geriatrics, the First Affiliated Hospital of Nanjing Medical University, Nanjing, China,

²Department of Oncology, Drum Tower Hospital Affiliated to Medical School of Nanjing University, Nanjing, China

Introduction Tetrandrine (Tet) has been reported as a novel anticancer agent. However, application of Tet is limited for its lower aqueous solubility. Accumulated evidences raise the possibility of developing nanoscale delivery systems of Trojan strategy with improved solubility, stability and cytotoxicity of lipophilic Tet.

Methods Tet-loaded nanoparticles (Tet-np) were prepared by a nanoprecipitation method basing on amphiphilic block copolymer (mPEG-PCL) and furthered evaluated for its in vitro anticancer effects and possible mechanisms.

Results We reported a simple way to efficiently produce controlled releasing Tet-np by amphiphilic mPEG-PCL block copolymers. The availability of Trojan strategy for Tet delivery was proved in Lovo cells. Compared to free Tet, Higher cellular uptake efficiency of the equivalent doses of Tet-np mediated by endocytosis, which leading to more intracellular Tet accumulation, inducing higher ROS level, and stimulating stronger activation of ROS-dependent JNK and caspase-3, can underlie the result that Tet-loaded nanoparticles at lower doses led to higher cell death than equivalent doses of free Tet in Lovo cells.

Conclusion The results suggest that Tet-loaded nanoparticles exert the anticancer effects through enhanced ROS-dependent JNK and caspase-3 activation, which could be a potential useful chemotherapeutic formulation for cancer therapy.

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Low-dose aspirin cannot prevent colorectal cancer: a meta-analysis of randomized controlled trials

KK TSOI, SC NG, HW HIRAI, FK CHAN, JJ SUNG

Institute of Digestive Disease, The Chinese University of Hong Kong

Introduction Aspirin reduces the risk of various cancers, but its use as a prevention for colorectal cancer (CRC) remains controversial.

Materials and methods Randomized controlled trials of aspirin for the prevention of colorectal neoplasia from 1950 to 2010 were identified. Meta-analyses were performed to combine the overall effect.

Results Five randomized-controlled trials that recruited a total of 70,656 subjects and 832 cases of CRC were included. The mean treatment duration was 7.83 years (range, 2.73–10.1 years), and the use of daily aspirin ranged from 50 mg to 1200 mg. Overall, the use of aspirin was not associated with a reduced risk of CRC (RR 0.94; 95% CI 0.82–1.07). In subgroup analyses, aspirin failed to reduce the risk of CRC in subjects taking aspirin less than 100 mg daily, or in subjects with treatment duration less than 5 years. Aspirin reduced CRC risk significantly only in subjects with high dose-years (>1000 mg-years) of aspirin (RR 0.74; 95% CI, 0.57–0.97) and in subjects taking at least 150 mg daily for a mean duration of five years over a latency of ten years (RR 0.71; 95% CI, 0.54–0.93).

Conclusion This meta-analysis shows that low dose or short-term treatment with aspirin does not reduce the incidence of CRC. The protective effect against CRC requires daily dosage of aspirin no less than 150 mg for at least five years of regular medication with a latency of about 10 years.

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The relationship between evolutions of detection rate of adenocarcinoma of esophagogastric junction (AEG) and reflux esophagitis (RE) in recent 10 years

KUN WANG

Department of Gastroenterology, Peking University Third Hospital

Backgrounds and aims There has been a rise in the incidence and prevalence of AEG and RE during recent decades. The aims of the current study were to determine the evolution of detection rates and demographic characteristics of AEG, esophageal carcinoma (EC) and gastric carcinoma (GC) in a tertiary medical center and to analyze the relationship between the AEG subtypes and RE, Hp infection.

Methods All the cases underwent gastroscopy in the past 10 years were reviewed. AEG, GC, EC, RE and Hp infection were diagnosed according to the results of gastroscopy and/or biopsy.

Results 70073 patients underwent gastroscopy in the past 10 years. Hp was tested by Warrson-Starry silver stain in all of those patients. There were 279 AEG patients (3.98%, M:F = 5.6:1), 794 GC patients (11.33%, M:F = 2:1), 366 EC patients (5.22%, M:F = 3.4:1) and 4681 RE patients (6.68%). The average age was higher in AEG patients (66.42 ± 10.03) than that of GC (60.05 ± 13.82) or EC (64.65 ± 11.07) patients and the proportion of male was superior to female in all these three cancer patients, especially in AEG (male:female = 5.6:1, $p < 0.001$). In the past ten years, the annual detectable rate of subtype I and II AEG ascended obviously and gastric cancer descended. The annual detectable rate of subtype I AEG and RE presented positive correlation ($r = 0.846$ and $p = 0.002$). But the rate of subtype I AEG and Hp infection appeared to be negative correlation ($r = -0.785$, $p = 0.007$). Also, the rate of RE and Hp infection was negative correlation ($r = -0.907$, $p = 0.000$). There was no relationship of the detectable rate between RE, Hp and subtype II and III AEG.

Conclusions In the past ten years, the annual detection rate of AEG and RE presented upward trending, and subtype I AEG appeared to be positive correlation with RE. The annual detection rate of GC and Hp infection appeared to descend, and subtype I AEG rate correlated to Hp infection negatively. RE may be one of important causal factors of subtype I AEG.

Pancreas

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Extracorporeal shock wave Lithotripsy and Endotherapy for Pancreatic Calculi—a large single center experience

M TANDAN, DN REDDY

Asian Institute of Gastroenterology, Hyderabad, India

Aim Large Pancreatic Ductal Calculi are a feature of Chronic Calcific Pancreatitis (CCP), especially Idiopathic and tropical pancreatitis and these patients often present with severe pain. This large single center study evaluates the role of Extracorporeal Shock Wave Lithotripsy (ESWL) in fragmentation of large pancreatic stones and subsequent relief in patients with CCP.

Methods All patients of CCP with pain as their presenting symptom and large pancreatic duct (PD) calculi (>5 mm diameter) not amenable to extraction at routine Endoscopic Retrograde Cholangio Pancreatography (ERCP) were taken up for ESWL using a 3rd generation lithotripter. Stones in the head & body were targeted at ESWL. 5000 shocks were given per session till calculi were fragmented to less than 3 mm size and were cleared subsequently at ERCP. Stents were placed where deemed necessary.

Results A total of 1006 patients fulfilling the above criteria underwent ESWL. Complete clearance was achieved in 76%, partial clearance in 17% while in the rest the procedure was unsuccessful. More than 90% of patients needed three or less sessions of ESWL. Follow-up at 6 months revealed significant relief of pain in 84% with decrease in analgesic use. Complications were minimal and mild.

Conclusion ESWL is an effective and safe modality for fragmentation of large PD calculi in patients with CCP and their subsequent clearance at ERCP provides significant pain relief.

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Clinical trial: comparative study of celiac plexus block, segmental epidural block and narcotic analgesics for control of severe pain in acute pancreatitis

D SANTOSH, R MOHAN, DN REDDY

Asian Institute of gastroenterology, Hyderabad, India

Introduction Effective management of severe pain in acute pancreatitis is an important issue in therapy. Not all patients get relief from opioid therapy. The other effective method of pain relief is segmental epidural block or celiac ganglion block. Aim of the study was to compare the effect of celiac plexus block, segmental epidural block and narcotic analgesics for control of pain in patients with acute pancreatitis using a visual analogue scale (VAS).

Materials and methods 179 patients admitted to the intensive care unit with acute pancreatitis having severe pain were randomized into three groups. One set of patients received celiac plexus block (Group A), the second set got segmental epidural block (Group B), and the third set received narcotic analgesics (Group C). Celiac plexus block was performed in the right lateral position. D6-D12 segments were blocked through an epidural catheter. Fentanyl was the narcotic administered.

Results Pre and post procedure pain scores were obtained. Subjects having pain relief were Fifty five (90%) undergoing celiac block, forty two (70%) in epidural group and thirty six (60%) in the narcotics group. The subjects with low VAS scores was seen in a group of the patients with alcohol ingestion as the etiology of pancreatitis.

Conclusion Celiac plexus block offers a more effective alternative for treatment of pain in acute pancreatitis than segmental epidural block or narcotics.

Psychosomatic GI Disease

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Treatment of functional dyspepsia with selective-serotonin receptor inhibitor in Chinese patients: a randomized placebo controlled study

VICTORIA PING YI TAN

Department of Medicine, Queen Mary Hospital, Hong Kong University

Objective To evaluate selective serotonin reuptake inhibitors in the treatment of patients with functional dyspepsia.

Methods Patients with a clinical diagnosis of functional dyspepsia according to the Rome II criteria with a Hong Kong Dyspepsia Index of greater than 16 were recruited and randomized to receive sertraline 50 mg or placebo daily for 8 weeks.

Main outcome measures Dyspepsia symptom scores, quality of life (SF-36) and Hospital Anxiety and Depression (HAD) scale and symptom relief were evaluated before, during and after treatment.

Results A total of 193 patients were randomized. At 8 weeks patients in the sertraline group demonstrated a statistically significant reduction in their Hong Kong Dyspepsia Index (from 25.83 to 20.53, $p = 0.02$). However, there was no statistically significant difference in overall quality of life measures or the hospital anxiety and depression scale related to treatment.

Conclusions Functional dyspepsia is a common condition where there is a paucity of effective treatments. This study is the first to suggest that sertraline is superior to placebo in the treatment of functional dyspepsia.

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Aberrant connectivity of brain centers during somatic pain and activation of endogenous pain modulation in IBS compared to healthy controls

C YANG,² S GRAHAM,¹ CH WILDER-SMITH,^{2,3} G SONG,² KY HO²

¹Dept. Psychology, National University, Singapore, Singapore, ²Dept. Medicine, National University, Singapore, Singapore

Introduction IBS patients demonstrate abnormal sensory function and abnormal activation of endogenous pain modulation. The latter may constitute a central underlying mechanism in IBS.

Methods The connectivity of the pain modulatory centers was examined by fMRI using heterotopic hand and foot stimulation for activation of endogenous pain modulation in 14 IBS patients and 14 controls. Voxels activated above threshold ($p < 0.001$ corrected) were selected and Granger Causality Mapping, GCM, was performed.

Results Heterotopic stimulation decreased hand pain by 16% in controls and by 0% in IBS ($p < 0.05$). Comparing IBS and controls, the most prominent cortical activation difference with heterotopic stimulation was in the left cingulate cortex. GCM indicated during pain in controls the brainstem was mainly influenced by the right insula, left thalamus, left anterior cingulate and cerebellum. In IBS, however, bilateral thalami, contralateral brainstem, left anterior cingulate and cerebellum were influenced by the primary brainstem activation area.

Conclusions Central processing of pain and of endogenous pain modulation differs between IBS and controls in the direction of connectivity of the major brainstem area activated. In controls the brainstem appears to be driven by cortical processing areas, whereas in IBS the modulatory brainstem area drives the cortical network. This could be characterized as top-down versus bottom-up drive. Further analysis of the communication direction between the endogenous pain modulatory and pain processing areas is warranted.

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Endogenous pain modulation and brain activity in Irritable Bowel Syndrome (IBS) and in healthy controls: individual correlations during fMRI

C YANG,¹ CH WILDER-SMITH,^{1,2} S GRAHAM,³ KY HO¹

¹Dept. Psychology, National University, Singapore, Singapore, ²Brain-Gut Research Group, Berne, Switzerland, ³Dept. Medicine, National University, Singapore, Singapore

Introduction IBS patients show abnormal sensory function and endogenous pain modulation. As the deficient brain pathways in IBS have not been characterized and the usual group analyses mask individual associations, we correlated individual pain intensities with fMRI brain activations in IBS patients and controls.

Methods In 14 female IBS and 14 female controls electrical hand and foot cold pain were applied alone or together (heterotopic stimulation) during fMRI. Random effects general linear model with conditions of interest were generated via the finite impulse response (FIR) deconvolution method and corrected using cluster threshold estimation.

Results The change in hand pain during heterotopic stimulation correlated with brain activation in the left ACC, right ACC, right anterior insula and the right dorsolateral prefrontal cortex during subliminal stimulation ($p < 0.05$, $r > 0.60$) only in controls. In IBS only, hand pain during endogenous pain modulation correlated with changes in activation in the right ACC (BA32), left ACC (BA24) and PAG during heterotopic stimulation ($p < 0.05$, $r > 0.55$).

Conclusions Individual correlations of pain ratings and brain activations within the homeostatic modulatory network show significant differences between healthy and IBS subjects, both during subliminal stimulation and activation of endogenous pain modulation. There is consistent evidence for a shift in the dynamic balance between inhibition and facilitation.

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The impact of acute stress on the oligomerization of serotonin transporter (SERT) in early life stress model

EFC LAM, WWT LAW, YY LEE, JJY SUNG, JCY WU

Department of Medicine and Therapeutics, the Chinese University of Hong Kong, Hong Kong, China

Introduction Serotonin transporter (SERT) plays the regulatory role of serotonin (5HT) signaling. The irritable bowel syndrome (IBS) patients encounter abnormal serotonin response upon acute stress. The relationship between psychological stress and SERT expression in brain is unclear.

Methods Non-handled (NH) rats and maternal separation stress (MS) rats ($N = 6$) were used in the study. Each rat group was exposed to 1-hour water avoidance stress (WAS). Control groups were caged for 1 hour individually. Post-WAS plasma 5HT profile (0–180 min) was determined. The rats were sacrificed after 3 hours and brain was harvested for mRNA and protein assay of SERT.

Results There is no different in SERT mRNA expression. Glycosylation of SERT (~64 kDa) was found in brain tissue (non-glycosylated SERT: ~58 kDa). Higher degree of SERT protein oligomerization (dimmer and tetrameric) was found in MS rats (Fig 1, lane 3 & 4), but only dimeric SERT was expressed in NH rats. Increased expression of SERT oligomer was observed in rats exposed to acute WAS stress. Significantly higher area under curve (AUC) of plasma 5HT was found in NH HCD rats compared to NH control rats (1611.8 ± 211.9 vs 888.9 ± 150.3 ng.hr/ul, $p = 0.02$) but in MS groups.

Conclusion Psychological stress in early life leads to different conformational change of SERT protein in rat brain, and this may explain the abnormal 5HT response in IBS subjects upon stress.

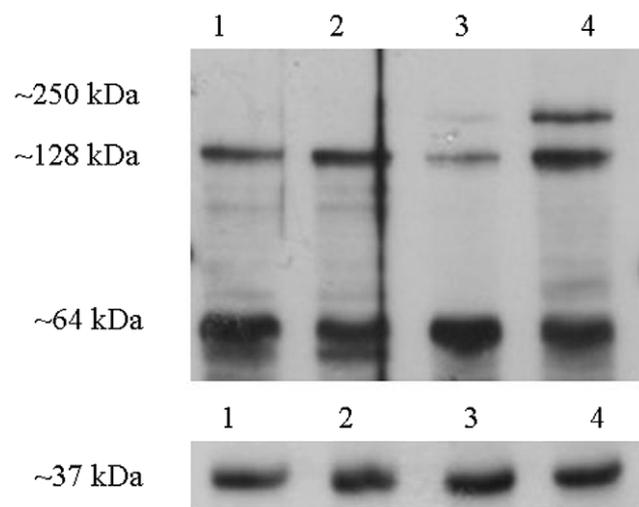


Figure 1: Western blot analysis of serotonin transporter (SERT) (upper blot) and beta actin (lower blot). Lane 1: Non-handled control rats (NH control); lane 2: Non-handled rats with water avoidance stress (NH WAS); lane 3: Maternal separation stress control rats (MS control); and lane 4: Maternal separation stress control rat with water avoidance stress (MS WAS). In upper blot, three major bands with size approximately 64, 128 and ~240kDa were monomeric, dimeric and tetrameric SERT respectively.

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Activation pattern in response to visual stimuli (Horror) in patients with functional bowel disease using functional magnetic resonance imaging

SHALIMAR, B CHOUDHARY, S SENTHIL KUMARAN, P SINGH, GK MAKHARIA, NR JAGANNATHAN
Department of Gastroenterology and Human Nutrition and Department of Nuclear Magnetic Resonance, All India Institute of Medical Sciences, New Delhi, India

Introduction Frequent co-occurrences of other functional disorders with irritable bowel syndrome (IBS) raises a question whether these disorder share a common pathogenesis. We tested the hypothesis that patients with IBS differ from healthy controls in the cerebral processing of non visceral stimuli such as visual cues using fMRI.

Patients and methods Six patients each with IBS-C, IBS-D, and healthy controls were included. We carried out BOLD mapping using fMRI with visual stimulus with horror content along with neutral baseline using binocular vision system (NordicNeuroLab, Norway) at 1.5 T (Avanto, M/s Siemens, Germany). The post-processing was done using SPM2.

Patients and methods 18 patients were recruited in IBS-C, IBS-D, and control group, with each group having 6 subjects. We carried out BOLD mapping using fMRI with visual stimulus with horror content along with neutral baseline using binocular vision system (NordicNeuroLab, Norway)

at 1.5 T (Avanto, M/s Siemens, Germany). The post-processing was done using SPM2.

Results On viewing horror visual stimulus, control subjects showed more activation of insula, cuneus and cerebellum, declive in left hemisphere and cuneus, thalamus, uncus and cerebellum posterior lobe on right side. On the same stimulus, patients with IBS-D showed significantly higher brain activation in left hemispheric precuneus, cuneus, superior occipital gyrus, right parahippocampal gyrus, and bilateral frontal and superior temporal gyrus than the controls. Higher level of anxiety, depression and neuroticism in IBS patient group could account for some of the observed differences in brain activation responses, especially in parahippocampal gyrus, fusiform gyrus. For horror paradigm the selective group of patient having FBS frequently complaining of gas going to head has significantly higher activation in fusiform cortex.

Conclusion IBS patients exhibit higher anxiety and invoke temporal-occipital pathway for the fear emotion.

Small Intestine

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Patients with irritable bowel syndrome exhales more hydrogen than healthy subject in fasting state

S KUMAR, A MISRA, UC GHOSHAL
Department of Gastroenterology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Road, Lucknow-226014, India

Background Irritable bowel syndrome (IBS) is a common disorder with significant morbidity and impairment of quality of life. 26–83% patients with IBS from Asia reported bloating. Bloating may result from increased amount or distribution of gas in the gut or exaggerated perception of distension. To evaluate whether patients with IBS produce more hydrogen even in fasting state, we conducted a study with the following aims, (a) to estimate fasting breath hydrogen (FBH) levels among patients with IBS as compared with healthy controls (HC), (b) to study relationship between symptoms of IBS and stool frequency and FBH levels.

Methods 81 patients with IBS (Rome III criteria) and 123 HC were included. Hydrogen breath test was performed using a gas analyzer after an overnight (12-h) fast. Both patients with IBS and HC controls had similar preparation before breath hydrogen estimation.

Results Of 93 patients with symptoms of functional gastrointestinal disorders, 81 (87.1%) met Rome III criteria and 12 (12.9%) were negative and hence, excluded from the study. Patients with IBS were comparable in age (35 ± 11.8 year vs. 37.5 ± 13.1 year, $p = \text{ns}$) and gender [male 61/81 (75.3%) vs. 77/123 (62.6%), $p = 0.67$] with HC. Average FBH was higher in patients with IBS as compared to HC (mean 10.1 ± 6.5 ppm vs. 5.5 ± 6.2 ppm, $p < 0.0001$). Number of stools per week correlated with average FBH excretion in patients with IBS ($r = 0.26$, $p = 0.02$).

Conclusion In spite of similar preparation for the test, FBH was higher in patients with IBS as compared to HC. Number of stools per week correlated with FBH levels among patients with IBS.

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The prevalence of small intestinal bacterial overgrowth in primary biliary cirrhosis

S SIDANI, C VINCENT, M BOUIN

Hopital Saint-Luc, Centre Hospitalier de l'Universite de Montreal, Quebec, Canada

Introduction An alteration of intestinal motility has been documented in liver cirrhosis, predisposing to small intestinal bacterial overgrowth (SIBO), but there are scarce data concerning the occurrence of SIBO in Primary Biliary Cirrhosis (PBC).

Aims 1) To determine the occurrence of SIBO in patients with PBC. 2) To identify characteristics of patients with SIBO.

Methods Prospective study from 2006 to 2008. All participants diagnosed with PBC had a lactulose hydrogen breath test to diagnose SIBO. The following parameters were studied: demographic data, digestive symptoms and signs, Child-Pugh and Mayo scores.

Results 52 patients were recruited (50 females, age 57 ± 11 years). The breath test was normal in 63% (n = 33) patients and suggestive of SIBO in 36% (n = 19). The 2 groups of patients were similar in terms of age, body mass index, presence of abdominal pain, bloating, transaminases, bilirubin and alkaline phosphatase levels, and Child-Pugh and Mayo severity scores. Diarrhea was less common in the group with SIBO (25 % vs. 64 %, p < 0.05).

Conclusion 36% of patients with PBC had a lactulose hydrogen breath test result in favor of SIBO. Besides fewer occurrence of diarrhea in patients with SIBO, no demographic or clinical factor was associated with SIBO. The high occurrence of SIBO in PBC suggests that intestinal transit alterations thus exist in PBC and need to be characterized further.

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Spectrum of malabsorption syndrome in northern Indian adults and factors differentiating celiac disease and idiopathic malabsorption in the tropics (tropical sprue)

UC GHOSHAL,¹ M MEHROTRA,¹ S KUMAR,¹ N KRISHNANI,² R AGGARWAL,¹ G CHOUDHURI¹

Departments of ¹Gastroenterology and ²Pathology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Road, Lucknow-226104, India

Background Etiology of malabsorption syndrome (MAS) differs in tropical and temperate countries over time; information on its causes in Indian adults currently is scanty.

Method Causes of MAS and factors differentiating tropical sprue (TS) from celiac disease (CD) were determined in 276 consecutive patients attending Luminal Gastroenterology Clinic at a tertiary center (2000 to 2010).

Results Using standard criteria, the causes of MAS in 276 patients (age 37.5 ± 13.2 years, 170, 61.5% male) were, TS 101 (37%), CD 53 (19%), small intestinal bacterial overgrowth 28 (10%), AIDS 14 (5%), giardiasis 13 (5%), hypogammaglobulinemia 12 (4%), intestinal tuberculosis 7 (2.5%), strongyloidiasis 7 (2.5%), immunoproliferative small intestinal disease 5 (2%), Crohn disease 6 (2%), amyloidosis 6 (2%), intestinal lymphangiectasia 3 (1%) and unknown 21 (8%). On univariate analysis, patients with CD were younger than TS (30.6 ± 12 years vs. 39.3 ± 12.6 years, p < 0.001), (age < 35 years: 37/53, 70% vs. 40/101, 40%, p = 0.0003), more often Punjabi (8/53, 15.1% vs. 3/101, 3%, p = 0.009), had lower body weight (41.3 ± 11.8 kg vs. 49.9 ± 11.2 kg, p < 0.001), longer diarrhea duration (median 36 month, inter-quartile range [IQR] 17.8–120 vs. 24 month, 8–48, p = 0.01), less frequent stool (6/day, IQR 5–8 vs. 8,

5–10, p = 0.03), lower hemoglobin (9.4 ± 3.2 g/dL vs. 10.4 ± 2.7 g/dL, p = 0.04), hepatomegaly (9/53, 17% vs. 4/101, 4%, p = 0.01), subtotal or partial villous atrophy or blunted villi (36/50, 72% vs. 28/87, 32%, p < 0.001). Younger age (<35 years), longer diarrhea duration, Punjabi race and villous atrophy were significant on multivariate analysis.

Conclusions TS and CD are common causes of MAS among Indian adults. Punjabi race, younger age (<35 years), longer diarrhea duration and villous atrophy were associated with CD.

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Narrow Band Imaging in the evaluation of villous morphology: a feasibility study assessing a simplified classification and observer agreement

R SINGH,^{1,2} G NIND,^{1,3} N NGUYEN,^{2,3} R HOLLOWAY,^{2,3} J BATES,³ W TAM^{1,2,3}

¹The Lyell McEwin Hospital, Adelaide, SA, Australia,

²University of Adelaide, SA, Australia, ³The Royal Adelaide Hospital, Adelaide, SA, Australia

Introduction To determine the utility of Narrow Band Imaging with optical magnification (NBI-Z) in the evaluation of villous morphology.

Methods Patients considered at risk of having Coeliac Disease (CD) were invited. After standard endoscopy, they underwent further evaluation with NBI-Z which was digitally recorded. Targeted biopsies of each videoed area with NBI-Z were performed and tissue sent for histopathological analysis. 2 expert endoscopists then selected the best representative videos (developmental phase). 41 representative images of these videos were classified as follows: villous patterns as present (N) or absent (A). Absent villi then classified as cerebiform (C) or flat (F) corresponding to partial or total villous atrophy respectively. 3 NBI-Z naive endoscopists then graded the videos. They first underwent an interactive training session (learning phase) with video and images from a digital library before embarking on the actual assessment. To test for reproducibility, all videos were randomly reordered and graded again after a week.

Results 41 videos (10 CD, 31 normal) from 21 patients (3 CD, 18 normal) were analysed. The overall Sensitivity (Sn) and Specificity (Sp) in correctly differentiating the presence or absence of villi was 93.3%, and 97.8% respectively with inter and intra observer agreement (kappa, k) at 0.82 and 0.86. The Sn and Sp in differentiating partial from total villous atrophy was 83.3% and 100%; k at 0.73 and 0.68 respectively.

Conclusions Using a simplified classification, we demonstrated that NBI-Z is feasible in revealing villous atrophy in patients presenting with suspicion of CD.

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Does capsule endoscopy (CE) predicts rebleeding rate and mortality in obscure gastrointestinal bleeding (OGIB)? Results from a long-term follow-up

LH LAI, JJY SUNG, FKL CHAN

Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong S.A.R., China

Introduction We investigated the performance of CE in predicting long-term outcome of OGIB patients.

Methods Consecutive OGIB patients referred for CE were enrolled. CE findings (“P0”—no abnormality, “P1”—probable relevant lesion, “P2”—highly relevant lesion), rebleeding (“overt rebleeding”, “overall rebleed-

ing*—overt rebleeding or drop in Haemoglobin > 2 g/dL from baseline), mortality and potential predictive factors were determined.

Results 103 patients (49.5% male, mean age 61.8 years) were followed up for a median of 50 months. 35 patients had negative CE (P0 only). Overall rebleeding rate (69.1% versus 28.6%) and mortality (30.9% versus 5.7%) were found to be higher in positive CE (either P1 or P2 lesions) than negative CE patients ($p < 0.05$, log-rank test). Cox regression analysis showed that positive CE (HR 3.1, 95%CI 1.6–6.3), lowest haemoglobin < 8 g/dL on presentation (HR 2.0, 95%CI 1.1–3.7) and age ≥ 65 years (HR 2.1, 95%CI 1.2–3.7) were independent risk factors for overall rebleeding, while positive CE (HR 4.5, 95%CI 1.0–19.2) and age ≥ 65 years (HR 6.0, 95%CI 1.7–20.4) were independent risk factors for death. OGIB patients with lowest risk (age < 65 years, lowest haemoglobin ≥ 8 g/dL and negative CE) had no recurrent bleeding nor mortality, while 64.8% and 27.3% of patients rebled or died in the remaining cohort (both $p < 0.05$ by log-rank test).

Conclusion Apart from CE finding, age and lowest haemoglobin are useful risk prognosticators for OGIB patients. Expectant approach could be safe in patients with age below 65 years, haemoglobin above 8 g/dL and negative CE.

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Effect of addition of short course steroid to gluten free diet on mucosal epithelial cell regeneration and apoptosis in celiac disease: a pilot randomized controlled trial

SHALIMAR,¹ PRASENJIT DAS,² SIDDHARTHA DATTA GUPTA,² GK MAKHARIA¹

Departments of ¹Gastroenterology and Human Nutrition and ²Pathology, All India institute of Medical Sciences, New Delhi, India

Introduction Addition of glucocorticoids to GFD in in-vitro studies have shown to reduce the harmful effects of gluten on the duodenal mucosa in celiac disease (CD). To see the exact effect of steroids over GFD on epithelial cell regeneration and apoptosis in CD was our interest.

Patients and methods Twenty-five treatment naïve patients of CD were randomized to either GFD alone (n = 14) or steroids and GFD (n = 11). Prednisolone (1 mg/kg) was given for a period of 4 weeks followed by rapid tapering. Both groups underwent duodenal biopsies at baseline, 1 and 2 months after initiation of therapy. To determine the cell proliferation index, the sections were labelled with Ki-67 antibody. Immunohistochemical stains (IHC) for different apoptotic markers as AIF (Apoptosis-inducing factor), XIAP (X-linked inhibitor of apoptosis), cleaved caspase-3, H2AX, p53, bcl2, ki67 and M30 CytoDeath were performed and compared between two treatment groups.

Results In the group treated with GFD+ steroid, p53, AIF and M30 expression were reduced or showed such a trend both in villi and crypts. Expression of H2AX and CC3 showed a trend of reduced expression in villi. XIAP expression was not different between the two groups. Bcl2 expression showed a trend of higher expression in patients treated with GFD alone. The area of distribution and stain intensity of Ki67 staining in the villous nuclei were significantly higher or showed a trend of higher expression in patients treated with GFD alone. In the crypts there were no difference of Ki67 index between the two groups.

Conclusion A short course of steroid with GFD decreases apoptotic activity in CD. Addition of steroid to GFD slows down the villous regeneration in comparison to those treated with GFD alone.

Stomach

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A practical model to stratify dyspeptic patients based on the risk of gastric cancer

TD QUACH,¹ MH LE,² TO NGUYEN,¹ ST NGUYEN,² N UEMURA³

Departments of ¹Endoscopy and ²Pathology, University Medical Center at HCMC, Vietnam, ³Department of Gastroenterology, International Medical Center of Japan, Japan

Background The severity of endoscopic gastric atrophy (EGA), high-stage OLGA gastritis (i.e. stage III–IV), and extensive intestinal metaplasia (IM) with incomplete subtype have been separately reported as high risk factors of gastric cancer (GC).

Aims To evaluate the associations among these characteristics and to develop a stratification model for GC risk.

Methods A cross-sectional study was conducted on 280 patients with non-ulcer dyspepsia. Biopsies were taken according to the updated Sydney system. EGA was assessed according to the Kimura-Takemoto classification and gastritis stage was assessed according to the OLGA system.

Results Moderate-to-severe EGA was significantly associated with high-stage OLGA gastritis, extensive IM, and incomplete IM subtype ($p < 0.001$). Extensive IM was also associated with incomplete IM subtype ($p = 0.01$). Consequently, a classification could be established as illustrated in table 1.

Conclusion This model could stratify patients with non-ulcer dyspepsia into 4 groups with different risk levels of developing GC and potentially help to individualize the follow-up strategies.

Table 1 Stratification model for gastric cancer risk based on EGA, OLGA stage and IM characteristics.

| GROUP | I (n = 13) | II (n = 23) | III (n = 90) | IV (n = 154) |
|------------------------|-----------------|----------------|-----------------|-----------------|
| EGA | Moderate–severe | Mild | | |
| OLGA stage | III–IV | I–II | 0–II | |
| IM characteristics | | | | |
| Rate | 92,3% | 100% | 38,9% | 7,1% |
| Extensive ^a | 84,6% | 100% | 0% | 1,3% |
| Incomplete subtype | 69,2% | 34,8% | 7,4% | 0,6% |

^aExtensive IM is defined as the presence of IM at ≥ 2 biopsy locations. Group II and III are differentiated based on this feature.

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Standard- versus high-dose proton pump inhibitor in peptic ulcer bleeding after combined endoscopic hemoostasis

C-C CHEN,¹ H-P WANG,^{1,2} J-M LIU,² C-Y LEE,¹ Y-J FANG,¹ M-L HAN,¹ S-J HSU,¹ T-L LIN,¹ J-T LIN, M-S WU²

¹Department of Internal Medicine, National Taiwan University Hospital, Yun-Lin Branch, Douliou, Taiwan,

²Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

Introduction The optimal dose of intravenous proton pump inhibitors (PPIs) for preventing ulcer rebleeding remains unclear.

Materials and methods 194 patients with bleeding ulcers were treated with combined endoscopic hemostasis, and randomized to receive intravenous PPIs according to a high-dose regimen (pantoprazole 8 mg/h continuous infusion for 72 h) or a standard-dose regimen (pantoprazole 40 mg bolus daily for 72 h). The primary end point was recurrent bleeding within 30 days after endoscopy.

Results The 30-day cumulative rebleeding rate was similar between the 2 groups (8.2% vs 9.3%, $P > 0.05$). There was no difference in hospital stay, need for surgery or interventional radiology and mortality rate between two groups. The results are illustrated in Table 1.

Conclusions Standard-dose pantoprazole infusion was as effective as a high-dose regimen in reducing the risk of recurrent bleeding after combined endoscopic hemostasis

Table 1 Results of pantoprazole therapy after endoscopic hemostasis

| | High-dose | Standard-dose | P Value |
|----------------------------------|-----------|---------------|---------|
| Rebleeding (%) | | | |
| Within 72 h | 5.2 | 8.2 | 0.39 |
| Within 7 day | 7 | 8.2 | 0.79 |
| Within 30 day | 8 | 9.3 | 0.80 |
| Hospital stay, days | 7.9 ± 7.8 | 5.8 ± 3.4 | 0.16 |
| Surgery or TAE within 30 day (%) | 1.1 | 0 | 0.32 |
| Death within 30 day (%) | 3.2 | 1.1 | 0.33 |