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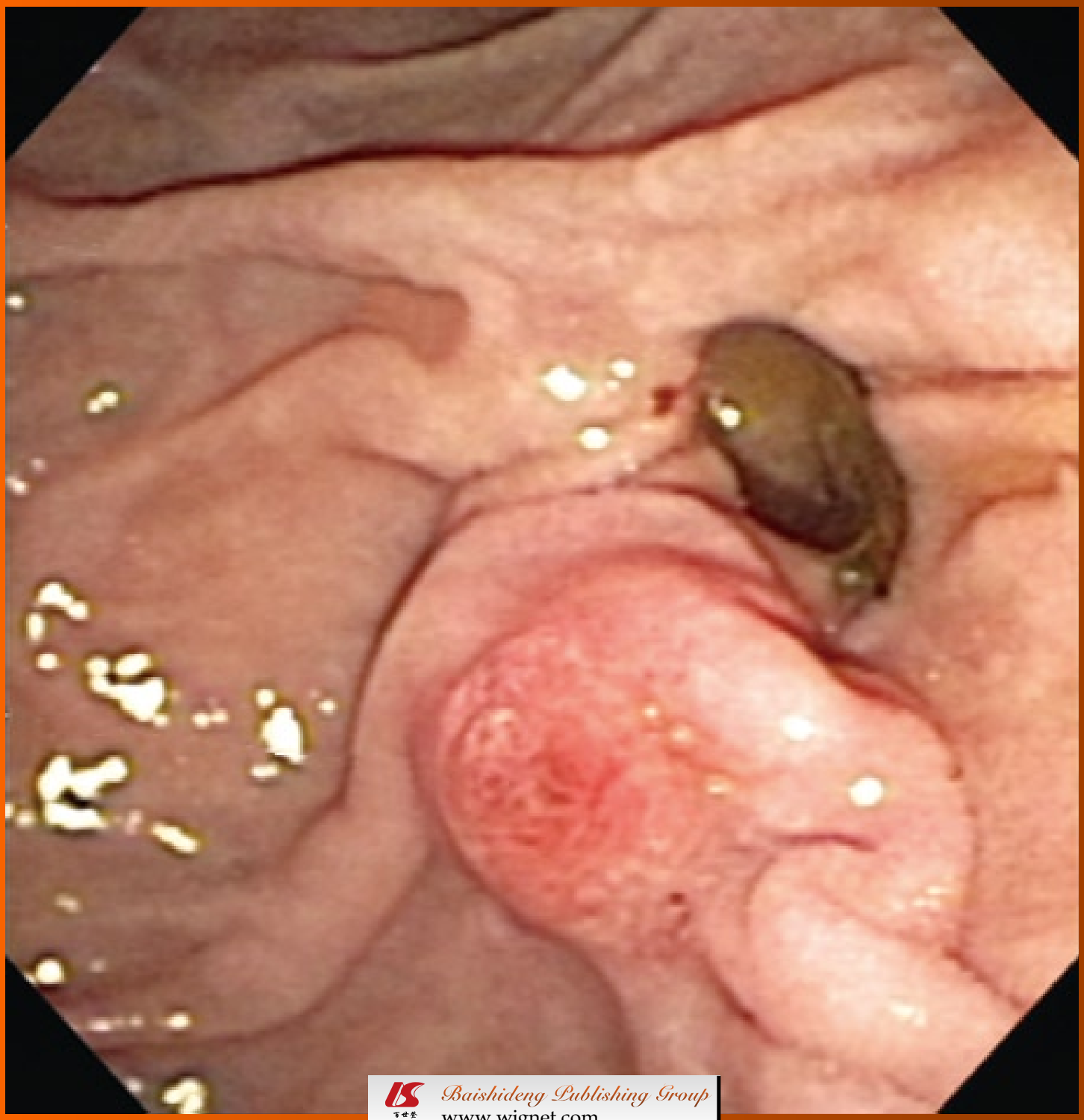

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No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: +86-10-8538-1892
Fax: +86-10-8538-1893
E-mail: baishideng@wjgnet.com
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EDITING
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Room 903, Building D, Ocean International Center,
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Fax: +86-10-8538-1893
E-mail: wjge@wjgnet.com
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EDITORIAL OFFICE
Hai-Ning Zhang, Director
World Journal of Gastrointestinal Endoscopy
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: +86-10-5908-0038
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EDITORIAL

Intravenous proton pump inhibitors for peptic ulcer bleeding: Clinical benefits and limits

Hsiu-Chi Cheng, Bor-Shyang Sheu

Hsiu-Chi Cheng, Bor-Shyang Sheu, Institute of Clinical Medicine, Medical College, National Cheng Kung University, Tainan 70428, Taiwan, China
Hsiu-Chi Cheng, Bor-Shyang Sheu, Department of Internal Medicine, National Cheng Kung University, Tainan 70428, Taiwan, China
Author contributions: Cheng HC composed the review with thoughtful discussion and refinement of the manuscript by Sheu BS .
Correspondence to: Bor-Shyang Sheu, MD, Professor of Internal Medicine, National Cheng Kung University Hospital, 138 Sheng Li Road, Tainan 70428, Taiwan, China. sheubs@mail.ncku.edu.tw
Telephone: +886-6-2353535 Fax: +886-6-2370941
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Abstract

Peptic ulcer bleeding is a common disease and recurrent bleeding is an independent risk factor of mortality. Infusion with proton pump inhibitors (PPIs) prevents recurrent bleeding after successful endoscopic therapy. A gastric acidic environment of less than pH 5.4 alters coagulation function and activates pepsin to disaggregate platelet plugs. Gastric acid is secreted by H^+, K^+-ATPase, naming the proton pump. This update review focuses on the mechanism and the role of PPIs in the clinical management of patients with peptic ulcer bleeding. An intravenous omeprazole bolus followed by high-dose continuous infusion for 72 h after successful endoscopic therapy can prevent the recurrent bleeding. In the Asian, however, the infusion dosage can possibly be diminished whilst preserving favorable control of the intragastric pH and thereby still decreasing rates of recurrent bleeding. Irrespective of the infusion dosage of PPIs, rates of recurrent bleeding remain high in patients with co-morbidities. Because recurrent peptic ulcer bleeding may be prolonged in those with co-morbidities, a low-dose infusion of IV PPIs for up to 7-day may result in better control of recurrent bleeding of peptic ulcers. Due to the inter-patient variability in CYP2C19 genotypes, the infusion form of new generation PPIs, such as esomeprazole, should be promising for the prevention of recurrent bleeding. This article offers a comprehensive review of clinical practice, highlighting the indication, the optimal dosage, the duration, and the potential limitation of PPIs infusion for peptic ulcer bleeding.

Key words: Peptic ulcer bleeding; Recurrent bleeding; Comorbidity; Cytochrome P-450 2C19; Proton pump inhibitor; Omeprazole

Peer reviewers: Michal Procke, MD, Department of Internal Medicine - Gastroenterology and Endoscopy, Charles University, second Medical School, Motol University Hospital, Prague, Czech Republic; Lucian Negreanu, MD, PhD, Assistant Professor, Gastroenterology Department, Emergency University Hospital, Carol Davila University Bucharest, 169 splaiul Independentei Street, Sector 5, Bucharest, Romania

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INTRODUCTION

Upper gastrointestinal bleeding is a rather common disease with prevalence rates of up to 102 per 100 000 people[1,2]. About 48% of upper gastrointestinal bleeding is related to peptic ulcer diseases[3]. Peptic ulcer bleeding is a potentially lethal disease, and recurrent bleeding is a considered and independent risk factor potentially leading to mortality[4,5]. Recurrent bleeding is positively linked with the presence of stigmata of recent hemorrhage, co-morbidities, and others[1,5-10]. In general, patients with underlying medical

co-morbidities have increased rates of recurrent bleeding and longer duration of risk for recurrent bleeding than those without co-morbidity[6,10].

Because the acid environment of stomach is rather hostile for ulcer healing, the clinical course of peptic ulcer bleeding is more complicated than skin wound bleeding. The recurrent bleeding rate of peptic ulcers varies widely, from as low as only 5% up to almost 100%[11]. Inhibition of gastric acid secretion by intravenous infusion of proton pump inhibitors (PPIs) has now been shown to prevent the recurrent bleeding after successful endoscopic therapy[12-15]. However, the mortality rate of peptic ulcer bleeding has still not decreased even after PPIs usage. Yavorski *et al* found that almost all patients who died from peptic ulcer bleeding have at least one underlying comorbid illness, and the major cause of mortality is thus the underlying comorbid illness which is exacerbated by peptic ulcer bleeding or recurrent bleeding[1]. Accordingly, it is very important to identify high risk patients with comorbidity. For such patients, the more aggressive application of intravenous (IV) PPI could be warranted to control the bleeding and also to prevent recurrent bleeding.

This article offers a comprehensive review of clinical practice highlighting the indication, the optimal dosage, the duration, and the potential limitation of PPIs infusion for peptic ulcer bleeding.

MECHANISM OF PROTON PUMP INHIBITORS

The risk of recurrent bleeding is higher and there is a more complicated healing process in peptic ulcer disease than in cutaneous wounds[11]. The major reason for this is the acid microenvironment of the stomach lumen. Intragastric hydrochloric acid (HCl) which provides the acid microenvironment is secreted by H^+, K^+-ATPase, which is a membrane-bound proton pump in parietal cells. The proton pump is an α, β heterodimer[16]. After parietal cells are activated on receptors, proton pumps translocate from tubulovesicles to the membranes of secretory canaliculi[16-18].

The gastric H^+, K^+-ATPase is an important target for development of drugs to inhibit gastric acid secretion[19,20]. Substitutes benzimidazoles are the first group of anti-secretory drugs, acting *via* inhibition of H^+, K^+-ATPase[21,22]. Omeprazole was the first benzimidazole to be launched for clinical use in the late 1980s[23-25]. Other analogues such as lansoprazole, rabeprazole, pantoprazole and esomeprazole have since been developed. These drugs are generically called PPIs.

PPIs are lipophilic and are inactive in the neutral environment of the bloodstream. After absorption, PPIs cross the plasma membrane, enter and accumulate in the secretory canaliculi of parietal cells, where they are protonated by acid, then converted into the active form, sulfenamide[26,27]. The activated sulfenamide reacts covalently with the cysteine sulfhydryl group on the extracellular surface of the α-subunit, the Src homology group of proton pumps, thus inactivates the pump and inhibits gastric acid secretion[25,28]. PPIs are very specific to inhibition of gastric proton pumps because they are activated only in the acidic environment of the stomach, whereas they are not activated for the similar enzyme found in the colon and the kidney[29].

INDICATIONS OF IV PPIs

Recurrent bleeding is an independent risk factor of mortality[4] and remains at a rate of about 15% to 20% even after endoscopic hemostasis. Therefore, the aim of acute treatment of peptic ulcer bleeding is to reduce recurrent bleeding. For both pharmacological and physiological reasons, anti-secretory drugs should be able to reduce rates of recurrent bleeding, given that bleeding sources are acid-related lesions. Because platelet aggregation and plasma coagulation are both abolished while the intragastric pH is below 5.4[30], adequate and sustained acid inhibition results in avoidance of the deleterious effect of acid secretions and pepsin activation on the hemostatic process.

Intravenous PPIs infusion can prevent recurrent bleeding in patients with high risk factors for bleeding peptic ulcers, such as active oozing, non-bleeding visible vessels, and adherent clots[31,32]. Intravenous omeprazole after endoscopic hemostasis shows better results than either cimetidine or placebo in reducing the rate of recurrent bleeding[12-14,33,34], the need for endoscopic treatment[12,13], the number of surgery[13,34], the need for blood transfusion, and the length of hospitalization[12].

Empirical therapy with intravenous PPIs should be considered in patients awaiting endoscopy. The use of intravenous PPIs before endoscopy in case of upper gastrointestinal bleeding was shown to accelerate the resolution of signs of bleeding in ulcers[35], reduce the need for endoscopic therapy and shorten hospital stay[36]. However, the recurrent bleeding rate, operation rate and mortality rate are similar in patients treated with intravenous PPIs and placebo[3]. Most recently, Tsoi *et al*[37] suggested pre-endoscopic administration of PPIs has a lower cost-effectiveness ratio per endoscopic therapy averted (USD $ 3561) than the placebo (USD $ 4117). Pre-endoscopic administration of PPIs may be cost-effective in certain situations[38,39]. Therefore, omeprazole infusion as an adjunct therapy to endoscopic hemostasis in actively bleeding peptic ulcers has a favorable overall clinical outcome.

IV PPIs FOR ULCER RECURRENT BLEEDING CONTROL

Platelet aggregation under different pH conditions

The major defense against hemorrhage is transient vasoconstriction and the subsequent formation of a platelet plug. In an acidic environment, the coagulation cascade and platelet aggregation are inhibited. Green *et al* showed there is a respective 2-fold and 4-fold prolongation of prothrombin time, activated partial thromboplastin time,

and thrombin time at pH 6.4 and pH 6.0 compared to pH 7.4[30]. More acid conditions result in greater prolongation of these assay times. In an acid milieu, not only the platelet aggregation profile is profoundly inhibited but also disaggregation of stable platelet plugs occurs. The extent of disaggregation is higher at pH 6.1 than at pH 7.3.

Pepsin control of platelet aggregation

Green *et al.* also showed not only the capability of acid to produce alterations in the coagulation cascade, but also the additive effect of pepsin in disaggregating platelets in pH as low as 5.5. At similar pH, the mean total percentage disaggregation is higher in the presence of pepsin than in the absence. In an *in vitro* study, the effect of pepsin on enhancement of platelet disaggregation increases with decreasing pH[30].

Goal of intragastric pH elevation

The acid environment in the stomach both promotes activation of pepsin and exacerbates gastric mucosal damage. Gastric acid-peptic activity exacerbates superficial mucosal damage into deep ulceration[40], interferes the ulcer healing[41], and adversely affects hemostatic mechanisms[30]. The physiological goal is to achieve an-acidity to arrest hemorrhage in acute gastroduodenal mucosal lesions.

Because platelet aggregation and plasma coagulation are both abolished at pH 5.4 *in vitro*, it is important to achieve intragastric pH higher than pH 5.4 to arrest hemorrhage[30]. However, endogenous buffers such as hemoglobin in the gut or tissue buffers may be not able to maintain the pH of gastroduodenal contents at or above the level necessary for hemostatic integrity.

Netzer *et al* tested the antisecretory effect of high-dose intravenous omeprazole, delivered either by infusion or injection, over the critical first 72 h. With omeprazole infusion, they found the percentage of time with intragastric pH 6 is 59% on day 1, 71% on day 2 and day 3[42]. An additional study in India showed that high-dose infusion of PPIs, such as omeprazole, rabeprazole, and pantoprazole achieves an intragastric pH $\geqslant$ 6 within 1 h of administration and which is maintained for more than 98% of the time in bleeding peptic ulcers[43]. Laine *et al* also demonstrated the antisecretory effect of high-dose lansoprazole infusion, which keeps intragastric pH >6 for 67.8% of the time[44].

The optimal dose of IV PPIs

Current guidelines suggest that patients with bleeding peptic ulcers should be treated with an intravenous omeprazole bolus followed by continuous infusion after endoscopic therapy[31]. Andersen *et al* evaluated the effect of an initial loading dose of 80 mg omeprazole in intragastric pH and found that it achieves a fast and sustained increase to above pH 4[45]. Additional studies showed that after an intravenous 80 mg omeprazole bolus, a high-dose continuous infusion, at 8 mg per hour for 72 h, achieves the necessary high intragastric pH-level from the first day to the third day either in healthy subjects[42] or in patients with bleeding peptic ulcers[46]. Four clinical trials suggested therapeutic benefit for high-dose PPIs in reducing recurrent bleeding or in achieving a favorable clinical outcome[12,13,33,34].

Controversy surrounds the optimal dose required to target intragastric pH and recurrent bleeding control. In Denmark, Kiilerich *et al* showed that low-dose omeprazole at 4 mg/h continuous infusion after a bolus of 80 mg is as effective as the high-dose in maintaining a consistent pH of around 4-6. However, for the low dose omeprazole there is considerable inter-subject variability in AUC and in time with intragastric pH $\geqslant$ 4[47]. Nevertheless, although individual intragastric pH response curves are more variable in low-dose omeprazole infusion[48], Udd *et al* showed a low-dose intravenous bolus of omeprazole of 20 mg daily for 3 d could be still as effective as the high-dose infusion in controlling peptic ulcer recurrent bleeding[49]. Because of the smaller parietal cells mass[50] and higher prevalence rate of a poor metabolizer of cytochrome P450 CYP2C19 alleles in Asian populations[51], it is rational to decrease omeprazole dose in these groups. In Taiwan, Sheu *et al* reported that a decreased dosage of omeprazole with an intravenous 80 mg omeprazole bolus followed with 40 mg bolus twice daily for the consecutive three days could maintain a favorable intragastric pH[52] and decrease recurrent bleeding[14]. Another trial in Taiwan also showed that a decreased dosage of omeprazole, 3.3 mg/h infusion or 40 mg injected every 12 h for 3 d could effectively decrease rates of recurrent bleeding[6,53]. An increase in intravenous dosage to 40 mg per 6 h showed marginally better recurrent bleeding control for Asian populations[54].

The infusion duration: at least 3 d and longer for some groups

The recurrent bleeding rate of peptic ulcers is related to the presence of the stigmata of recent hemorrhage[11]. The fading time of non-bleeding visible vessels is around 3 to 6 d[55]. Commonly, recurrent bleeding may develop within 2-3 d[56,57]. Accordingly, the common duration of omeprazole infusion is 3 d, applied after the endoscopic therapy[6,12-14,34,52,58]. Nonetheless, even with continuous infusion of omeprazole for 3 d, recurrent bleeding rates remain high in certain patients such as those with the presence of underlying medical co-morbidities [1,4,6,10,56]. Clinical trials showed that control of recurrent bleeding following 3-day omeprazole infusion is worse in patients with co-morbidities than in patients without co-morbidities[6,10]. Moreover, we reported that the duration of peptic ulcer recurrent bleeding is prolonged up to the 14th day after the first bleeding episode in patients with co-morbidities[6,10]. To prevent recurrent bleeding in such high risk patients, we advocated the therapeutic benefit of a prolonged 7-day course of low-dose intravenous omeprazole which can exert better recurrent bleeding control for up to 1 mo[59].

Patients with co-morbidities often have a high Rockall risk score $\geqslant$ 6, which indicates that the mean hospital day after acute upper gastro-intestinal hemorrhage should be more than 10 d[60]. Thus, the cost of the prolonged

admission required for giving a 7-day course of omeprazole infusion is not significant. It should be emphasized that costs associated with a recurrent bleeding event far outweigh costs of PPIs therapy[61]. The shift to 7-day prolonged low-dose omeprazole treatment does not increase the cost of omeprazole itself, as the amount given is equivalent to 3-day high-dose infusion. Therefore, for such high risk patients, the prolonged duration intravenous PPI should be cost-effective, especially in Asian patients.

Factors related with the poor control of IV PPIs: CYP2C19 story

Several risk factors for recurrent bleeding have been demonstrated in a variety of studies. Inter-patient variability in responsiveness to PPIs therapy may be a factor in failed healing of severe esophagitis[62], and higher recurrent bleeding rates of peptic ulcers[63]. One of the reasons maybe because of different metabolizer phenotypes of (*S*)-mephenytoin 4'-hydroxylase (Cytochrome P-450 2C19), by which omeprazole is metabolized to an inactive form[64,65]. According to the single nucleotide polymorphism and enzyme activity, subjects are divided into extensive metabolizers (EM), intermediate metabolizers, and poor metabolizers (PM). The increasing potency of gastric acid suppression and increasing intragastric pH with oral omeprazole is dependent on the CYP2C19 genotype status in the rank order of homo-EM ≤ hetero-EM ≤ PM[66]. There are pronounced geographic and interracial differences in the distribution of this polymorphism. The prevalence rate of PM in Chinese and Japanese is higher than in Caucasians and African descents[67-73].

In addition to the inter-patient variability in responsiveness to omeprazole therapy, a poor disease background or a poor nutrition status also has negative impact on recurrent bleeding control of peptic ulcers. Patients with two or more co-morbid diseases or with hypoalbuminemia < 3.0 g/dL have a significantly higher risk of recurrent bleeding[6,10]. Emerging evidence suggests that the incidence of idiopathic peptic ulcers, defined as patients without *H. pylori* infection and no exposure to NSAIDs, is high in the West (between 11% and 44%), and is also increasing in the Asia (from 4.2% to 18.8%)[74-79]. More than 70% of idiopathic peptic ulcers have comorbid illnesses, half of which are severe or life-threatening systemic disorders, defined as American Society of Anesthesiology score ≥3[74,80]. Current evidences indicate that idiopathic peptic ulcers increase the risk of ulcer recurrence and bleeding. Two studies in Hong Kong showed the probability of peptic ulcer recurrence or bleeding in either 12-month or 7-year follow-up is higher in patients with idiopathic peptic ulcers than those with *H. pylori* infection after eradication. One of the two factors associated with recurrent bleeding is comorbidity with severe or life-threatening systemic disorders[75,80].

The most important systemic disorders are renal failure, liver failure, and disseminated malignancy[4]. Similarly, a retrospective cohort study found that renal failure and liver disease are two independent prognostic factors of an unfavorable clinical course, including persistent or recurrent bleeding, required interventional therapy, and death[81]. Although most recurrent bleeding develops within 72 h[56,57], uremic patients have a higher delayed recurrent bleeding risk for 7 to 30 d [10,82].

DIFFERENCES BETWEEN THE ORAL AND IV PPIs

The intragastric 24-h median pH is 4.93 in patients taking oral 40 mg omeprazole once daily, which is significantly higher than baseline median pH of 1.68 in *H. pylori*-negative healthy subjects. However, probably because of diurnal rhythm, the intragastric pH in patients on oral omeprazole falls to a median pH of 3.03 during the night period from 22:00 to 06:00[83]. Therefore, oral omeprazole 40 mg once daily does not suppress gastric acid secretion completely throughout the 24 h period [84].

Several studies have shown that oral administration of high-dose PPIs is just as effective in raising the intragastric pH to above 6 and reducing recurrent bleeding as intravenous administration[43,44,53]. To achieve similar acid control, the dose of oral lansoprozole should be 120 mg bolus then 30 mg per 3 h for 8 times. Results had shown intragastric pH is greater than 6 during 64.8% of the study period, which is similar to 67.8% achieved with intravenous lansoprazole 90 mg bolus injection, followed by 9 mg/h continuous infusion. Therefore, frequent oral PPIs therapy may be able to replace bolus plus constant intravenous PPIs infusion for patients with peptic ulcer bleeding[44].

LIMITS OF IV PPIs TO CONTROL BLEEDING

As discussed previously, the intravenous bolus and continuous infusion of PPIs following endoscopic therapy is effective in reducing recurrent bleeding in most patients[6,12-14,34,52,58]. However, not all patients receiving high-dose omeprazole infusion achieve a mean intragastric pH of more than 6. The 30% of patients with high-dose omeprazole infusion who have a mean pH value of less than 6 tend to have a higher recurrent bleeding rate within the first 3 d than those with mean pH values of 6 or greater[63]. This may reflect inter-patient variability in responsiveness to PPIs therapy[62,63].

In addition, the presence of co-morbidities and poor nutrition status such as uremia and hypoalbuminemia are also the significant indicators of a higher recurrent bleeding rate even when applying intravenous omeprazole infusion[6,10,82]. Kamada *et al* found that only one-third of patients with *H. pylori*-negative idiopathic duodenal ulcers may have acid hypersecretion[85]. Moreover, despite favorable intragastric pH control, patients with comorbid illnesses still have higher recurrent bleeding[10]. In addition to PPIs, certain host factors should be identified and corrected to prevent recurrent bleeding of peptic ulcers in

such high risk patients[86].

As described previously, pre-endoscopy administration of PPIs may be cost-effective in certain situations[38,39]. However, pre-endoscopy administration of PPIs cannot replace urgent endoscopy in managing patients with upper gastrointestinal bleeding[31].

Because of inter-patient variability in responsiveness to omeprazole therapy[47,62], there is a need to find a therapy that provides even more effective control of gastric acid secretion and also reduces the variation in acid inhibition between patients. Esomeprazole, the *S*-isomer of omeprazole[87], has an improved pharmacokinetic profile leading to greater acid suppression than that produced by omeprazole, pantoprazole, lansoprazole, and rabeprazole[88]. Because the metabolism of omeprazole is stereoselective, the sum of the intrinsic clearance values is 3 times lower for *S*-omeprazole than for *R*-omeprazole[89-91]. Following an intravenous bolus of 80 mg and then 8 mg/h continuous infusion, the AUCt and Cmax of esomeprazole is higher than that of omeprazole[92]. The inter-subject variability of esomeprazole for AUCt is also significantly lower and time with intragastric pH > 4 is less than with omeprazole. Although similar acid suppression achieved by i.v. esomeprazole and i.v. omeprazole, the former has a tendency for a faster onset of action (2 h shorter to the target pH > 6) and significantly lower variability in pharmacodynamic response than the later[92]. Moreover, the median intragastric pH of esomeprazole 40 mg i.v. is significantly higher than that of pantoprazole 40 mg i.v. infusion and bolus injection[93]. The duration to achieve elevation of pH > 4 is longer in the former than in the later (1.7 h *vs.* 0.6 h, $P < 0.0001$)[94].

In clinical studies, the greater acid suppression produced by esomeprazole has been translated into higher healing rates and more effective symptom relief when compared to other PPIs in patients with gastro-esophageal reflux disease[95-98]. In a multiethnic study, Sung *et al* showed the high-dose intravenous esomeprazole infusion given after successful endoscopic therapy to patients with high-risk peptic ulcer bleeding has a lower recurrent bleeding rate and a better clinical outcomes than placebo[99]. Therefore, because the variability in the pharmacodynamic response of intravenous esomeprazole is lower, intravenous esomeprazole could be applied in different CYP2C19 genotypes in preventing recurrent bleeding. However, clinical benefits of intravenous esomeprazole for high risk patients such as those with co-morbidities should be further investigated.

CONCLUSION

In summary, an intravenous omeprazole bolus followed by high-dose continuous infusion for 72 h after successful endoscopic therapy has been shown to inhibit gastric acid secretion effectively and have clinical benefits on the prevention of recurrent bleeding in most patients. In the Asian, low-dose omeprazole infusion can effectively decrease rates of recurrent bleeding. Nevertheless, patients with co-morbidities such as renal failure, liver disease, and hypoalbuminemia or who are extensive metabolizers of CYP2C19 genotype may experience higher rates of recurrent bleeding. The prolonged 7-day course of low-dose intravenous omeprazole may decrease recurrent bleeding in such patients with medical comorbidities. There is a need to validate whether intravenous esomeprazole can improve the control of peptic ulcer recurrent bleeding, especially for patients with different CYP2C19 genotypes and with underlying comorbidities.

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Endoscopic and anesthetic feasibility of EUS and ERCP combined in a single session versus two different sessions

Juan J Vila, Marcos Kutz, Silvia Goñi, Miriam Ostiz, Edurne Amorena, Carlos Prieto, Cristina Rodriguez, Ignacio Fernández-Urien, Francisco J Jiménez

Juan J Vila, Marcos Kutz, Silvia Goñi, Miriam Ostiz, Edurne Amorena, Carlos Prieto, Cristina Rodriguez, Ignacio Fernández-Urien, Francisco J Jiménez, Endoscopy Unit, Gastroenterology Department, Complejo Hospitalario de Navarra, Pamplona 31008, Spain

Author contributions: Vila JJ was responsible for the study design, manuscript draft and coordination; Kutz M was responsible for writing corrections and data collection; Ostiz M and Amorena E were responsible for data collection; Prieto C and Rodríguez C performed statistical analysis and interpretation; Fernández-Urien I provided a critical review; and Jiménez FJ gave the final approval.

Correspondence to: Juan J Vila, MD, Endoscopy Unit, Gastroenterology Department, Centro Hospitalario de Navarra, Pamplona 31008, Spain. juanjvila@gmail.com

Telephone: +34-848-422114 Fax: +34-848-422303

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Abstract

AIM: To discuss the feasibility of single session endoscopic ultrasonography (EUS) to discuss and endoscopic retrograde cholangiopancreatography (ERCP) execution.

METHODS: Retrospective endoscopic and anesthetic outcome comparison of performing both EUS and ERCP in a single endoscopic session (Group Ⅰ) versus performing each procedure in two different sessions (Group Ⅱ) was made. The following variables were evaluated: epidemiological variables, American Society of Anesthesiologists Physical Status Classification (ASA) level, procedural time, propofol dose, anesthetic complications, endoscopic complications and diagnostic yield, and therapeutic procedures on both groups. T-student, Chi-Square and Fisher test were used for comparison.

RESULTS: We included 39 patients in Group Ⅰ (mean age: 69.85 ± 9.25; 27 men) and 46 in Group Ⅱ (mean age: 67.46 ± 12.57; 25 men). Procedural time did not differ significantly between both groups (Group Ⅰ *vs* Group Ⅱ: 93 ± 32.78 *vs* 98.98 ± 38.17; P >0.05) but the dose of propofol differed (Group Ⅰ *vs* Group Ⅱ: 322.28 ± 250.54 mg *vs* 516.96 ± 289.06 mg; P = 0.001). Three patients had normal findings on both explorations. Three anesthetic complications [O_2 desaturation (2), broncoaspiration (1)] and 9 endoscopic complications [pancreatitis (6), bleeding (1), perforation (1), cholangitis (1)] occurred without significant differences between both groups (P > 0.05). We did not find any significant difference regarding age, sex, ASA scale level, diagnostic yield or therapeutic maneuvers between both groups.

CONCLUSION: The performance of EUS and ERCP in a single session offers a similar diagnostic and therapeutic yield, does not entail a higher complication risk and requires a significantly smaller dose of propofol for sedation compared with performing each exploration in a different session.

Key words: Endosonography; Endoscopic Retrograde Cholangiopancreatography; Feasibility Studies; Endoscopy; Gastrointestinal; Anesthesia

Peer reviewer: Perminder Phull, MD, FRCP, FRCPE, Gastrointestinal and Liver Service, Room 2.58, Ashgrove House, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN, United Kingdom

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INTRODUCTION

Endoscopic ultrasonography (EUS) and endoscopic retrograde cholangio-pancreatography (ERCP) have become two essential diagnostic and therapeutic tools in patients with biliary and pancreatic diseases. Performing both procedures in a single anesthetic and endoscopic session has theoretical advantages, as reported by some authors[1]. But this tandem approach is currently a topic of debate and is discouraged by other authors based on the observation of complications seen after performing EUS with fine needle aspiration (EUS-FNA) followed by ERCP[2,3]. Development of cardiac complications has also been described in relation with prolonged ERCP procedures[4].

Despite encouraging results referring to feasibility of tandem procedures described in some series[5,6], comparative studies are lacking, so controversy still remains and this issue should be further clarified. Thus, the aim of this study was to compare the feasibility, clinical, endoscopic and anesthetic outcomes of performing EUS and ERCP in a single session versus performing each procedure in a different session. Although retrospective, this is the first comparative study to our knowledge reported in the literature regarding this topic.

MATERIAL AND METHODS

We compared the outcomes of a group of consecutive patients who underwent EUS and ERCP in a single session (Group Ⅰ) versus a group of consecutive patients who underwent EUS and ERCP in two different sessions (Group Ⅱ) from January 2006 until May 2009. Data were collected retrospectively from a review of the electronic medical record and endoscopy database from our hospital. Patients included in Group Ⅱ underwent EUS and ERCP as part of the diagnostic and therapeutic work-up for the same disease. The decision to perform both explorations on the same day or on two different days was made by the referring clinician.

In Group Ⅰ, both explorations were performed in a fluoroscopy suite specifically dedicated to this type of intervention during the same sedation procedure. In Group Ⅱ, EUS was performed in an endoscopy unit lounge without fluoroscopy equipment and ERCP was performed some days later in the same suite as Group I. All the explorations were performed under sedation with propofol, administered by an anesthetic team comprised of an anesthesiologist and a nurse. To reduce duodenal motility during ERCP, intravenous hyoscine butylbromide was given following the anesthesiologist's criteria.

EUS was accomplished first in all patients, followed by ERCP. EUS explorations were performed by two endoscopists and ERCP by three endoscopists, assisted on both explorations by a nurse. EUS was done using a radial echoendoscope (Pentax EG3630UR, Pentax Europe, Hamburg, Germany) with evaluation of the entire pancreas, ampulla, extrahepatic bile duct, liver, retroperitoneal space and posterior mediastinum. When a pancreatic mass, liver metastasis or distant lymph nodes in patients with oncological disease were seen, FNA was performed with a linear array echoendoscope (Pentax EG3830UT, Pentax Europe, Hamburg, Germany) using a 22 G needle (Echo-Tip, Wilson-Cook medical, Inc., Winston-Salem, NC, USA). When a thickened extrahepatic bile duct was found, brush cytology or biopsy was obtained during ERCP following our team's policy. ERCP was performed using a lateral view duodenoscope with therapeutic channel (Olympus TJF160VR, Olympus Medical Systems Corp, Tokyo, Japan). When EUS-FNA was performed, the specimens were immediately assessed on-site for adequacy by a dedicated cytopathologist.

The following variables were recorded: age, gender, American Society of Anesthesiologists Physical Status Classification (ASA), procedural time, administered propofol dose, cardiopulmonary complications, endoscopic complications and diagnostic yield of both explorations. The procedural time was considered from the moment that cardiopulmonary monitorization was initiated before sedation to the moment the patient left the exploration room. In Group Ⅱ, the procedural time and total propofol dose were calculated by adding the values of each individual exploration. All ERCPs were performed on an in-patient basis, observing the patient for at least 24 h after ERCP before discharge.

Statistical analysis

Quantitative variables are presented as mean value ± standard deviation. T-student test was used for the comparison of quantitative variables and Fisher exact test was used for the comparison of qualitative variables. The normal distribution of quantitative variables was evaluated with the Kolgomorov-Smirnoff Z test. Statistical significance was considered for P values under 0.05.

RESULTS

A total of 39 patients were included in Group Ⅰ with a mean age of 69.85 ± 9.25 years. Twenty-seven of these patients were men. On the other hand, 46 patients were included in Group Ⅱ. This group mean age was 67.46 ± 12.57 years and 25 were men. The indication for endoscopic study was suspected choledocolithiasis in 9 patients (11%), pancreatic cancer in 18 patients (21%), ampulloma in 5 patients (6%), cholangiocarcinoma in 4 patients (5%), chronic pancreatitis in 3 patients (3%), pancreatic pseudocyst in 1 patient (1%) and suspected pancreatobiliary disease without definitive diagnosis prior to endoscopic explorations in 45 patients (53%). Seventy three patients (86%) were studied with transabdominal ultrasonography prior to the endoscopic procedure, 61 (72%) with a CT and 25 (30%) with magnetic resonance cholangiopancreatography. No significant differences regarding age, sex and indication of endoscopy were seen between both groups.

ASA scale distribution of patients is shown in Table 1. When we analyzed patients regrouped as low ASA grade (including patients with ASA Ⅰ and Ⅱ) and high

Table 1 ASA Physical Status Classification distribution of patients in Group Ⅰ and Group Ⅱ

	American Society of Anesthesiologists (ASA) Physical Status Classification			
	Ⅰ	Ⅱ	Ⅲ	Ⅳ
Group Ⅰ	3	19	15	2
Group Ⅱ	4	17	23	2

ASA: American Society of Anesthesiologists

ASA grade (ASA Ⅲ and higher), no differences between both groups were found, with 21 patients with a low ASA grade in Group Ⅰ and 22 patients in Group Ⅱ.

During ERCP, brush cytology was obtained in 20 patients (23%), retrieving an adequate specimen in 14 of them (diagnostic yield of 70%). Nine of these patients were included in Group Ⅰ and 11 in Group Ⅱ. Forceps biopsy was taken in 15 patients, 4 from Group Ⅰ and 11 from Group Ⅱ. The histological study was diagnostic in all of them. Eight of these patients had an ampullary tumor. EUS-PAAF was required in 19 patients in Group Ⅰ and 13 in Group Ⅱ, resulting in a correct specimen extraction in 17 patients in Group Ⅰ and 12 patients in Group Ⅱ. No significant differences were seen regarding the distribution or the diagnostic yield of EUS-FNA, brush cytology or forceps biopsy between both groups ($P > 0.05$).

Mean procedural time was 93 ± 32.78 min in Group Ⅰ and 98.98 ± 38.17 min in Group Ⅱ, without significant differences between them. Regarding the amount of administered propofol, patients included in Group Ⅰ received a mean dose of 322.28 ± 250.54 mg while the dose administered to patients included in Group Ⅱ was 516.96 ± 289.06 mg, significantly higher ($P = 0.002$). Age, procedural time and propofol dose variables followed a normal distribution.

Three patients in Group Ⅰ suffered desaturation during the tandem exploration. Two episodes resolved after increasing inhaled oxygen flow and jaw thrust and the other required oro-tracheal intubation. One of the former was later diagnosed with aspiration pneumonia and had an uneventful recovery. Only one patient in Group Ⅱ suffered desaturation which resolved with jaw thrust and oro-pharyngeal cannulation. No other cardiopulmonary complications were seen. None of these complications prevented our team from completing the endoscopic procedure.

Endoscopic complications appeared in 9 patients (11%), all of them related to ERCP. In Group Ⅰ, one patient developed post-ERCP pancreatitis and another suffered sphincterotomy bleeding requiring endoscopic therapy. In Group Ⅱ, five patients developed post-ERCP pancreatitis, one developed post-ERCP cholangitis and one suffered a retroperitoneal perforation. This latter patient developed a retroperitoneal abscess and required percutaneous drainage. The rest of the patients had an uneventful recovery with conservative management.

No significant differences between both groups were seen with regard to presentation of cardiopulmonary or endoscopic complications ($P > 0.05$).

Table 2 Therapeutic maneuvers performed on Group Ⅰ and Ⅱ

		Group Ⅰ	Group Ⅱ	P
Sphincterotomy	Yes	17	22	0.69
	No	22	24	
Common bile duct	Yes	9	5	0.13
stone extraction	No	30	41	
Biliary plastic stent	Yes	14	24	0.18
	No	25	22	
Biliary metallic stent	Yes	6	3	0.29
	No	33	43	
Pancreatic plastic stent	Yes	0	3	0.24
	No	39	43	
Endoscopic therapy	Not Necessary	8	1	0.006
	Necessary	31	45	

Final diagnosis after both explorations was pancreatic cancer in 30 patients, cholangiocarcinoma in 9, ampulloma in 8, choledocolithiasis in 23, chronic pancreatitis in 7 and other findings in 3 patients. Three patients had normal findings on both explorations. No significant differences between Group Ⅰ and Ⅱ were observed regarding the final diagnostic yield.

Patients who did not undergo any therapeutic procedures were more common on Group Ⅰ ($P < 0.05$). No other therapeutic differences were seen between both groups (Table 2).

DISCUSSION

EUS and ERCP are currently two complementary techniques in the diagnosis and therapeutic work-up of patients with pancreatic and biliary diseases. Performing both explorations in the same session is an appealing policy which is in common use in some tertiary centers and is supported by published data and expert opinion[1,5,6]. This policy has important advantages for endoscopists as has been previously stated[1]. These advantages include performing EUS in naïve conditions which might be important in pancreatic and biliary cancer staging[7,8]. Only one sedation procedure would be necessary for the same patient and this, in the opinion of some authors, could reduce the demand on anesthetic resources[5]. Performing EUS initially could guide the biliary or pancreatic access and therapy on ERCP since the endoscopist gets useful clinical and anatomical information. Cost-effectiveness could be another advantage of the tandem approach since the procedure time and endoscopic and anaesthetic resources could be lowered. To these theoretical advantages reported previously, we would add the lowering of social costs by means of reducing the length of hospital admissions and avoiding the attendance of the patient and relatives at the hospital for two days for each individual exploration. This policy would also facilitate the endoscopy room's workload planning, resulting in a more efficient organization of endoscopic resources.

But all these are theoretical advantages not previously proved since a prospective comparative study of single

versus a two session approach is lacking. Two feasibility studies have been published supporting the tandem approach[5,6]. The first one published by Tarantino *et al*[6] aimed to report the complication rate of performing EUS-FNA followed by ERCP in 25 patients with biliary or pancreatic disease. No early or late complications were seen in this series. The authors concluded that performing both explorations the same day was feasible and safe and should be considered the reference standard. Ross *et al*[5] also published a feasibility retrospective study including 114 jaundiced patients who underwent EUS ± FNA followed by ERCP. They concluded that combined EUS and ERCP is a feasible approach to establish a tissue diagnosis, complete local staging and relieve biliary obstruction in a single session with a complication rate no greater than that for the component procedures.

These feasibility studies were preceded by discouraging clinical observations. Mergener *et al*[2] published a case of a 77 year old woman who developed pneumoperitoneum after EUS-FNA of a peripancreatic lymph node followed by ERCP. This complication was asymptomatic and no intervention was required so the clinical importance of this observation remained unclear. The authors postulated that the pneumoperitoneum resulted from insufflated air tracking through the FNA site during ERCP and recommended that in a tandem approach, ERCP should precede FNA. Di Matteo *et al*[3] reported two cases of biliary leakage complicating ERCP performed after EUS-FNA of a pancreatic head mass. They postulated that FNA would create subclinical bile duct injuries which would be aggravated by manipulation during ERCP. Furthermore, Fisher *et al* reported a significant association between myocardial ischemia or injury, defined by the release of cardiac troponin I, with a longer duration of ERCP (37.7 ± 28.9 min *vs* 24.2 ± 12.3 min in this study, $P = 0.007$). This was true only for patients older than 65 years and predominant in men. The critical time cut-off value in this study was 30 min of duration for ERCP. Although there are other investigators[9,10] who, based on ECG intraoperative studies, concluded that, even in patients with severe coronary artery disease, ERCP and other endoscopic procedures do not increase the risk of myocardial ischemia. Taking into account these data, the benefits of the tandem approach would be questioned by a potentially higher risk of cardiac and endoscopic complications.

With this background, we decided to evaluate the benefits and complications of the tandem approach compared with the two session approach by means of a comparative retrospective study, including consecutive patients who underwent EUS and ERCP in our endoscopy unit for a 41 mo period. In our study, both groups were comparable regarding age, sex, indication for endoscopy and ASA grade, and no significant differences were seen regarding diagnostic yield, cardiopulmonary complications, endoscopic complications or procedural time between both groups. This latter aspect might be surprising since it has been previously postulated that the tandem approach would lower the procedure time[5,6]. Ross *et al* reported a mean procedure time for the combined procedure of 73.6 ± 30 min and Tarantino *et al* 58.6 ± 16.14 min. In our study, the mean intervention time for the tandem procedure reached 93 ± 32.78 min, lower although not significantly different than the mean 98.98 ± 38.17 min corresponding to the two session group. The explanation for this "high" procedure time can be found on the retrospective nature of our study since the procedural time we registered ranged from the moment the patient was monitored to the moment he left the endoscopic room which includes a large period without any endoscopic maneuver. In this sense, we think that our study does not properly clarify this aspect.

The only significant difference we found between both approaches was the propofol requirements, favoring the tandem approach which required a lower propofol dose. This is undoubtedly an important issue and supports the tandem approach, confirming the previous hypothesis raised by other authors[5].

We performed EUS with FNA in 32 patients without related complications and with a diagnostic yield of 90.6%. No pneumoperitoneum or biliary leakage was detected after EUS-FNA and the only perforation in our series occurred in a patient in Group Ⅱ.

The main limitation of our study lies in its retrospective nature, as already discussed. Moreover, it is a single center study including a heterogeneous group of patients, resulting in a selection bias since the decision to perform combined or separated EUS and ERCP depended on the referring physician. Referring clinicians were, in many cases, non-specialized gastroenterologists who were not implicated in the trial and many were not familiarized with the latest high-level endoscopic innovations. Therefore, their choice of exploration was determined either by their usual clinical practice or by the latest information on the subject that had reached them. This makes a selection bias which could not be controlled due to the characteristics of the study.

In conclusion, our results show that the performance of EUS followed by ERCP in a single session is feasible and safe, does not entail a higher cardiopulmonary or endoscopic complication risk and requires a significantly smaller dose of propofol for sedation compared with performing each exploration in two different sessions. Furthermore, the tandem approach does not lower the diagnostic yield of EUS or ERCP.

COMMENTS

Background

Nowadays patients with pancreatobiliary disease undergo endoscopic retrograde cholangiopancreatography (ERCP) and Endoscopic ultrasonography (EUS) more frequently as part of their diagnostic and therapeutic management. To perform both explorations in a single anesthetic and endoscopic session has been discouraged by some authors for a possible higher risk of complications.

Research frontiers

To our knowledge, the feasibility and outcomes of performing both explorations in the same session has never been compared with performing them in different endoscopic and anesthetic sessions.

Innovations and breakthroughs

The dose of Propofol administered to patients was the only variable significantly different when comparing both groups. Procedural time, incidence

of complications, diagnostic yield and therapeutic procedures showed no difference between the groups. This is an important finding since the major drawback described to perform ERCP and EUS in the same session was that it may increase the risk of perforation and systemic complications. This has not been confirmed in this study.

Applications

According to our data, to perform both explorations in a single session does not entail a higher risk of complication. This policy can have some advantages and may be important regarding costs and endoscopy room daily work plan organization. In any case, prospective and comparative studies are warranted.

Terminology

ERCP is an endoscopic procedure which allows drainage of the bile and pancreatic ducts through the papilla. It is also useful to diagnose biliary and pancreatic disease and to obtain material for cytological or histological analysis. EUS is also an endoscopic procedure which combines endoscopic and ultrasonographic view, with higher frequencies than transabdominal ultrasonography and thus with a higher resolution. It allows tissue to be obtained for pathological diagnosis and transmural therapeutic procedures to be performed with a low risk of complication.

Peer review

This paper describes a retrospective study of patients undergoing tandem EUS plus ERCP versus separate procedures. No difference was demonstrated in the outcome parameters.

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CASE REPORT

Duodenal diverticulum and associated pancreatitis: Case report with brief review of literature

Mian Muhammad Rizwan, Harpeet Singh, VP Chandar, Maria Zulfiqar, Veera Singh

Mian Muhammad Rizwan, Harpeet Singh, VP Chandar, Maria Zulfiqar, Veera Singh, Department of Internal Medicine, Prince George's Hospital, MD 20785, United States

Author contributions: Rizwan MM, Singh H and Chandar VP supplemented the data about the patient; Zulfiqar M and Singh V reviewed the literature and analyzed the data; and Rizwan MM wrote the paper.

Correspondence to: Mian Muhammad Rizwan MD, Department of Internal Medicine, Prince George's Hospital, 3001 Hospital Drive, Cheverly, MD 20785, United States. mmrizwan1@hotmail.com

Telephone: +1-301-6183776 Fax: +1-301-6182986
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Abstract

Pancreatitis in the elderly is a problem of increasing occurrence and is associated with severe complications. Periampullary diverticula (PAD) are extraluminal outpouchings of the duodenum rarely associated with pancreatitis. The presence of PAD should be excluded before diagnosing idiopathic pancreatitis, particularly in the elderly. However, when a duodenal diverticulum is found in the absence of any additional pathology, only then should the symptoms be attributed to the diverticulum. We describe a case of duodenal diverticulum presenting with pancreatitis to emphasize the importance of this commonly neglected etiology.

Key words: Duodenal diverticulum; Periampullary duodenal diverticulum; Pancreatitis

Peer reviewers: Jiang-Fan Zhu, MD, Professor of Surgery, Department of General Surgery, East Hospital of Tongji University, Pudong, Shanghai 200120, China; Maher Aref Abbas, MD, FACS, FASCRS, Associate Professor of Surgery, Chief, Colon and Rectal Surgery, Center for Minimally Invasive Surgery, Kaiser Permanente, 4760 Sunset Blvd, third Floor, Los Angeles, CA 90027, United States; Wahid Wassef, MD, MPH, FACG, Professor of Medicine, Division of Gastroenterology, Department of Medicine, University Campus, 55 Lake Avenue, North, Worcester, MA 01655, United States

Rizwan MM, Singh H, Chandar VP, Zulfiqar M, Singh V. Duodenal diverticulum and associated pancreatitis: Case report with brief review of literature. *World J Gastrointest Endosc* 2011; 3(3): 62-63 Available from: URL: http://www.wjgnet.com/1948-5190/full/v3/i3/62.htm DOI: http://dx.doi.org/10.4253/wjge.v3.i3.62

INTRODUCTION

Duodenal diverticulum is a well known entity since the early eighteenth century when it was first reported by a French pathologist, Chomel, in 1710. The duodenum is the second most common site of diverticula in the small bowel following the jejunum[1,2]. It is difficult to ascertain the true prevalence of duodenal diverticula; they are seen in 1%-6% of upper gastrointestinal contrast studies[2,3], 12%-27% of endoscopic studies[2,4] and in 15%-22% of autopsies. Diverticula are rare below age 40 and the prevalence rate increases with age.

Diverticula occur at weak spots in the duodenal wall such as the site of entry of the common bile duct, pancreatic duct and perivascular connective tissue sheath. The exact etiology is not clear; however, it might be the end result of disordered duodenal motility. Advancing age, progressive weakening of intestinal smooth muscles and increase in intraduodenal pressure may all encourage the outpouching of the duodenum.

About 70%-75% of all duodenal diverticula are periampullary. Diverticula arising within 2-3 cm radius of the ampulla but not containing it are referred to as juxtapapillary diverticula. However, if the papilla arises within a diverticulum it is called an intradiverticular papilla. In the majority of cases, diverticula arise on the inner or pancreatic border of the duodenum. The possibly of PAD should be kept in mind while interpreting any bile duct imaging. It can create a filling defect in biliary passage; hence, can be mistaken for periampullary tumors or biliary stones. It can also be misinterpreted as pancreatic pseudocyst when it is large and fluid filled.

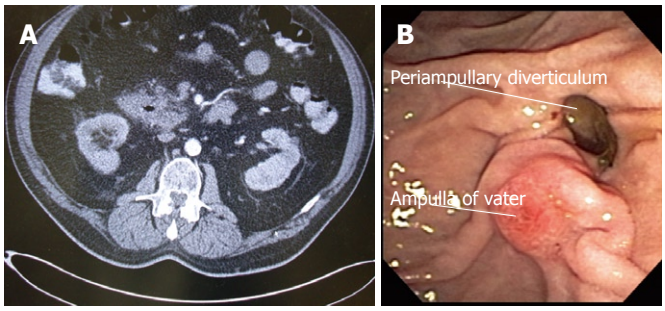

Figure 1 A duodenal diverticulum with ampulla. A: Computed tomography scan of abdomen with gas collection in pancreatic head representing periampullary diverticulum penetrating in pancreatic tissue; B: Periampullary diverticulum

CASE REPORT

A 69 year old Caucasian male presented to our hospital because of worsening abdominal pain for 3 d. The pain was initially in the upper abdomen but later radiated to the back. Epigastric tenderness was evident on physical examination. He had a history of similar painful episodes occurring infrequently for a few years but the pain had never been so severe. He had never previously sought medical attention for this pain. He also had a past medical history of constipation, hemorrhoids, dementia and hypertension.

The patient was given nil per mouth while workup for abdominal pain was started. His pancreatic enzymes were found to be elevated and a subsequent CT scan showed an irregular pancreatic outline consistent with pancreatitis. Interestingly, CT of the abdomen showed gas collection in the pancreatic head which raised the suspicion of a duodenal diverticulum. Sigmoid diverticulum and a small inguinal hernia were also incidental findings on the CT scan. HIDA scan was performed which showed normal transit of bile through the common bile duct (CBD).

A subsequent ERCP showed a duodenal diverticulum with ampulla in the mouth of diverticulum (Figure 1A, B). There was no evidence of any CBD stones or strictures on cannulation of the CBD. No intervention was needed since the patient's condition started to improve with conservative management and the patient was found to be doing well at his 1 year follow-up visit.

Pancreatitis in the elderly is a problem of increasing occurrence and is associated with severe complications. The possibility of the presence of PAD should be kept in mind in the differential of pancreatitis, particularly in the elderly population. In this patient, we believe chronic constipation was the factor responsible for hemorrhoids, sigmoid and duodenal diverticulum. The diverticulum might have been a major contributing factor in repeated attacks of mild self-resolving pancreatitis in the past.

DISCUSSION

With lengthening of the life span, diverticulosis has come to occupy a more important position in the sphere of clinical gastroenterology. The majority of duodenal diverticula are asymptomatic. Clinical presentation may be characterized by non-specific abdominal symptoms. However, complications are responsible for presentation in most cases. When drainage in the neck is inadequate or the neck is narrow, these conditions favor inflammation and may even lead to hemorrhage or perforation.

There have been anecdotal accounts implicating PAD in the pathogenesis of acute and chronic pancreatitis. Compression of CBD, dysfunction of the ampulla or a poorly emptying diverticulum with a narrow neck can all lead to pancreatico-biliary disease and possible pancreatitis. However, the relationship with pancreatitis remains tenuous as biliary calculus disease is also more common in PAD. It is debatable whether the pancreatitis is caused by the PAD per se or by the associated biliary calculi. It has been proposed that PAD may be responsible for transient biliary symptoms and alterations in liver function[5]. It is possible in the above mentioned case that distension of a diverticulum with inspissated food might have caused compression of the pancreatic duct leading to pancreatitis which resolved spontaneously.

To date, there are no hard and fast guidelines regarding management of such diverticulum. Earlier this century, surgical diverticulectomy was frequently carried out for non-specific symptoms. There is now consensus that elective surgical treatment of asymptomatic or minimally symptomatic diverticulum is not justified. Operative procedures for diverticula in the second part of duodenum are particularly cumbersome since often it requires mobilization of the duodenum which is retroperitoneal. Dennesen and Rijken reviewed 45 reported cases of perforation of duodenal diverticula and found an overall mortality rate of 31%[2]. Surgical or endoscopic interventions should only be reserved for symptomatic diverticulum[6]. Diverticulectomy for vague pain and abdominal discomfort is dangerous and unrewarding; it carries a high morbidity and mortality[3,6]. Furthermore, only 50% of patients treated with diverticulectomy were relieved of their symptoms [6,7].

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CASE REPORT

Stent-in-stent through a side hole to prevent biliary metallic stent migration

Wiriyaporn Ridtitid, Rungsun Rerknimitr, Surachai Amornsawadwattana, Yuwadee Ponauthai, Pinit Kullavanijaya

Wiriyaporn Ridtitid, Rungsun Rerknimitr, Surachai Amornsawadwattana, Yuwadee Ponauthai, Pinit Kullavanijaya, Division of Gastroenterology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand
Author contributions: Ridtitid W and Rerknimitr R contributed equally to this work; Ridtitid W and Rerknimitr R developed the concept; Ridtitid W, Rerknimitr R; Amornsawadwattana S and Ponauthai Y contributed to acquisition of data; Rerknimitr R and Kullavanijaya P revised the paper for important intellectual content; and Ridtitid W and Rerknimitr R wrote the paper.
Correspondence to: Wiriyaporn Ridtitid, MD, Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. wiriyaporn_r@yahoo.com
Telephone: +66-2-2564265 Fax: +66-2-2527839
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Abstract

The covered self-expandable metallic stent (SEMS) has been developed to overcome the problem of tissue ingrowth, However, stent migration is a well-known complication of covered SEMS placement. Use of a double pigtail stent to lock the movement of the SEMS and prevent migration has been advised by many experts. Unfortunately, in our case this technique led to an incidental upward migration of the SEMS. We used APC to create a side hole in the SEMS for plastic stent insertion as stent-in-stent. This led to a successful prevention of stent migration.

Key words: Metallic stent migration; Distal biliary obstruction

Peer reviewers: Tony Chiew Keong Tham, MD, Consultant Gastroenterologist, Ulster Hospital, Dundonald, Belfast BT16 1RH, Northern Ireland, United Kingdom; Iruru Maetani, MD, Professor and Chairman, Division of Gastroenterology, Department of Internal Medicine, Toho University Ohashi Medical Center, 2-17-6 Ohashi Meguro-ku, Tokyo 153-8515, Japan

Ridtitid W, Rerknimitr R, Amornsawadwattana S, Ponauthai Y, Kullavanijaya P. Stent-in-stent through a side hole to prevent biliary metallic stent migration. *World J Gastrointest Endosc* 2011; 3(3): 64-66 Available from: URL: http://www.wjgnet.com/1948-5190/full/v3/i3/64.htm DOI: http://dx.doi.org/10.4253/wjge.v3.i3.64

INTRODUCTION

Self-expandable metallic stent (SEMS) placement is widely accepted for palliative management of patients with unresectable malignant biliary obstruction. However, complications such as tumor ingrowth, overgrowth, food debris, and mucosal hyperplasia can occur. The use of covered SEMS is clearly effective in preventing tumor ingrowth[1-3]. Nevertheless, in two recently published randomized trials of covered versus uncovered metal biliary stents, outcomes such as stent patency were no different between the two stents but the risk of migration was higher with the covered stents[4,5]. Here, we report a case of stent-in-stent insertion through a side hole to prevent migration of a covered self-expandable metallic stent in a patient with distal malignant biliary obstruction.

CASE REPORT

A 35-year-old man presented with obstructive jaundice resulting from metastatic pancreatic cancer. The diagnosis was confirmed by intraductal biopsy. Endoscopic retrograde cholangiopancreatography (ERCP) demonstrated a distal biliary stricture 1.5 cm in length with upstream dilatation. Placement of a 4-cm-long covered SEMS (Wallstent, Boston Scientific, Natick, MA) under conscious sedation was initially performed. Three weeks later, the patient was re-admitted due to acute cholangitis. ERCP demonstrated distal migration of the SEMS (Fi-

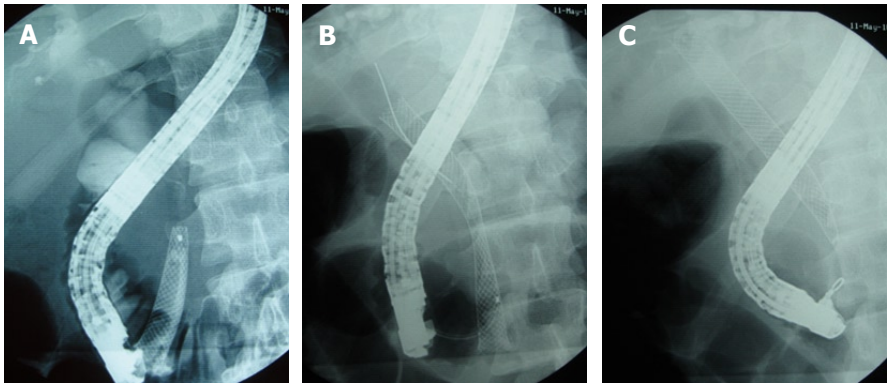

Figure 1 Endoscopic retrograde cholangiopancreatography after re-admission. A: Distal migration of self-expandable metallic stent (SEMS); B: 8-cm-long partially covered SEMS replacement; C: Retrieving the stent using a rat-toothed forceps after upward migration of SEMS.

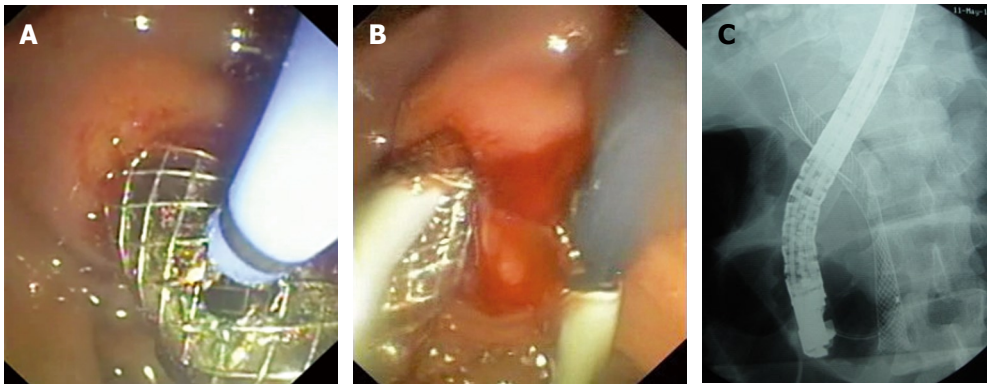

Figure 2 Stent-in-stent through the side hole. A: Creating a side hole at the distal end of the self-expandable metallic stent with argon plasma coagulation trimming; B: Insertion of plastic stent through the side hole; C: After the successful procedure for the prevention of stent migration.

gure 1A). Successful removal of the first SEMS was performed using a snare and this was replaced with a new SEMS (Wallstent, Boston Scientific, Natick, MA), 8 cm in length (Figure 1B). Subsequently, placement of a double pigtail 10 Fr 10 cm plastic stent (PS) was attempted as stent-in-stent to prevent migration. However, even with cautious deployment the SEMS was accidentally displaced upwards during PS insertion. Using a rat-toothed forceps we were able to move the stent downwards to the proper position (Figure 1C). Argon plasma coagulation (APC) was then applied to create a side hole at the distal end of the SEMS (Figure 2A) and a PS was inserted through the side hole (Figure 2B). This side hole insertion was helpful in preventing the upward movement of the previously deployed SEMS (Figure 2C). Six months later the patient was doing well and was without clinical sign of biliary obstruction.

DISCUSSION

Covered SEMS placement is widely accepted for use in palliative management of patients with unresectable malignant distal biliary obstruction. Although covered stents are designed to overcome tissue ingrowth, failure to embed in the bile duct wall can result in proximal and distal migration, at a reported frequency of 6%-8%[1-5]. Migration of a biliary SEMS may occur proximally or distally after stent insertion and may cause complications such as ulceration, perforation and intestinal obstruction[1-3].

Generally, correct positioning of the SEMS at the initial stent placement is important in preventing migration. Nevertheless, a high shortening ratio of the covered SEMS is thought to favour migration after deployment of the stent[6]. New covered stents, therefore, have been developed for the prevention of stent migration. These include the nitinol SEMS (Wallflex; Boston Scientific, Natick, Massachusetts, USA or Niti-S; Taewoong Medical, Seoul, South Korea) which is flared at the uncovered ends and the fully-coverd Zeostent (Zeon Medical Inc., Tokyo, Japan) which has a wavy contour after full expansion[6,7]. Some previous work of expert endoscopists suggested that putting a double pigtail stent as stent-in-stent to lock the movement of the SEMS could prevent migration[8]. However, this technique for preventing biliary stent migration has not been well established. We have reported a case with malignant distal biliary obstruction after covered SEMS placement. In our case, the insertion of a double pigtail stent was perform to lock the movement of the SEMS and thereby prevent its migration. However, due to upward force exerted during PS insertion as stent-in-stent, this technique led to an incidental upward migration of the covered SEMS.

Argon plasma (APC) has been described as a useful tool for trimming the stent or making a hole[9-12]. Studies done on Wallstent, have recommended a power setting of 70-80 W and argon flow of 0.8 L/min. In this case, we used APC to make a side hole in the SEMS for PS insertion without complication. After the force angle of PS insertion was changed, the distal end of double pigtail stent was able to lock the distal end of the SEMS and to prevent upward migration of SEMS during PS placement.

In conclusion, we report a successful technique of stent-in-stent insertion through the side hole to change

an angle of PS insertion for preventing upward covered SEMS migration in a patient with distal malignant biliary obstruction. With this tangential stent insertion, the chance of upward stent migration during deployment should be less.

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Maher Aref Abbas, MD, FACS, FASCRS, Associate Professor of Surgery, Chief, Colon and Rectal Surgery, Chair, Center for Minimally Invasive Surgery, Kaiser Permanente, 4760 Sunset Blvd, third Floor, Los Angeles, CA 90027, United States

Iruru Maetani, MD, Professor and Chairman, Division of Gastroenterology, Department of Internal Medicine, Toho University Ohashi Medical Center, 2-17-6 Ohashi Meguro-ku, Tokyo 153-8515, Japan

Lucian Negreanu, MD, PhD, Assistant Professor, Gastroenterology Department, Emergency University Hospital, Carol Davila University Bucharest, 169 splaiul Independentei Street, sector 5, Bucharest, Romania

Michal Procke, MD, Department of Internal Medicine - Gastroenterology and Endoscopy, Charles University, 2nd Medical School, Motol University Hospital, Prague, Czech Republic

Perminder Phull, MD, FRCP, FRCPE, Gastrointestinal & Liver Service, Room 2.58, Ashgrove House, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN, United Kingdom

Tony Chiew Keong Tham, MD, Consultant Gastroenterologist, Ulster Hospital, Dundonald, Belfast BT16 1RH, Northern Ireland, United Kingdom

Wahid Wassef, MD, MPH, FACG, Professor of Medicine, Division of Gastroenterology, Department of Medicine, University Campus, 55 Lake Avenue, North, Worcester, MA 01655, United States.

Jiang-Fan Zhu, MD, Professor of surgery, Department of General Surgery, East Hospital of Tongji University, Pudong, Shanghai 200120, China

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Meetings

Events Calendar 2011

January 14-15, 2011
AGA Clinical Congress of Gastroenterology and Hepatology: Best Practices in 2011
Miami, FL 33101, United States

January 20-22, 2011
Gastrointestinal Cancers Symposium 2011
San Francisco, CA 94143, United States

January 28-29, 2011
9. Gastro Forum München
Munich, Germany

February 04-05, 2011
13th Duesseldorf International Endoscopy Symposium
Duesseldorf, Germany

February 13-27, 2011
Gastroenterology: New Zealand CME Cruise Conference
Sydney, NSW, Australia

February 24-26, 2011
Inflammatory Bowel Diseases 2011-6th Congress of the European Crohn's and Colitis Organisation
Dublin, Ireland

February 24-26, 2011
2nd International Congress on Abdominal Obesity
Buenos Aires, Brazil

February 26-March 1, 2011
Canadian Digestive Diseases Week
Westin Bayshore, Vancouver
British Columbia, Canada

March 03-05, 2011
42nd Annual Topics in Internal Medicine
Gainesville, FL 32614, United States

March 14-17, 2011
British Society of Gastroenterology Annual Meeting 2011
Birmingham, England, United Kingdom

March 17-19, 2011
41. Kongress der Deutschen Gesellschaft für Endoskopie und Bildgebende Verfahren e.V.
Munich, Germany

March 17-20, 2011
Mayo Clinic Gastroenterology & Hepatology 2011
Jacksonville, FL 34234, United States

March 25-27, 2011
MedicReS IC 2011 Good Medical Research
Istanbul, Turkey

April 07-09, 2011
International and Interdisciplinary Conference Excellence in Female Surgery
Florence, Italy

April 15-16, 2011
Falk Symposium 177, Endoscopy Live Berlin 2011 Intestinal Disease Meeting, Stauffenbergstr. 26
Berlin 10785, Germany

April 18-22, 2011
Pediatric Emergency Medicine: Detection, Diagnosis and Developing Treatment Plans
Sarasota, FL 34234, United States

April 20-23, 2011
9th International Gastric Cancer Congress, COEX, World Trade Center, Samseong-dong
Seoul 135-731, South Korea

April 25-27, 2011
The Second International Conference of the Saudi Society of Pediatric Gastroenterology, Hepatology & Nutrition
Riyadh, Saudi Arabia

April 28-30, 2011
4th Central European Congress of Surgery
Budapest, Hungary

May 07-10, 2011
Digestive Disease Week
Chicago, IL 60446, United States

May 12-13, 2011
2nd National Conference Clinical Advances in Cystic Fibrosis
London, England, United Kingdom

May 21-24, 2011
22nd European Society of Gastrointestinal and Abdominal Radiology Annual Meeting and Postgraduate Course
Venise, Italy

May 25-28, 2011
4th Congress of the Gastroenterology Association of Bosnia and Herzegovina with international participation, Hotel Holiday Inn
Sarajevo, Bosnia and Herzegovina

June 11-12, 2011
The International Digestive Disease Forum 2011
Hong Kong, China

June 13-16, 2011
Surgery and Disillusion XXIV Spigc II ESYS, Napoli, Italy

June 22-25, 2011
ESMO Conference: 13th World Congress on Gastrointestinal Cancer
Barcelona, Spain

September 10-11, 2011
New Advances in Inflammatory Bowel Disease
La Jolla, CA 92093, United States

September 10-14, 2011
ICE 2011-International Congress of Endoscopy, Los Angeles Convention Center, 1201 South Figueroa Street
Los Angeles, CA 90015, United States

September 30-October 1, 2011
Falk Symposium 179, Revisiting IBD Management: Dogmas to be Challenged, Sheraton Brussels Hotel
Brussels 1210, Belgium

October 19-29, 2011
Cardiology & Gastroenterology Tahiti 10 night CME Cruise
Papeete, French Polynesia

October 22-26, 2011
19th United European Gastroenterology Week
Stockholm, Sweden

October 28-November 02, 2011
ACG Annual Scientific Meeting & Postgraduate Course
Washington, DC 20001, United States

November 11-12, 2011
Falk Symposium 180, IBD 2011: Progress and Future for Lifelong Management, ANA Interconti Hotel, 1-12-33 Akasaka, Minato-ku
Tokyo 107-0052, Japan

December 01-04, 2011
2011 Advances in Inflammatory Bowel Diseases/Crohn's & Colitis Foundation's Clinical & Research Conference
Hollywood, FL 34234, United States

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Instructions to authors

GENERAL INFORMATION

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3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

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4 **Diabetes Prevention Program Research Group**. Hyperten sion, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

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6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

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Books

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15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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