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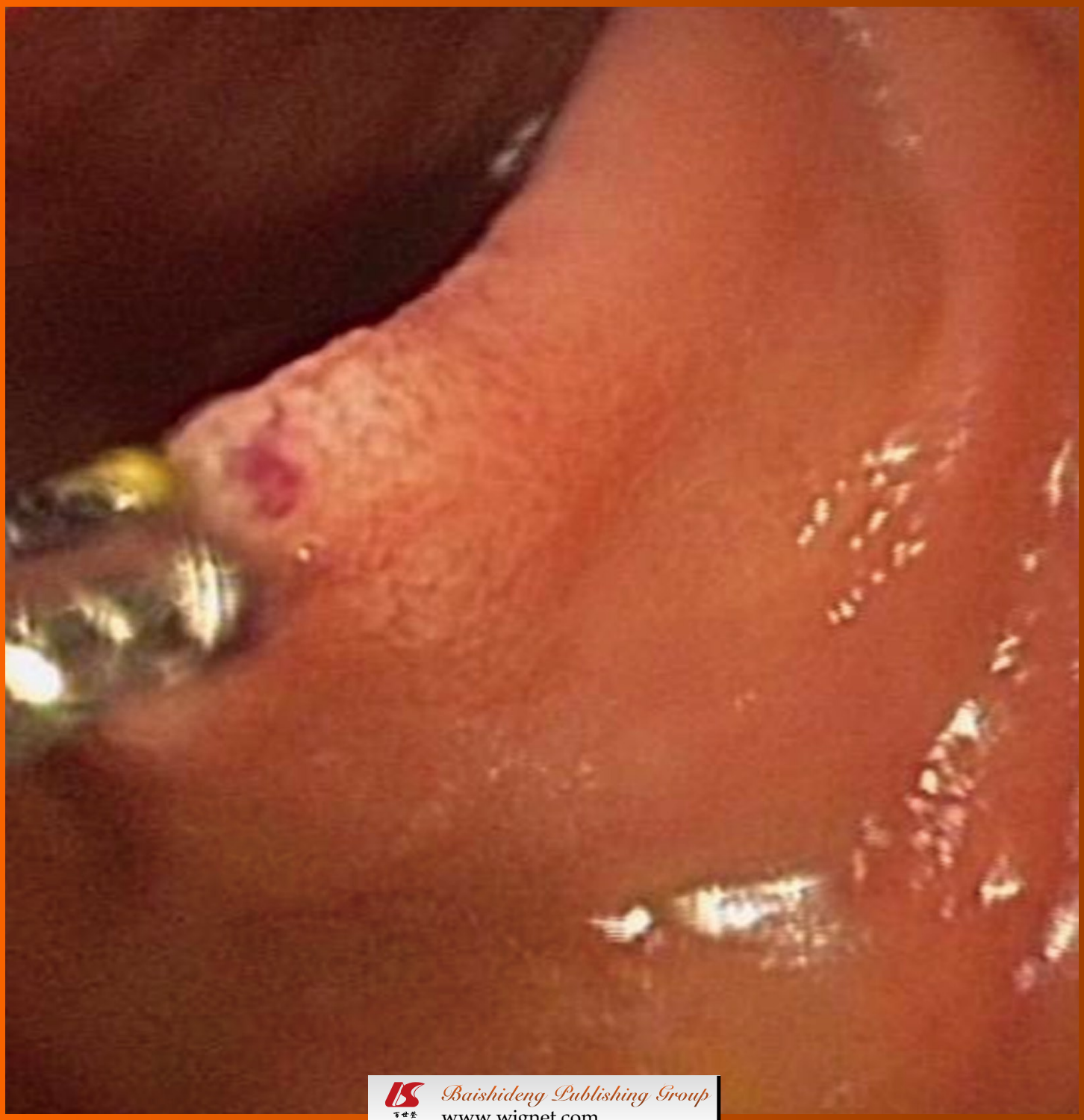

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No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: +86-10-8538-1892
Fax: +86-10-8538-1893
E-mail: baishideng@wjgnet.com
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EDITING
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Room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

Small bowel video capsule endoscopy in Crohn's disease: What have we learned in the last ten years?

Alfredo J Lucendo, Danila Guagnozzi

Alfredo J Lucendo, Danila Guagnozzi, Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso 13700, Ciudad Real, Spain
Author contributions: Lucendo AJ and Guagnozzi D contributed equally to this paper.
Correspondence to: Alfredo J Lucendo, MD, PhD, Department of Gastroenterology, Hospital General de Tomelloso, Vereda de Socuéllamos, s/n, Tomelloso 13700, Ciudad Real, Spain. alucendo@vodafone.es
Telephone: +34-926-525926 Fax: +34-926-525870
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Abstract

Since its introduction in 2001, capsule endoscopy (CE) has become the most important advance in the study of small bowel disease, including Crohn's disease (CD). This technique has been demonstrated to be superior to all other current forms of radiological investigation in detecting mucosal abnormalities of small bowel non-stricturing CD. CE has proven to be extremely useful in diagnosing CD in patients with inconclusive findings from ileocolonoscopy and x-ray-based studies. Almost half of all patients with CD involving the ileum also present lesions in proximal intestinal segments, with the small bowel being exclusively involved in up to 30% of all CD cases. Despite the widespread use of CE, several questions concerning the utility of this technique remain unanswered. The lack of commonly agreed diagnostic criteria for defining CD lesions with the aid of CE may have had an influence on the variation in diagnostic results for CE reported in the literature. The utility of CE in monitoring CD and in guiding therapy has also been proposed. Furthermore, CE could be a useful second-line technique for patients with an established diagnosis of CD and unexplained symptoms. Finally, as no threshold for CD diagnosis has been agreed upon, a severity scale of mucosal disease activity has not been universally followed. None of the available activity indexes based on CE findings has been independently validated. This article discusses several cutting-edge aspects of the usefulness of CE in CD 10 years after its introduction as a sensible method to study the small intestine.

Key words: Capsule endoscopy; Crohn's disease; Inflammatory bowel disease

Peer reviewers: Robert J Richards, MD, Gastroenterology/Hepatology, Stony Brook University HSC, Stony Brook, NY 11793, United States; Reena Sidhu, MRCP, MD, Department of Gastroenterology, Royal Hallamshire Hospital, 15 Barncliffe Road, Fulwood, Sheffield S10 4DF, United Kingdom

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INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disorder with complex phenotypes regarding age of onset, location, and disease behavior. The diagnosis of CD is based on clinical history and a physical exploration with compatible data, suspicious x-ray images, and the presence of endoscopic lesions with a compatible histology[1]. This combination of diagnostic methods is necessary because there is no single gold standard diagnostic test for CD and, therefore, no isolated finding is sufficient to diagnose this disease accurately.

The most frequent location of CD is in the terminal ileum and the colon. As such, an effective diagnosis can be made with the aid of ileocolonoscopy and biopsies in most cases. However, in one third of all CD patients the

disease is confined to the small bowel[2,3]. For many of these individuals, diagnosis and follow-up management with traditional endoscopic and radiological procedures is of limited value. In fact, the small bowel is the most difficult area to access for diagnostic purposes via endoscopy or x-rays. Capsule endoscopy (CE), a recently introduced diagnostic procedure, thus represents an extremely important technical advance in the identification of mucosal lesions in the small bowel. Initially recommended for the investigation of obscure gastrointestinal bleeding after inconclusive upper endoscopy and colonoscopy results[4],the extensive availability of CE has allowed diagnosticians to extend its use to other small bowel pathologies, including CD, malabsorption syndromes[5], some cases of abdominal pain with unclear origin[6,7], small bowel transplantation, and graft-versus-host disease[8,9].

Although it was only approved by the Food and Drug Administration in 2001, CE has already proven to be more accurate in the diagnosis of CD than radiological techniques[10-13]. The use of CE has facilitated the detection of previously unknown proximal small bowel lesions in half of all patients with a previous diagnosis of CD involving the distal ileum[14]. In addition, CE may be useful for correctly classifying patients diagnosed with ulcerative colitis and atypical features or with unclassified inflammatory bowel disease[15,16].

CE poses specific risks in patients with CD, the main complication being the retention of the capsule, defined as the failure to progress along the gastrointestinal tract (i.e. a capsule remains in the bowel for a minimum of 2 wk or even permanently, unless extracted surgically or endoscopically)[17]. Capsule retention occurs in 1% of patients with suspected CD, but retention ratios of between 4% to 6% have been reported in patients with confirmed CD[18]. A detailed clinical history for occlusive symptoms and possibly an Agile patency capsule exam should be carried out in higher risk patients as this has been demonstrated to be as safe and effective method for minimizing the risk of capsule retention[19].

USEFULNESS OF CE IN SUSPECTED CD

Several studies have been published recently on the usefulness of CE in diagnosing suspected CD patients, particularly those in whom there remains a high clinical suspicion of CD despite negative results from ileocolonoscopy and/or radiological examinations[18].

In fact, CE has proven to be superior to all current forms of radiological testing of the small intestine in detecting the mucosal abnormalities of nonstricturing CD[16,20]. It shows an incremental diagnostic yield of 20% to 40% over other diagnostic modalities such as barium studies and CT scanning, and a high negative predictive value in cases of suspected CD[21]. A review published in 2005 estimated a diagnostic yield for CD of over 70% in patients with negative or inconclusive findings from previous ileocolonoscopy and x-ray studies[18].

Nevertheless, the success rate of CE is low when performed in patients with either abdominal pain alone or with abdominal pain and diarrhea. The presence of biochemical markers of inflammation in patients with symptoms suggestive of CD as opposed to the presence of suggestive symptoms alone increases the diagnostic success rate of CE[22]. For this reason, and on the basis of ICCE consensus, patients with these symptoms plus either extraintestinal manifestations, inflammatory markers, or abnormal imaging results from SB series, CT scans, *etc*, should be considered as possible CD sufferers. Indeed, when any one of these criteria is added, the CE diagnostic success rate increases. These results were recently corroborated in a meta-analysis[23] which demonstrated that CE was superior to small bowel radiography, CT scans, and ileocolonoscopy in evaluating patients with suspected CD. There is also increasing evidence of the utility of magnetic resonance (MR) in the assessment of small bowel CD, with positive preliminary results indicating it as a frontline technique for CD diagnosis and follow up[24]. Unfortunately, comparative studies between CE and MR have not been carried out on patients suspected of having CD[23]. Larger prospective studies are thus needed to define the proper place of CE in the diagnostic algorithm for CD.

CE findings specific to CD

One of the main problems which arose after the spread of CE as a diagnostic tool was the lack of commonly accepted terminology to describe endoscopic findings during explorations. This led to the proposal of structured terminologies in order to standardize the description and definition of CE results[25,26].

This is especially important since previous studies which used various diagnostic criteria to define CD lesions in the small bowel produced extremely varied results, probably due in large part to the absence of a unified terminology. CD-associated lesions described using CE results are thus in great need of more precise definitions and of commonly accepted defining criteria as, currently, the definition of CD through CE could, to some extent, be considered arbitrary[27].

Currently, the most widely and commonly used diagnostic criterion for CD is the presence of more than 3 ulcerations in the absence of nonsteroidal anti-inflammatory drugs (NSAIDs), as proposed by Mow *et al*[28] in 2004. In addition, the location and length of the intestinal segments involved and the topographical distribution of lesions along the small intestine should be considered as relevant diagnostic criteria for CD since the number of ulcers tends to increase progressively as CE approaches the distal ileum[29]. Using the presence of 3 or more ulcers to indicate an abnormal CE result, a recent article set out to define the utility of CE in patients with suspected CD after inconclusive CT scans, small bowel follow-through, and endoscopy. The authors observed a sensitivity of 77% and a specificity of 89%, with a positive predictive value of 50% and a negative predictive value of 96%[30].

Voderholzer *et al*[31] suggested that finding more than 10 aphthae in a CE examination was also strongly

suggestive of CD. The presence of several small alterations such as villous edema, villous denudation (loss of villi), erosions, erythema, vasculitis, cobblestone appearance, nodular lymphoid hyperplasia, and lymphangiectasia have been considered to be early manifestations of CD in some series[12,20,22,32,33], but not in others[34-36]. The finding of previously undetected stenosis has also been considered an important diagnostic criterion by some authors[36-38].

The various CE-based criteria outlined above are not considered to be of equal value in diagnosing CD. Thus, while ulcers and multiple aphthae may directly lead to a CD diagnosis in a suitable clinical context, an isolated simple mucosal edema or mucosal erythema is probably insufficient to establish a clear diagnosis. Different observers report that the discovery of mucosal breaks such as ulcers and aphthae (which can be described as 'major findings'), as well as of circumferentially ulcerate stenosis, have a high diagnostic correlation[37,39] while the presence of more subtle lesions ('minor findings') is less well correlated with a diagnosis of CD[39]. Nevertheless, observing only 'minor findings' in patients clinically and/or analytically suspected of having CD should not definitively exclude a diagnosis of CD, since such patients can show clinical improvement when treated for CD[20]. This further obliges medical professionals to develop standardized, prospectively validated diagnostic criteria and to perform more follow-up studies.

CD-like findings on CE

It is important to note that the accuracy of CE in diagnosing CD is limited by the lack of specificity of mucosal findings. In fact, up to 14% of healthy subjects have mucosal breaks and erosions in the small bowel[40], which only serves to bolster the idea that CE mucosal findings alone are insufficient to confirm a diagnosis of CD.

It is also worth noting that not all mucosal breaks found in the small intestine are due to CD. Several lesions properly described as CD are actually non-specific and can be found in a large proportion of patients treated with NSAIDs[41,42] as well as in patients with other types of small bowel disorders. For this reason, recent intake of NSAIDs should be excluded in all patients undergoing CE, and, if possible, such therapy should be interrupted several weeks before the CE exploration to ensure accuracy. Such measures would help improve the predictive values of the technique.

CE AS A CD MONITORING TECHNIQUE

CE has also been proposed as a method for determining the extent and severity of lesions, postoperative recurrence, and mucosal healing under therapies in patients with an established CD diagnosis. Because CE is also more sensitive than x-ray-based techniques in monitoring CD, some authors have proposed that CE be used to assess the activity or recurrence of the disease, thereby limiting a patient's exposure to unnecessary radiation[16]. However, the exact role of CE for this indication has yet to be established[27]. In fact, some of the available data are contradictory and in clinical practice, indications for CE are limited to patients with a proven diagnosis of CD.

CE and mucosal healing

The major goals for medical therapies to combat CD should include modifying the clinical course, halting the progression of the disease, and avoiding the need for surgery, hospitalization, and the use of corticosteroids. In this context, early healing of the intestinal mucosa has recently been proposed as the primary objective of medical therapies[43]. In fact, early healing has been demonstrated to be a strong predictor for improved long term outcome in CD, with fewer complications and surgical interventions[44]. CE may have a potential role in assessing mucosal healing after drug therapy[27], but it is still unclear whether the presence of endoscopic lesions in the small bowel mucosa identified with the aid of CE in CD patients is directly related to the activity of the disease itself. It remains to be seen whether CE findings can lead to a change in the therapeutic management of CD patients[45] similar to that of ileocolonoscopy during CD flare-ups. Part of the problem is that the clinical response does not always correlate with mucosal healing in patients with small bowel CD[46].

A study published by Mehdizadeh *et al*[29] in 2010, retrospectively analyzed 147 CE procedures performed on 134 patients who had previously been diagnosed with CD and who exhibited symptoms suggestive of active disease. CE identified lesions indicative of activity in about half the symptomatic patients, with the number of lesions progressively increasing as the CE approached the distal ileum. This study concluded that a clear correlation between symptoms and endoscopic lesions cannot be established in CD patients since symptoms suggesting activity may occur in the absence of small bowel lesions.

In contrast, another study by Lorenzo-Zúñiga *et al*[47] showed that therapy was changed in 64% of patients previously diagnosed with CD after a CE exam was performed due to anemia, abdominal pain, or because the location of the disease needed to be reevaluated. These results indicate that CE findings can bring about a change in therapeutic approach in a large number of CD patients. However, further research must be done on the usefulness of CD in monitoring mucosal healing during the natural course of small bowel CD[45].

CE in assessing postoperative recurrence of CD

Diagnosis of post-operative recurrence may be based on clinical symptoms and/or endoscopic findings. To date, ileocolonoscopy is viewed as the gold standard for defining the presence and severity of morphologic recurrence and predicting the clinical course of the disease. Recent studies have shown that performing a CE exam 6 to 12 mo after surgery seems to have comparable sensitivity, specificity, and positive/negative predictive values to ileocolonoscopy in diagnosing post-operative recurrence of CD[48,49]. The advantage of CE is that it has higher tolerability and a better probability of reaching the neoileum, which is not always accessible *via* colonoscopy.

Table 1 Lewis capsule endoscopy scoring table[38]

	Regions[1]				
	Duodenum	Jejunum	Proximal ileum	Distal ileum	
	Lesions				
	Number	Distribution pattern	Longitudinal extent	Shape	Size (by circumference)
Erythema		Localized = 1 Patchy = 2 Diffuse = 3	Short segment = 1 Long segment = 2 Whole region = 3		
Edema		Localized = 1 Patchy = 2 Diffuse = 3	Short segment = 1 Long segment = 2 Whole region = 3		
Nodularity	Single = 1 Few = 2 Multiple = 3	Localized = 1 Patchy = 2 Diffuse = 3	Short segment = 1 Long segment = 2 Whole region = 3		
Ulcer	Single = 3 Few = 5 Multiple = 7	Localized = 3 Patchy = 5 Diffuse = 7	Short segment = 1 Long segment = 2 Whole region = 3	Circular = 3 Linear = 5 Irregular = 7	< ¼ = 3 ¼ - ½ = 5 > ½ = 7
Stenosis	None = 0 Single = 10 Multiple = 20	Traversed = 10 Not traversed = 20	Nonulcerated = 5 Ulcerated = 10		

[1]Score by region by adding points listed.

However, the value of CE in diagnosing post-operative recurrence in the ileum and particularly in the jejunum has not yet been systematically studied. Further studies are thus needed before a definitive conclusion can be reached.

Indexes for evaluating the severity of CD

Once CE had been widely accepted as a good diagnostic tool, several activity indexes were developed to assess the severity and extension of small bowel CD. The various CE proposed indexes primarily assess 4 parameters to define CD severity: (1) the presence of mucosal lesions that are felt to explain the patient's reasons for referral (including disturbances in villous appearance and presence of ulcers); (2) the size of ulcers; (3) the location and extension of ulcers; and (4) the presence of stenosis with or without mucosal lesions. Apart from these parameters, each index has its own particularities.

The first index created to evaluate CD severity was proposed in 2004 by Kornbluth *et al*[38]. It makes use of five parameters previously defined in structured terminology developed specifically for CE: erythema, edema, nodularity, ulcers, and stenosis. This Lewis Capsule Endoscopy Score[38] exhaustively analyses each parameter over four small bowel segments (duodenum, jejunum, proximal ileum, and distal ileum) (Table 1), adding up the individual points to obtain the final score by region. The complete score highlights the distribution and longitudinal extent of lesions found through CE.

In 2005, Gralnek *et al*[39] carried out a study in order to develop and test a simple, user-friendly CE scoring index for CD activity based on the previously proposed endoscopic findings associated with the disease. These were individually scored as three equal parts (or tertiles) into which the small bowel transit time was divided (Table 2). The final scoring index included three endoscopic variables among which the authors found excellent inter-observer agreement: villous edema, ulcers, and stenosis. Index parameters are measured by number, longitudinal extent, and additional descriptors. Using these parameters, the authors established a score ranging from 8 to 4800 points: a score < 135 was designated as normal or clinically insignificant mucosal inflammatory change while a score between 135 and 790 was considered to indicate mild CD and a score ≥ 790 indicated moderate to severe CD.

In 2008, a new activity index was developed by Gal *et al*[37]. The CECDAI (Capsule Endoscopy Crohn's Disease Activity Index) (Table 3) uses a methodology similar to that of the previously described index, but with two important differences. First, small bowel transit time is divided into proximal and distal parts. In both the proximal and distal bowel, three parameters are calculated separately by multiplying the inflammation score (A) by the extent-of-disease score (B) and adding the stricture score (C). The second particularity of this index is that villous appearance and ulcers are considered to be opposite extremes of a wide range of inflammation rather than as independent variables, as was the case in the Gralnek index. Furthermore, and in contrast to both of the aforementioned indexes, the number of lesions is not considered in calculating the score. In the case of identifying different inflammatory lesions in the same bowel segment (i.e. moderate edema and a large ulcer in the distal section), the more serious lesion is used for calculating the index. The same occurs with regard to the stricture index.

An important limitation in the use of CE severity indexes is that none of them has been independently validated and no studies comparing the different indexes have been conducted to date. Another important disadvantage of the use of indexes in CD is that clinical indexes do not

Table 2 Parameters and weightings for the capsule endoscopy scoring index[39]

	Parameters	Number	Longitudinal extent	Descriptors
First tertile	Villous appearance	Normal = 0 Edematous = 1	Short segment = 8 Long segment = 12 Whole segment = 20	Single = 1 Patchy = 14 Diffuse = 17
	Ulcer	None = 0 Single = 3 Few = 5 Multiple = 10	Short segment = 8 Long segment = 12 Whole segment = 20	< ¼ = 9 ¼ to ½ =12 > ½ = 18
Second tertile	Villous appearance	Normal = 0 Edematous = 1	Short segment = 8 Long segment = 12 Whole segment = 20	Single = 1 Patchy = 14 Diffuse = 17
	Ulcer	None = 0 Single = 3 Few = 5 Multiple = 10	Short segment = 8 Long segment = 12 Whole segment = 20	< ¼ = 9 ¼ to ½ = 12 > ½ = 18
	Villous appearance	Normal = 0 Edematous = 1	Short segment = 8 Long segment = 12 Whole segment = 20	Single = 1 Patchy = 14 Diffuse = 17
	Ulcer	None = 0 Single = 3 Few = 5 Multiple = 10	Short segment = 8 Long segment = 12 Whole segment = 20	< ¼ = 9 ¼ to ½ =12 > ½ = 18
Third tertile	Villous appearance	Normal = 0 Edematous = 1	Short segment = 8 Long segment = 12 Whole segment = 20	Single = 1 Patchy = 14 Diffuse = 17
	Ulcer	None = 0 Single = 3 Few = 5 Multiple = 10	Short segment = 8 Long segment = 12 Whole segment = 20	< ¼ = 9 ¼ to ½ =12 > ½ = 18
Stenosis-rated for whole study	Stenosis	None = 0 Single = 14 Multiple = 20	Ulcerated = 24 Non-ulcerated = 2	Traversed = 7 Not traversed = 10

Table 3 Capsule endoscopy Crohn's disease activity index scoring system[37]

	Proximal	Distal
A. Inflammation score	0 = None 1 = Mild to moderate edema/hyperemia/denudation 2 = Severe edema/hyperemia/denudation 3 = Bleeding, exudates, aphthae, erosion small ulcer (< 0.5 cm) 4 = Moderate ulcer (0.5 cm - 2 cm), pseudopolyp 5 = Large ulcer (> 2 cm)	
B. Extent of disease score	0 = None 1 = Focal disease (single segment) 2 = Patchy disease (multiple segments) 3 = Diffuse disease	
C. Narrowing (stricture)	0 = None 1 = Single-passed 2 = Multiple-passed 3 = Obstruction	
Segmental score = A × B + C Total score = (A1 × B1 + C1) + (A2 × B2 + C2)		

estimate the severity of mucosal lesions while endoscopic indexes only assess small bowel mucosal changes, not necessarily their effect on the disease. Indeed, the main advantage of having different types of indexes available is their prognostic value, as they allow medical professionals to observe the changes caused by the disease over time.

CONCLUSION

CE represents the most important technical advance in the diagnosis of small bowel diseases and constitutes an irreplaceable method for studying CD. However, difficulties in clearly establishing commonly accepted diagnostic criteria and the possibility of finding typical lesions of CD without histological confirmation in subjects not suffering from the disease have limited the diagnostic success of this method. Diagnostic yield of CE in CD increases when finding are interpreted within a suitable clinical and analytical context. Some studies suggest that CE may be a useful technique for monitoring CD as well as an interesting tool in guiding treatment. Proposed activity indexes could be useful for predicting the prognosis of CD by assessing mucosal changes caused by the disease or the therapy, although further research should be carried out to confirm this potential.

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TOPIC HIGHLIGHT

Konstantinos Triantafyllou, MD, PhD, *Series Editor*

Endoscopic retrograde cholangiopancreatography training in the United Kingdom: A critical review

Peter Isaacs

Peter Isaacs, Gastroenterology Unit, Victoria Hospital, Blackpool, FY38NR, United Kingdom
Author contribution: Isaacs P contributed solely to this work.
Correspondence to: Peter Isaacs, MD, Gastroenterology Unit, Victoria Hospital, Blackpool, FY38NR, United Kingdom. dr.isaacs@bfwh.nhs.uk
Telephone: +44-01253-303614 Fax: +44-01253-306936
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Abstract

Endoscopic retrograde cholangiopancreatography training used to be in virtually all district general hospitals, resulting in a large number of trainees with an inadequate case load and achieving poor levels of skill. Training is now restricted to a small number of trainees working in approved units. Continuous audit of outcomes and the appointment of a training lead in the unit are essential. Use of the global rating scale helps clinicians advise hospital administration on the priorities for a quality training program.

Key words: Endoscopic retrograde cholangiopancreatography; Endoscopy training; Endoscopy quality and safety

Peer reviewer: Majid Abdulrahman Al Madi, MBBS, FRCPC, Gastroenterology Division, McGill University Health Center, McGill University, Royal Victoria Hospital, 687 Pine Ave West, Montreal QC H3A 1A1, Canada

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) remains an important tool in the management of biliary and pancreatic disease. Although supported by endoscopic ultrasound (EUS) and magnetic resonance imaging (MRI), ERCP is still frequently required to treat biliary diseases, often in acutely ill and elderly patients. High standards of training and practice are very necessary.

Gastrointestinal endoscopy in the health services of the UK have undergone major investment and reforms in the last ten years driven by the need to massively expand the provision of endoscopy and improve the quality of the service. The investment has been successful in that the initial targets for waiting times have been achieved, resulting in more stringent targets. The reforms of service provision have been paralleled by reform of training systems.

The quality and safety of ERCP was examined by the national confidential enquiry into patient outcome and death (NCEPOD)[1] in 2004 as part of its examination of deaths after therapeutic endoscopy. It found that 68% of ERCP examinations were futile and that complications were unacceptably high.

This prompted the british society for gastroenterology (BSG) to undertake a survey of ERCP practice in the UK in 2005[2] which found that there were some shortcomings of clinical practice and training. Of the 5264 ERCPs performed by 213 endoscopists, 94% were with therapeutic intent and in only 70% was the therapeutic aim was achieved. There was a complication rate of 5.1%, including a 1.6% incidence of pancreatitis and a procedure-related mortality of 0.4%. Patient selection was appropriate. The group concluded that the number of operators and possibly the number of units performing ERCP was too high and that a small number of trainees should be selected and given focused programs. They recommended that the selected trainees should have a firm intention of providing ERCP services after the completion of their training. The working group predicted a

need for 0.9 ERCP procedures per 1000 population per annum and, given the number of units requiring at least 2 ERCPists and the predicted retirement rate, concluded that about 30 per annum should complete ERCP training in the UK.

In the USA a similar situation was pertaining, with a majority of trainees concluding that their training had been inadequate even though they were intending to practice ERCP[3].

Standards for training and service quality in the UK are set by the royal colleges joint advisory group (JAG)[4]. Comprising of representatives from the Royal Colleges of Physicians, Surgeons, Radiologists and General Practitioners, JAG advises the department of health (DoH) and thereby the national health service (NHS) on the provision of endoscopic services. JAG certifies the competence of endoscopists.

The DoH appointed Dr Roland Valori as National Endoscopy Lead and he introduced GRS[5] as the self-assessment tool for endoscopic services. The JAG has adopted the global rating scale (GRS) as the structure for their assessment. Using GRS, units gather documentary evidence to prove their quality. The four GRS domains are clinical quality (scores for consenting, safety, comfort, quality of the procedure, appropriateness, communication of findings), quality of patient experience (equality of access, patient experience, booking and choice, privacy, aftercare, feedback), training (the training environment and opportunities, trainers, assessment, equipment and educational materials) and the workforce (skill-mix, orientation, appraisal, caring for staff). JAG inspection of endoscopy services has had real effects. Failure to receive approval would have disastrous results on the income of an endoscopy unit, both *via* a negative effect on patient referral numbers and on staff because trainees can only be allocated to approved units.

The JAG has set standards for units performing ERCP: a unit is required to have all the standard ERCP accessories, hemostasis equipment and an emergency lithotripter present for all procedures.

The role of ERCP must be agreed in a local protocol, including the use of prophylactic antibiotics, a consultant must write that ERCP is indicated and all patients must be assessed by suitably trained staff. A contemporaneous report of the ERCP must be written in the record and complications recorded for audit.

The staffing for the procedure must be a minimum of 3 appropriately trained assistants, usually gastroenterology nurses.

Auditable records for the unit must show less than 10% of procedures without therapeutic intent (less now with EUS and MRI), decompression of obstructed bile duct in > 80% and, if ERCP failed, decompression by alternative method within 5 d (within 1 d if severe cholangitis present). The complications should be < 1% transfusion-requiring sphincterotomy bleeding, < 2% perforation, < 5% pancreatitis and procedure-related mortality of < 1%.

The initial accreditation inspection of a unit is rigorous and is preceded by a so-called pre-JAG visit by a local gastroenterologist who advises on the potential shortcomings of the unit. This is useful in helping the unit to acquire adequate resources from their hospital management, including equipment or administrative staff to ensure that the unit has the best chance of passing the JAG inspection. If a unit is clearly in the process of development, a provisional accreditation may be given and the inspection team will visit again after a 6 mo interval to ensure that the standards are met. Once full accreditation has been achieved, the unit reports its GRS ratings to JAG which may decide on a re-inspection after a longer interval of up to 5 years.

Growing out of the JAG and GRS initiatives, the NHS recognized the need for a national endoscopy training system (NETS) which serves the needs of all staff including endoscopists, nurse endoscopists, endoscopy nurses and endoscopy unit administrators.

Units wishing to establish themselves as training units in countries which do not yet have training and a service quality program should certainly consider appointing an endoscopy training lead and an audit program. The endoscopists must all use the electronic endoscopy management system (EMS) and agree on and use a robust system for the recording of complications. Such records are difficult to achieve and only are meaningful if fully agreed by the ERCPists of a unit. Because ERCP may be performed on patients who are day cases (admitted to the hospital for a period of 8 h only) or on patients in surgical or geriatric wards as well as in the gastroenterology service, complications such as respiratory infection and pancreatitis may not always be reported to the endoscopists. Ideally all ERCP patients should be contacted or seen 30 d after the procedure. Many units depend on case notes retrieval and review to obtain outcome data which would be more efficiently analyzed if it had been entered in the EMS contemporaneously. Responsibility for this rests with the trainer endoscopists who could delegate data input to the trainee.

TRAINING OF ENDOSCOPISTS

For trainees there have also been major changes. Specialty training, including that in gastroenterology, is regulated by the general medical council (GMC) which, since April 2010, has incorporated the Postgraduate Medical Education Training Board.

The GMC has the authority to approve training programs which are delivered in the NHS under the direction of the Dean of Postgraduate Medical Education. The training program delivers the competences laid out in a specialty curriculum approved by the joint committee on higher medical training (JCHMT)[6] which consults the Royal Colleges and the British Society for Gastroenterology.

Postgraduate training changed in 2006 by the DoH initiative modernising medical careers (MMC)[7], which

moved to widen the experience in early postgraduate years with a compulsory 2 year foundation program (FY1-2), then selection into a 2 year core medical or surgical training (CMT1-2), followed by competition for 5 years as a Specialty Registrar (StR1-5). CMT and StRs rotate through hospitals in one of the 12 UK Deaneries. The Deanery establishes a specialty training committee (STC) for each specialty.

After a disastrous start of MMC occasioned by a complex selection process further marred by computer system failures, the mechanisms are now established. However, shift work enforced by the European Working Time Directive together with MMC has sometimes had adverse effects on the amount of time the trainee has in endoscopy.

UK trainees in gastroenterology are StRs training to both the specialty training curriculum in gastroenterology and the general internal medicine (GIM) curriculum laid down by the JCHMT[6]. StRs are required to undergo an annual review of competence progression (ARCP) with their STC. At the third year, the Specialty Training Committee of the Deanery will select the required number from the StRs who wish to undergo ERCP training. Within the endoscopy units of a Deanery, there will be other staff members undergoing ERCP training, such as other gastroenterologists on the permanent staff and visiting fellows.

It is the responsibility of the Endoscopy Training Lead of the unit to ensure that anyone undergoing training in their unit has a training plan which includes learning objectives and assessments. After their 5 years of gastroenterology/GIM training, StRs pursuing the ERCP track may also obtain further experience and skills as an Endoscopy Fellow in a UK or foreign unit. The BSG stakeholder group recommended that such fellowships should be of 6 to 12 mo of 7-8 sessions of highly specialized endoscopy per week.

The group also recommended that the number of trainees should be reduced and at present there are 2 in each of the 16 deaneries. Trainees now decide whether they wish to be considered for the ERCP training track to match an interest in hepatobiliary disease or to take an interest, for example in colonoscopy or nutrition, as special subspecialty interests. This has been accepted by UK trainees as a practical way to ensure that they all have a special interest and that training in these is kept to a high standard.

The group did not recommend that trainees participate in a mandatory workshop on ERCP technique which has been shown to reduce training time in the USA[8] and China[9]. The UK has not introduced computerized endoscopy simulators which have also proved to be an effective way of rapidly increasing the basic competences of trainees[10].

The number of UK SpRs undergoing official ERCP training has certainly reduced from approximately 50 to 25 with a consequent improvement in the clinical experience of trainees. Anecdotal evidence suggests that the rationalization of ERCP training has produced more satisfied trainees and proof of their ability may be evident in the next national audit of ERCP.

For a unit to be accredited as a training unit, it would have to deliver a minimum of 200 ERCPs per annum (either within the unit or as a network of units currently taking trainees) including sufficient complex cases to ensure breadth of training.

The trainers in ERCP should be personally carrying out at least 75 procedures per annum and have continuous audit showing a therapeutic procedure completion rate of > 90% and a complication rate of < 5%. At least once every 5 years, trainers would be expected to participate in an ERCP training course as an observer or a member of faculty.

At the completion of their StR training, trainees will be awarded certificates of completion of training (CCTs) in GIM and gastroenterology. A CCT can only be awarded to a doctor who has been allocated a National Training Number (NTN) by competitive appointment to a training program designed to lead to the award of a CCT and who has successfully completed that program.

Their competence in endoscopy is certified by the JAG which receives the evidence of competence from the endoscopy unit training lead supported by a log book of all ERCP endoscopic procedures performed. JAG had previously specified a minimum number of ERCPs but from 2010 the requirement is competence rather than number of procedures.

Assessment of competence of the trainee in performing ERCP is recorded by completing directly observed procedural skills (DOPS) evaluation forms during the training lists. The DOPS process evaluates the trainee under 4 headings: consent, safety and sedation, insertion, diagnostic and therapeutic ability. The assessor also rates the difficulty of the case. The trainee is given feedback on their technique during the list and in writing on the DOPS form. At the end of training, a so-called summative DOPS must be performed by two ERCP trainers who are not the trainee's usual trainer to certify competence in basic ERCP. The trainee must produce a record certified by the supervisor which, for provisional JAG accreditation, should show a complication rate (death, transfusion-requiring hemorrhage or perforation) of < 5%, satisfactory completion of intended therapeutic procedure of > 80% and more than 75 procedures performed in the last 12 mo.

The endoscopists may then proceed into "continued practice" during which the same minimum standards must be achieved. In continued practice, the supervisor must be available in the endoscopy unit for the next 50 procedures, within the hospital for the next 50 and there must be "targeted training" for complex cases, an annual peer review with a summative DOPS by consultant trainers over four cases and then full JAG certification is granted. After full certification, the ERCPist works independently but should maintain continued endoscopic professional development which would entail attending a master class or an ERCP training course as a member of faculty every three years.

It remains to repeat the national audit and to assess the effects of the reforms.

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TOPIC HIGHLIGHT

Konstantinos Triantafyllou, MD, PhD, *Series Editor*

Deep sedation for endoscopic retrograde cholangiopacreatography

Irene G Chainaki, Maria M Manolaraki, Gregorios A Paspatis

Irene G Chainaki, Maria M Manolaraki, Departments of Anesthesiology, Benizelion General Hospital, Heraklion, Crete 71409, Greece
Gregorios A Paspatis, Departments of Gastroenterology, Benizelion General Hospital, Heraklion, Crete 71409, Greece
Author contributions: Chainaki IG and Paspatis GA participated directly in manuscript writing; and Manolaraki MM provided supportive work.
Correspondence to: Gregorios A Paspatis, MD, Department of Gastroenterology, Benizelion General Hopsital, L.Knossou, Heraklion, Crete 71409, Greece. paspati@admin.teiher.gr
Telephone: +30-2810-368017 Fax: +30-2810-368017
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Chainaki IG, Manolaraki MM, Paspatis GA. Deep sedation for endoscopic retrograde cholangiopacreatography. *World J Gastrointest Endosc* 2011; 3(2): 34-39 Available from: URL: http://www.wjgnet.com/1948-5190/full/v3/i2/34.htm DOI: http://dx.doi.org/10.4253/wjge.v3.i2.34

Abstract

Sedation and analgesia comprise an important element of unpleasant and often prolonged endoscopic retrograde cholangiopacreatography (ERCP), contributing, however, to better patient tolerance and compliance and to the reduction of injuries during the procedure due to inappropriate co-operation. Although most of the studies used a moderate level of sedation, the literature has revealed the superiority of deep sedation and general anesthesia in performing ERCP. The anesthesiologist's presence is mandatory in these cases. A moderate sedation level for ERCP seems to be adequate for octogenarians. The sedative agent of choice for sedation in ERCP seems to be propofol due to its fast distribution and fast elimination time without a cumulative effect after infusion, resulting in shorter recovery time. Its therapeutic spectrum, however, is much narrower and therefore careful monitoring is much more demanding in order to differentiate between moderate, deep sedation and general anesthesia. Apart from conventional monitoring, capnography and Bispectral index or Narcotrend monitoring of the level of sedation seem to be useful in titrating sedatives in ERCP.

INTRODUCTION

Sedation and analgesia comprise an important element of endoscopic procedures. They reduce pain, discomfort and stress in patients undergoing unpleasant and prolonged procedures such as endoscopic retrograde cholangiopacreatography (ERCP) and contribute to better patient tolerance and compliance[1]. Moreover, they reduce the danger of injuries during ERCP due to inappropriate co-operation and facilitate the endoscopist's task[2].

According to the american society of anesthesiologists (ASA)[3] (Table 1), sedation is defined as a continum of progressive impairment in consciousness ranging from minimal to moderate, deep sedation and general anesthesia. This continuum indicates the concept that patients can move in a fluid manner between the states of sedation[3]. Furthermore, moving from a state of consciousness to deep sedation is a dose-related continuum that depends on patient response and, consequently, the state originally intended might not be the one ultimately achieved[4-6]. This is due to a wide variability in the pharmacokinetics and pharmacodynamics of sedative drugs. Thus, a standard dose of sedatives may produce undersedation in some patients and oversedation in others[4].

Table 1 American society of anesthesiologists physical status classification system

ASA PS	Health status	Comments-examples
1	Normal healthy patient	No organic, physiological or psychiatric disturbance; excludes the very young and very old; healthy with good exercise tolerance
2	Patients with mild systemic disease	No functional limitations; has a well-controlled disease of one body system; controlled hypertension or diabetes without systemic effects, cigarette smoking without chronic obstructive pulmonary disease (COPD); mild obesity, pregnancy
3	Patients with severe systemic disease	Some functional limitation; has a controlled disease of more than one body system or one major system; no immediate danger of death; controlled congestive heart failure (CHF), stable angina, old heart attack, poorly controlled hypertension, morbid obesity, chronic renal failure; bronchospastic disease with intermittent symptoms
4	Patients with severe systemic disease that is a constant threat to life	Has at least one severe disease that is poorly controlled or at end stage; possible risk of death; unstable angina, symptomatic COPD, symptomatic CHF, hepatorenal failure
5	Moribund patients who are not expected to survive without the operation	Not expected to survive > 24 h without surgery; imminent risk of death; multiorgan failure, sepsis syndrome with hemodynamic instability, hypothermia, poorly controlled coagulopathy
6	A declared brain-dead patient who organs are being removed for donor purposes	

ASA: American society of anesthesiologists.

Minimal sedation (anxiolysis) signifies a drug-induced state at which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are unaffected. At a moderate level of sedation (conscious sedation), the patient is able to respond purposefully to verbal commands or tactile stimulation. At this level of sedation, spontaneous ventilation is adequate and no interventions are required to maintain a patent airway. Cardiovascular function is usually maintained. At a deep sedation level, the patient responds only to repeated or painful stimuli but keeps intact spontaneous respiration and protective reflexes. Spontaneous ventilation may be inadequate and the patient may require assistance to maintain a patent airway. Cardiovascular function is usually maintained but may be compromised. The level of care for patients on deep sedation must be the same as general anesthesia[3]. Non responding patient to painful stimuli and loss of protective airway reflexes characterizes general anesthesia. Cardiovascular function may be impaired.

Since the first report[7] of the cannulation of major papilla endoscopically in 1968, ERCP has evolved from being a simple diagnostic procedure to becoming a therapeutic one of increasing duration and complexity, requiring a high degree of patient co-operation. Reports[8] have underlined that those complications such as duodenal perforation and pancreatitis result as a consequence of poor patient cooperation manifested by restlessness and anxiety during the procedure. Moreover, the spectrum of therapeutic applications of ERCP continues to expand, enabling treatment of more complex pancreatobiliary disease. The requirement for open surgical and percutaneous techniques has diminished and almost all biliary diseases are now amenable to endoscopic treatment. As a result, many patients who were previously considered inoperable or with life-threatening conditions are opting for therapeutic ERCP. Thus, sedation for therapeutic ERCP should be not only inevitable but also appropriate, effective and safe.

DECIDING ON THE LEVEL OF SEDATION

Successful performance of ERCP has been achieved with patients in either moderate or deep sedation or general anesthesia. Deciding on whether to use moderate, deep sedation or general anesthesia depends on patient characteristics, procedure demands and existence of the required structural conditions[9,10]. Common practice is the performance of ERCP under conscious sedation so most of the studies are targeted to a moderate level of sedation. Nevertheless, Patel *et al*[6] reported that even when the target level of sedation was a moderate one, deep sedation episodes of all sedation-level observations occurred in 35% for ERCP while they occurred at least once in 85%. ERCP was recognized as an independent risk factor of deep sedation.

General anesthesia is usually administered during ER CP after prior attempts using conscious sedation have failed[11,12]. A study by Raymondos *et al*[12] assessed the indications for carrying out ERCP examinations under general anesthesia or conscious sedation. Patients with primary sclerosing cholangitis, liver transplants and those in whom painful dilations were planned received general anesthesia more frequently while conscious sedation was provided more frequently in patients with neoplasms and cholelithiasis. The failure rate for ERCP was double under conscious sedation in comparison with general anesthesia (14% *vs* 7%). This was mainly due to inadequate sedation. For patients in whom ERCP had failed under conscious sedation, a repeated procedure under general anesthesia had a success rate of 83%. A large retrospective analysis from Germany[12] found that painful dilatations were performed more frequently on patients under general anesthesia and that under conscious sedation the ERCP failure

rate was double that of general anesthesia. In another large study from the USA[13], it was noted that the overall complication rate associated with therapeutic interventions during ERCP was significantly lower in patients who had received general anesthesia. It was thought that patient immobility and duodenal aperistalsis due to general anesthesia made the procedure technically easier and contributed to a lower complication rate. Conscious sedation seems to be adequate for octogenarians[14,15].

Despite all of this, ERCP under general anesthesia has several limitations. The procedure is often prolonged as a result of extra time required for patient preparation, induction of anesthesia, tracheal intubation and recovery. In addition, the cost per procedure may be higher. However, the efficacy of ERCP with general anesthesia supports a continued preference for general anesthesia rather than conscious sedation when complex and painful interventional ERCP procedures are planned. One group from New York[16] looked at the feasibility of using the laryngeal mask airway (LMA) instead of the endotracheal tube during ERCP. LMA use was associated with shorter extubation time compared with endotracheal (7.2 min *vs* 12 min) and there were no airway complications. A therapeutic duodenoscope was passed beyond the LMA with little or no resistance in all cases. Nevertheless, the use of LMA in the prone position requires more care because it can easily be removed by manipulation during the procedure and it does not secure the patient's airway in case of aspiration of gastric fluids.

Deep sedation, on the other hand, is an alternative that is used by specific centers[15,17] under anesthesiologist supervision instead of general anesthesia. Deep sedation has the advantage of offering the extra time required for general anesthesia and better procedure conditions in relation to conscious sedation. Moreover, pharyngeal reflexes are kept intact, preserving some protection against aspiration. The major risks in deep sedation constitute unintended general anesthesia and apnea. Studies about ERCP performed under deep sedation[15,18] target the reduction of the minimum effective dose for deep sedation and improvement of sedation and ventilation monitoring using devices such as Bispectral index (BIS) and capnography respectively. The sedative agent used in deep sedation is propofol, either alone[18] or in combination with midazolam[15] and remifentanil[19]. A combination of propofol and midazolam significantly reduces the total propofol amount required and consequently reduces the risk of apnea but prolongs recovery time in association to propofol alone. In another study by Paspatis *et al*[18], BIS monitoring also reduced the total propofol dose required. Deep sedation holds some advantages over general anesthesia as far as required time and cost are concerned and is a good alternative to general anesthesia for ERCP. Naturally, the risk of aspiration is greater as the airway is not secured. Therefore, patients with increased risk of aspiration (pregnant women, patients with full stomach, active bleeding or ascites) should have their airway secured with an endotracheal tube. Also, the presence of an anesthesiologist is still a limiting factor. According to Athens international statements[20], ASA Ⅰ, Ⅱ and many Ⅲ patients can be safely sedated to the level of conscious sedation by nurses qualified in cardiopulmonary resuscitation as far as OGD and colonoscopy procedures are concerned but there are no data for deep sedation by nurses in ERCP.

DECIDING ON THE AGENT

Debate over the ideal sedative agent and dosage regimen continues. The most commonly used sedatives in ERCP are benzodiazepines, opiates, propofol and droperidol[21] as monotherapy or in combination. Ketamine has also been used in difficult to sedate patients[22]. Midazolam, either as the only agent or in combination with an opiate such as meperidine, is the benzodiazepine mostly used because of the shorter duration of action and better amnesic properties compared with diazepam. Nevertheless, the synergistic sedation caused by this combination increases the duration of the effects of these drugs, the likelihood of ventilatory depression and prolongs recovery time[23,24]. Moreover, sedation with benzodiazepines is unsuitable for alcoholic and stressed patients as well as for patients with chronic use of benzodiazepines. Endoscopies failed in up to 30% in those patients[13].

Propofol is a lipophilic anesthetic agent with fast distribution and fast elimination time without a cumulative affect after infusion. Its therapeutic spectrum, however, is much narrower than that of midazolam so careful monitoring is much more demanding in order to differentiate between moderate, deep sedation and general anesthesia. Propofol has been evaluated in a variety of regimens[25-29] in ERCP and has been shown to provide the same or superior sedation quality as midazolam with the advantage of better patient cooperation and shorter recovery time. Similar conclusions revealed by a meta-analysis[30] of randomized studies compared propofol and conventional sedatives and did not show a higher complication rate for propofol but did reveal significantly faster recovery after propofol as well as a trend toward a lower incidence of hypoxia and hypotension, although this finding was not statistically significant. Conclusively, propofol is at least as safe as the generally accepted conventional sedatives, even for administration by non-anesthesiologists[31]. Specifically, all studies for ERCP under deep sedation used propofol solo or combined as a sedative.

Muller *et al*[32] compared dexmetomidine with propofol and fentanyl for providing conscious sedation during ERCP and found that dexmetomidine alone was not as effective as propofol combined with fentanyl. Furthermore, dexmetomidine was associated with greater hemodynamic instability and a prolonged recovery.

Based on the study by Varadarajulu *et al*[22] concerning difficult to sedate patients undergoing ERCP and endoscopic ultrasound (EUS), Wehrmann *et al*[33] suggest the combination of ketamine and propofol in order to reduce the total propofol dose. Wehrmann suggests ketamine instead of midazolam or opioids because ketamine holds analgesic properties and does not add further cardiorespiratory depressant action.

ASSESSING SEDATION-RELATED COMPLICATIONS

One large multicenter study from North America[34] demonstrated that the leading cause of death from ERCP was cardiopulmonary complications and in a large audit of upper endoscopy from the UK[35], cardiopulmonary complications resulted in mortality for one in 2000 procedures. The cardiopulmonary mortality of endoscopy likely exceeds that of general anesthesia. Sedation related complications were attributed to high doses of sedatives and lack of adequate monitoring. In a retrospective analysis, Sharma *et al*[36] showed that the incidence for cardiopulmonary complications in ERCP was double in relation to colonoscopy (2.1% *vs* 1.1%) and triple in relation to EGD (2.1% *vs* 0.6%). In a meta-analysis by Qadeer *et al*[30], propofol sedation correlated with 14.5% of complications while with the classical regimen of midazolam it was 16.9%. The target level of sedation was moderate. In a risk factor analysis, Wehrmann *et al*[33] identified as independent risk factors for sedation-related side-effects the emergency endoscopic examination and a propofol dose > 100 mg. In the previous study, most cases with adverse events concerned haemostatic procedures of UGI (72/4252) and ERCP (56/3937).

In a study with 41 patients undergoing ERCP under conscious sedation, Johnston *et al*[37] revealed that one quarter of patients had myocardial ischemia and over half of them had no previous cardiac history and normal baseline electrocardiography results.

AVOIDING COMPLICATIONS

Several guidelines for gastroenterologists-directed propofol use and training have been published. Whereas the German guidelines[10] have been written in collaboration with representatives of the German Society for Anesthesiology and Intensive Care, the US guidelines[38] were released without the involvement of anesthesiologists. When those guidelines were compared with the guidelines published by the American Society of Anesthesiologists in 2002[3] and reviewed in 2004 and 2006, several issues common to all three guidelines could be seen. Common issues concern the definition of the different levels of sedation, the need for structured pre-procedure patient evaluation including informed consent, the use of specific monitoring of sedation, the clinical assessment of the depth of sedation and the presence of one individual dedicated to patient monitoring and trained in advanced life support skills.

PRE-PROCEDURE PATIENT EVALUATION AND PROCEDURE EVALUATION

Patients should be assessed thoroughly before the ERCP and give their informed consent to the procedure and sedation. If deep sedation is the target level of sedation, all patients undergoing ERCP should be additionally assessed by an anesthesiologist. Furthermore, for patients ASA Ⅲ-Ⅳ or patients with probable difficulty in ventilation or intubation or patients in high risk for aspiration such as pregnant women or patients with ascites, an anesthesiologist's assessment should be mandatory and general anesthesia should be planned.

As far as procedure concerns, urgent procedures should be considered high risk for complications and should be assessed by an anesthesiologist. General anesthesia should be considered in long lasting procedures and procedures in patients with primary sclerosing cholangitis, liver transplants and those in whom painful dilations are planned[12,33].

SPECIALIZED EQUIPMENT AND QUALIFIED PERSONNEL

According to Austrian guidelines[39], as regards sedation in endoscopy, deep sedation and propofol use require the existence of special equipment in the endoscopy suite. Specifically, equipment for mask respiration and endotracheal intubation must be available; the medication for resuscitation should be at hand and there should be oxygen and vacuum connections. Also a defibrillator should be promptly available as well as special monitor devices.

As far as personnel are concerned, it is obvious that the endoscopist cannot be expected to simultaneously perform the ERCP which may be very complex, administer an anesthetic with narrow therapeutic spectrum and monitor a deeply sedated patient in a dimly lit endoscopy unit. Athens statements support that there must be an additional person present with those responsibilities. That person could be an anesthesiologist or specially trained nurses. The specially trained nurses must be familiar with the agent administered, be able to maintain respiration when complications occur or during the transition from deep sedation to general anesthesia and be able to handle cardiovascular side effects or complications caused by the agent administered. Lichtenstein *et al*[38] stated that the benefit of involving anesthesiologists in ASA Ⅳ or higher patients and in patients with a difficult airway or history of inadequate response to sedation is unclear. This statement contrasts with the literature and puts high risk patients at a potentially fatal risk. Sedation of such patients by non-anesthesiologists cannot be justified. Moreover, all studies in deep-sedated ERCP were performed in the presence of an anesthesiologist.

PREREQUISITES FOR MONITORING

ERCP, deep sedation and propofol use as sedative need more sophisticated monitoring. Both anesthesiology and gastrointestinal literature conclude that the primary causes of morbidity during sedation are respiratory depression and airway obstruction. A recent ASA closed claims study[40] on monitored anesthesia care in non-operating room locations reaffirmed this finding but also noted that respiratory events were twice as likely to cause morbidity in non-operating locations compared to the operating room. The vast majority of incidents in this study took

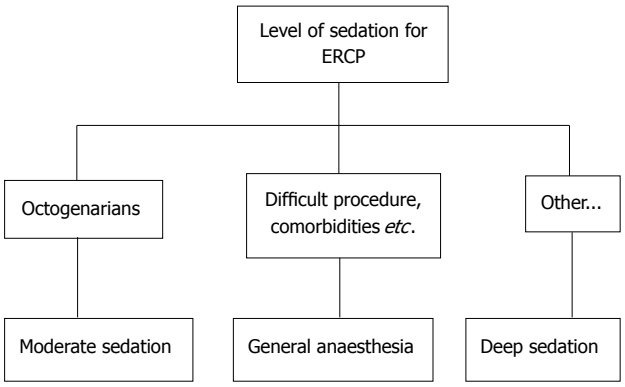

Figure 1 Level of sedation for endoscopic retrograde cholangiopacreatography. ERCP: endoscopic retrograde cholangiopacreatography.

place in an endoscopy room (82%). A recent review of the gastrointestinal Clinical outcomes research initiative (CORI) database[41] also found that cardiopulmonary events were the leading cause of unplanned events during gastrointestinal endoscopy.

Therefore, monitoring of respiration, cardiac rhythm and a non invasive blood-pressure measurement is mandatory. Methods to monitor respiration include direct observation of chest wall movement, capnography and ECG analysis of respiratory rate *via* impedance pneumography. Observation in a dark gastrointestinal suite is difficult. Moreover, chest wall movement as well as impedance pneumography does not detect actual airflow at the oropharynx. Capnography seems to be a more precise measure of ventilation[41]. The role of capnographic monitoring during endoscopy has been examined in several studies. One randomized study[42] involving adults having ERCP or EUS, demonstrated that the use of capnography detected more episodes of disordered ventilation and reduced the number of hypoxemic events compared with visual assessment and monitoring of standard physiological parameters.

Monitoring of depth of sedation could reduce the total amount of infused sedative and therefore the complication rate. The depth of sedation could be monitored *via* an electroencephalogram (EEG), by the spectral edge frequency, by the bispectral index and using the Narcotrend device. An EEG in itself is not practical during endoscopic procedures as it requires time and special knowledge for interpretation.

The computer generated BIS ranging from 0 (coma) to 100 (fully awake) reflects the level of sedation regardless of the patient's demographics and the type of hypnotic drug used. For obtaining a deep sedation level, BIS 50-60 is required. Paspatis *et al*[18] demonstrated a significant reduction in the used total propofol dose and a correspondingly shorter recovery time when using BIS monitoring in ERCP instead of conventional sedation. In a study where Al-Sammak *et al*[43] used midazolam and meperidine for ERCP, BIS reduced the total sedative dose.

The Narcotrend device also uses a multiparametric mathematical algorithm for analyzing the EEG rhythm. There is one randomized controlled study[44] showing that the use of this device during propofol sedated ERCP in 80 patients enables a more effective titration of propofol and is correspondingly associated with faster patient recovery.

CONCLUSION

In contrast to upper gastrointestinal endoscopy, ERCP is a complex, often time consuming diagnostic and therapeutic endoscopic procedure that requires a high degree of patient cooperation in order to facilitate an intervention requiring precision from the endoscopist. Any movement by the patient could considerably affect the success of the procedure. It may be difficult for moderate sedation itself to fulfill these requirements. Therefore, deep sedation is preferable in ERCP. General anesthesia should be considered in patients difficult to sedate, or having difficulty in ventilation and intubation or in high risk for aspiration. Also, it should be considered in lengthy procedures. Conscious sedation seems to be adequate in octogenarians (Figure 1).

As far as the proper sedative agent is concerned, propofol seems to provide the same or superior sedation quality as conventional regimens with the advantage of shorter recovery time and better patient tolerance in ERCP. Ketamine could also be used in difficult to sedate patients in order to avoid general anesthesia.

Cardiorespiratory events are considered the major complications of sedation in ERCP. Therefore, monitoring is much more demanding and sophisticated in those endoscopic procedures. Capnography, monitoring of the level of sedation and a presence of a qualified anesthesiologist could contribute to the reduction of cardiorespiratory complications.

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CASE REPORT

A typical presentation of a rare cause of obscure gastrointestinal bleeding

Stefan Reuter, Dominik Bettenworth, Sören Torge Mees, Jörg Neumann, Torsten Beyna, Wolfram Domschke, Johannes Wessling, Hansjörg Ullerich

Stefan Reuter, Department of Internal Medicine D, University Hospital Münster, Albert-Schweitzer Str. 33, Münster 48149, Germany
Dominik Bettenworth, Torsten Beyna, Wolfram Domschke, Hansjörg Ullerich, Department of Internal Medicine B, University Hospital Münster, Albert-Schweitzer Str. 33, Münster 48149, Germany
Sören Torge Mees, Department of General and Visceral Surgery, University Hospital Münster, Albert-Schweitzer Str. 33, Münster 48149, Germany
Jörg Neumann, Gerhard Domagk Institute of Pathology, University Hospital Münster, Albert-Schweitzer Str. 33, Münster 48149, Germany
Johannes Wessling, Department of Radiology, University Hospital Münster, Albert-Schweitzer Str. 33, Münster 48149, Germany
Author contributions: Reuter S and Bettenworth D contributed equally to this work; Reuter S, Bettenworth D, Domschke W, and Ullerich H wrote the paper; and Beyna T, Mees ST, Neumann J, and Wesseling J provided data.
Correspondence to: Stefan Reuter, MD, Department of Internal Medicine D, University Hospital Münster, Albert-Schweitzer Str. 33, Münster 48149, Germany. sreuter@uni-muenster.de
Telephone: +49-251-8356983 Fax: +49-251-8356973
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Abstract

A 52-year-old white woman had suffered from intermittent gastrointestinal (GI) bleeding for one year. Upper GI endoscopy, colonoscopy and peroral double-balloon enteroscopy (DBE) did not detect any bleeding source, suggesting obscure GI bleeding. However, in videocapsule endoscopy a jejunal ulceration without bleeding signs was suspected and this was endoscopically confirmed by another peroral DBE. After transfusion of packed red blood cells, the patient was discharged from our hospital in good general condition. Two weeks later she was readmitted because of another episode of acute bleeding. Multi-detector row computed tomography with 3D reconstruction was performed revealing a jejunal tumor causing lower gastrointestinal bleeding. The patient underwent exploratory laparotomy with partial jejunal resection and end-to-end jejunostomy for reconstruction. Histological examination of the specimen confirmed the diagnosis of a low risk gastrointestinal stromal tumor (GIST). Nine days after surgery the patient was discharged in good health. No signs of gastrointestinal rebleeding occurred in a follow-up of eight months. We herein describe the complex presentation and course of this patient with GIST and also review the current approach to treatment.

Key words: Gastrointestinal stromal tumor; Gastrointestinal neoplasms; Gastrointestinal hemorrhage; Computed tomography

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INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors in the GI tract. The clinicopathology and appearance of GISTs vary considerably

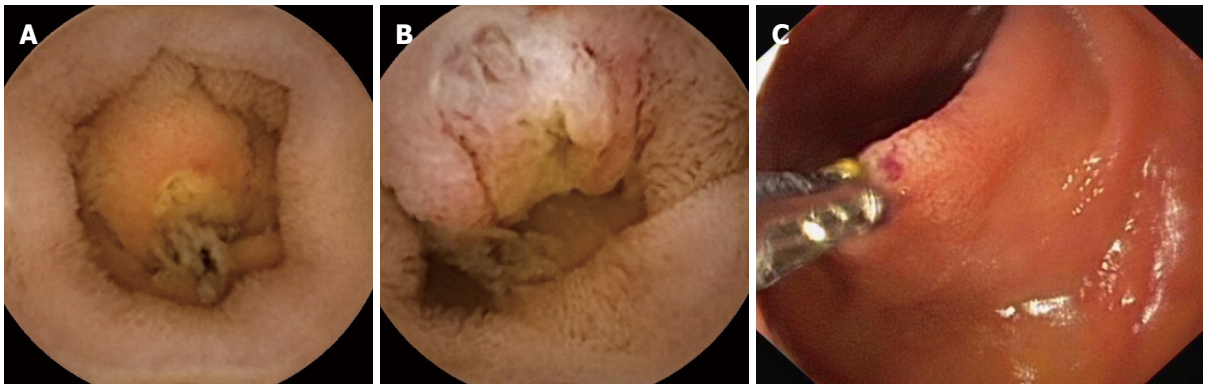

Figure 1 Endoscopic images. A, B: Video-capsule endoscopy detected a jejunal ulceration without bleeding signs. Subsequently, the patient was transferred to our hospital for further diagnostic work-up; C: We performed double-balloon enteroscopy which confirmed the suspected ulcerous lesion.

and symptoms might result from both small incidental nodules and large tumors. Symptomatic GISTs have often grown large before they are discovered and that is why their diagnosis frequently results from emergency surgery for gastrointestinal (GI) perforation or GI bleeding. Small GISTs often form solid subserosal or intramural masses, sometimes ulcerating or eroding vessels but rarely growing into the lumen. This is why the GISTs are sometimes hard to diagnose. However, GI bleeding (acute or chronic) is the most common clinical presentation of GISTs.

We report the case of a 52-year-old female who presented with intermittent GI bleeding for one year. Due to its submucosal location, multiple endoscopic approaches failed to diagnose the tumor correctly. However, a multidetector row computed tomography (MDCT) study with 3D reconstruction disclosed a homogeneous, hypervascularized abdominal mass showing arterial contrast enhancement and extravasation of contrast media into the intestines. This striking case illustrates that MDCT is a useful tool for diagnosis and localization in cases of acute obscure GI bleeding when diagnosis may be missed by endoscopy.

CASE REPORT

A 52-year-old female patient had suffered from intermittent GI bleeding (melena) for one year. Therefore, she underwent upper GI endoscopy and colonoscopy and peroral double-balloon enteroscopy (DBE) in a community hospital, the results of which were unremarkable. In video capsule endoscopy (PillCam^{TM} SB2 and Rapid 5 workstation, Given Imaging, Hamburg, Germany), a jejunal ulceration without bleeding signs was suspected (Figure 1). However, the blood hemoglobin level dropped slowly from 140 g/L to 92 g/L over 12 mo.

On admission to our hospital, physical examination of the hemodynamically stable patient (blood pressure 110/70 mmHg) showed regular motility of the gut without evidence of tenderness or any pathological abdominal mass. There was slight percussion pain in the right upper abdominal quadrant and melena on rectal exam. Her past medical history revealed uterine myomas, a diaphragmatic hernia, an iron deficiency anemia, and an appendectomy in her twenties. Laboratory findings included a white cell count of 4.5 × 10^9/L, a red cell count of 4.0 × 10^{12}/L, hemoglobin 92 g/L, hematocrit 32%, mean corpuscular volume 79.2 fl, ferritin 4 μg/L, blood iron 120 μg/L, transferrin 3 g/L, and transferrin saturation index 3%. Serum creatinine was 61 μl/L. Abdominal sonography results were unremarkable. Upper GI endoscopy and colonoscopy did not detect any bleeding source, suggesting obscure GI-bleeding. Peroral DBE was performed revealing a small ulceration (6-8 mm) without bleeding signs at 260 cm post-pylorus, confirming the jejunal ulceration previously suspected from video capsule endoscopy (Figure 1). Following negative biopsy results, the patient received packed red blood cells and was discharged from our hospital in good general condition. A second peroral and peranal DBE (insertion depth around 200 cm post-pylorus and peranal), conducted two weeks later because of persistent melena, did not reveal any significant findings. After a further two weeks later she was readmitted because of another episode of acute bleeding. An MDCT study (Figure 2) with 3D reconstruction was then performed (Figure 3).

Biphasic MDCT findings disclosed a homogeneous, hypervascularized, smoothly outlined abdominal mass (transverse diameter of about 2.8 cm × 3 cm, Figure 1: large arrow) showing arterial contrast enhancement and extravasation of contrast media into the intestines (Figure 2: small arrows) with washout in the venous phase. There were no signs of additional lesions or suspicious abdominal lymph nodes. 3D reconstruction of CT data was instrumental in determining site, size and vascularization of the bleeding origin (Figure 3). The adjacent intestinal wall for 3-5 cm on either side of the mass appeared to be hyperaemic. Due to multiple arteries arising from A. mesenterica superior and A. iliaca communis dextra feeding the tumor, arterial embolisation which might reduce the risk of intraoperative bleeding was not indicated (Figure 3, arrows). Carcinoembryonic antigen was within the normal physiological range.

For definite histopathological diagnosis, surgery was indicated. On exploration, a mass (3.6 cm × 3.2 cm × 2.8 cm) arising from the jejunum (240 cm behind the plica

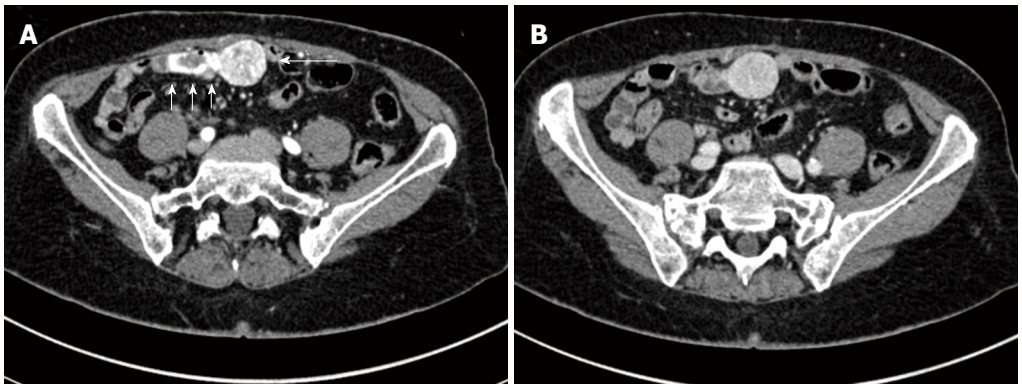

Figure 2 Biphasic MDCT in the arterial and venous phase. A: Smoothly outlined abdominal mass (transverse diameter of about 2.8 cm x 3 cm, long arrow) showing considerable arterial contrast enhancement and intraluminal contrast medium extravasation (shot arrows); B: Washout in the venous phase.

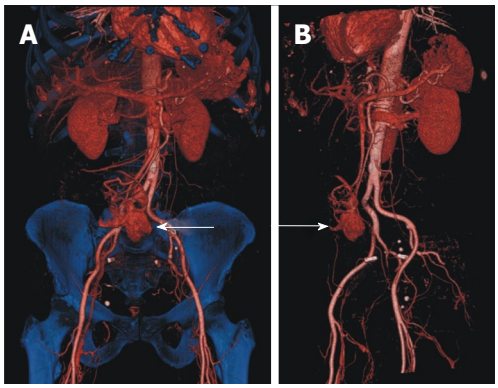

Figure 3 3D volume rendered reconstructions in the arterial phase (A, B). Note that the tumour (arrows) is supplied by vessels from the superior mesenteric and iliac arterial territories.

duodenalis superior/Treitz´s ligament) (Figure 4A) was revealed. A partial jejunal resection (Figure 4B) with end-to-end jejunostomy for reconstruction was performed showing a transmurally growing and bleeding tumor. There was no evidence of pathological lymph nodes or metastases.

Macroscopically, the tumor appeared as a lobulated, hypervascularized red-white mass infiltrating and ulcerating the intestinal wall (Figure 4C, arrow). Histological assessment revealed proliferation of whorls of spindle cells (uniform elongated cells with syncytial-appearing eosinophilic cytoplasm and uniform ovoid nuclei) with fibers, vessels and a mononuclear inflammatory infiltrate (Figure 5A). Using immunohistochemical staining techniques, nearly all tumor cells showed a positive reactivity for CD117 (c-kit) (Figure 5B) and CD34 (Figure 5C). Analysis by PCR amplification revealed a c-kit gene mutation in the exon 9. Staining against smooth muscle antigen (SMA) was negative and less than 5% of cells were positive for Ki-67 protein (cells expressing this protein are thought to be actively dividing). Because of the low mitotic rate [number of mitoses per 50 high-power fields (HPF): 5] and a size between 2 and 5 cm, the neoplasm was classified as a low risk gastrointestinal stromal tumor (GIST)[1]. Thus, therapy was exclusively surgical. Nine days after surgery the patient was discharged in good health. No signs of gastrointestinal rebleeding occurred in a follow-up of eight months.

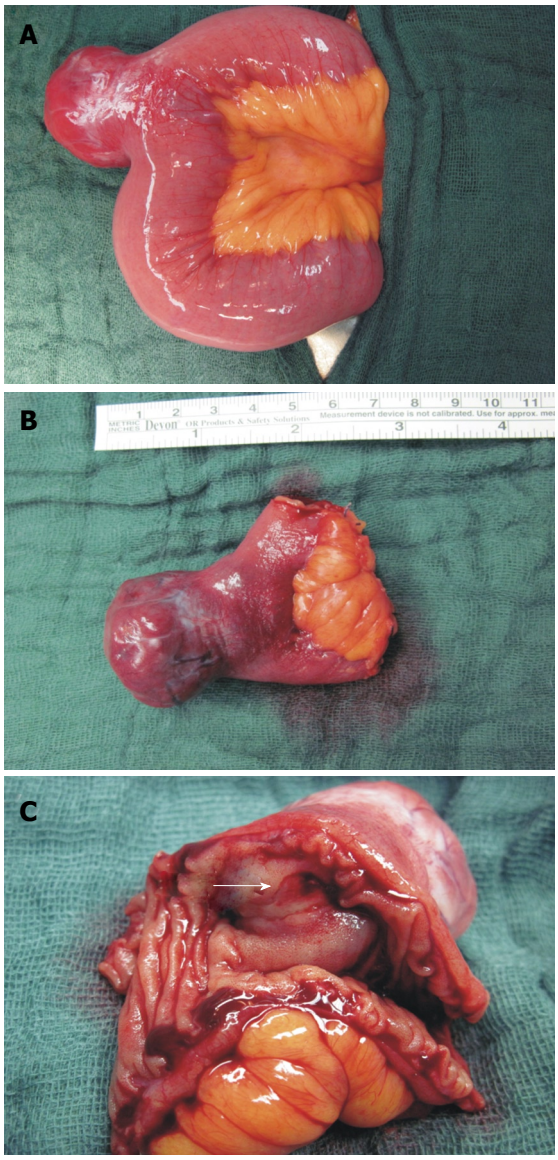

Figure 4 Surgical specimens. A: Tumor of 3.6 cm × 3.2 cm × 2.8 cm arising from the jejunum (240 cm behind the plica duodenalis superior/ Treitz's ligament); B:removal of the tumor *via* a partial jejunal resection; C: sliced preparation of the jejunum with a view of the GIST related ulcer (arrow).

DISCUSSION

GIST are extremely rare neoplasms, with an incidence

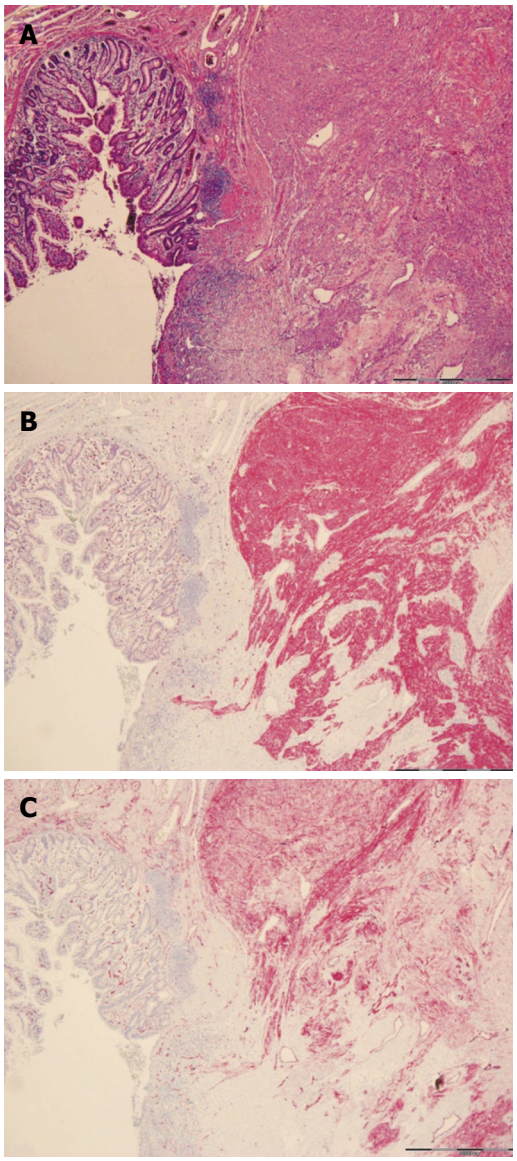

Figure 5 Histological assessment of surgical specimen revealed an ulcerated spindle-celled gastric stromal tumor with well marked margin and a positive staining for CD117 and CD34. A: HE-; B: CD117-; C: CD34-staining.

of 10-15 per million people per year, which usually occur in adults in their fifth or sixth decade (median age 55-60 years). They occur throughout the gastrointestinal tract with 60%-70% in the stomach, 25%-35% in small intestine, and less than 5% in rectum, esophagus, omentum, and mesentery[2,3]. GISTs are the most common mesenchymal tumors in the GI tract and comprise about 1%-3% of all malignant GI tumors. Interestingly, GIST can occur as classical familial GIST syndrome, GIST or as part of multi-neoplastic disease[4]. A debate on nomenclature, cell types of origin, and pathological subclassification was recently published by Miettinen and Lasota[2,3] and Fletcher *et al*[1].

The clinicopathology and appearance of GISTs vary considerably and as symptoms might result from both small incidental nodules and large tumors. Interestingly, up to 80% of patients with GISTs are without any symptoms at the time of diagnosis as smaller GISTs are frequently asymptomatic and are identified incidentally during surgery, radiologic or endoscopic studies[3]. Thus, symptomatic GISTs have often grown large before they are discovered and that is why their diagnosis frequently occurs following emergency surgery for GI perforation or GI bleeding. Small GISTs often form solid subserosal or intramural masses, sometimes ulcerating or eroding vessels but rarely growing into the lumen. Therefore, GI bleeding (acute or chronic) is the most common clinical presentation of GISTs while nonspecific symptoms, such as obstruction, invagination, perforation or anemia occur in approximately 20% of cases[5]. It is most likely that the jejunal ulceration seen on VCE and DBE is part of the GIST. The location of the endocopically detected lesion (distal part of the jejunum, insertion depth 260 cm post-pylorus) is consistent with the MDCT data and surgical resection specimen.

Recently, the diagnostic role of MDCT in upper and lower GI bleeding has been markedly extended due to its high spatial and temporal resolution, acquisition of arterial- and venous phase images as well as depiction of active extravasation of contrast medium. A presumed bleeding site or potential causative pathology was detected and localized by MDCT in > 80% of patients and active contrast media extravasation was apparent during most examinations[6-8]. Thus, in addition to the endoscopic standard work-up, MDCT seems to be recommended for obscure bleeding indications[9]. It is currently the imaging modality of choice for patients with suspected abdominal mass or biopsy-proven GIST[10]. Differential diagnoses of GIST include lymphoma, leiomyosarcoma, adenocarcinoma or metastases. Unlike the latter tumor entities, lymphadenopathy is not a common sign of GISTs. Metastases, if they occur, have been described as multiple smooth and not calcified (prior to therapy) masses with features distinguishing them from carcinoids. As luminal obstruction frequently occurs in adenocarcinomas (including clinical signs of constipation or paradoxical diarrhea) but not in GISTs (excepting large tumors), this might also help in differential diagnosis[11].

Up to one fourth of gastric GISTs and half of all small intestinal GISTs are clinically malignant with metastases commonly occurring intra-abdominally, i.e. preferentially in the liver; rarely in soft tissues, bones or skin; and even less frequent in lymph nodes and lungs. Metastases may develop a long time (> 15 years) after primary surgery and long-term follow-up is,therefore, encouraged[3]. Morphological features such as tumor size and mitotic activity (Ki-67 staining) have gained greatest acceptance for predicting outcome and distinguishing benign from malignant GISTs[1]. Histological features are site dependent with a majority being spindle cell tumors (70%) and a minority presenting with an epithelioid (20%) or mixed spindle, epithelioid, or a nested paraganglioma-like or carcinoid-like growth pattern or,rarely, a cytological pleomorphism (2%-3%)[1]. Further immunohistochemical charac-

terization of the tumor in this case revealed a key feature of GISTs (Figure 5B, C) - positivity for CD117 (c-kit or KIT) and CD34.

It is generally accepted that all GISTs are malignant regardless of tumor size or mitotic index[1]. Usually, the primary therapy of localized GISTs is surgical. Nevertheless, about 50% of patients treated by resection relapse within 5 years. Using the most important prognostic risk factors, tumor size and mitotic index, a system for classification of patients has been validated[1]. At present, further prognostic factors such as localisation, presence and type of c-kit mutation have been suggested for stratification of relapse risk (overview in[12] and[13]).

In cases of very low and low/intermediate grade GI STs, surgical resection has a good prognosis[14,15]. In patients with intermediate/high-risk GISTs increased recurrence and decreased survival rates occur despite complete surgical resection[16]. GIST is considered to be an extensively chemotherapy-resistant soft-tissue sarcoma subtype[17]. The standard systemic treatment for soft-tissue sar comas is a Doxorubicin-based chemotherapy, which achieves a 2-year survival rate of only 20% in patients with GIST[18]. For these patients, the development of imatinib, a tyrosine kinase inhibitor targeting both c-kit and platelet-derived growth factor alpha (PDGFRA), has considerably improved the outcome. In advanced disease this is now the standard firstline therapy[19].

Interestingly, due to secondary resistance often related to secondary c-kit or PDGFRA mutations, most patients initially responding to imatinib treatment will eventually develop tumor progression[20,21]. Nevertheless, for patients requiring cytoreductive therapy before resection, neoadjuvant treatment with imatinib is an emerging option[20]. There are established guidelines for the follow-up of a patient, such as ours, after resection with curative intent. According to the GIST Consensus Conference for low- or very low risk GIST, i.e. tumors < 5 cm and with a mitotic index < 5/50 high power fields, a systematic follow-up with CT scan every 6 mo for 5 years would be reasonable. At present, however, there is no evidence indicating that these are the optimal time intervals, and whether follow-up with CT is beneficial or not in these patients[10].

In conclusion, findings of the present report indicate that GI-bleeding is a typical presentation of GIST. In these cases MDCT is a useful tool for (initial) diagnosis and quick localization of submucosal GI tumors, since endoscopic diagnostic tools such as VCE and DBE may miss these lesions. In cases of very low and low/intermediate grade GISTs surgical resection has a good prognosis. However, novel therapeutic targets have been identified which may lead to potential new treatment options in the future.

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CASE REPORT

Endoscopic transpapillary gallbladder drainage with replacement of a covered self-expandable metal stent

Kazumichi Kawakubo, Hiroyuki Isayama, Naoki Sasahira, Yousuke Nakai, Hirofumi Kogure, Takashi Sasaki, Kenji Hirano, Minoru Tada, Kazuhiko Koike

Kazumichi Kawakubo, Hiroyuki Isayama, Naoki Sasahira, Yousuke Nakai, Hirofumi Kogure, Takashi Sasaki, Kenji Hirano, Minoru Tada, Kazuhiko Koike, Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo 113-8655, Japan

Author contributions: Kawakubo K, Isayama H, Sasahira N, Kogure H and Nakai Y designed the research; Sasaki T, Hirano K and Tada M criticized the paper for important intellectual content; Koike K finally approved the paper; Kawakubo K wrote the article.

Correspondence to: Hiroyuki Isayama, MD, Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. isayama-2im@h.u-tokyo.ac.jp
Telephone: +81-3-38155411 Fax: +81-3-38140021
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Abstract

Endoscopic self-expandable metal stent (SEMS) placement has become a standard palliative therapy for patients with malignant biliary obstruction. Acute cholecystitis after SEMS placement is a serious complication. We report a patient with an acute cholecystitis after covered SEMS placement, who was managed successfully with endoscopic transpapillary gallbladder drainage (ETGBD) and replacement of the covered SEMS. An 85-year-old man with pancreatic cancer suffered from acute cholecystitis after covered SEMS placement. It was impossible to perform percutaneous transhepatic gallbladder drainage. After removal of the covered SEMS with a snare, a 7Fr double pigtail stent was placed between the gallbladder and duodenum, subsequently followed by another covered SEMS insertion into the common bile duct beside the gallbladder stent. The cholecystitis improved immediately after ETGBD. ETGBD with replacement of the covered SEMS thus proved to be effective for treatment of patients with acute cholecystitis after covered SEMS placement.

Key words: Self-expandable metal stent; Cholecystitis; Endoscopic transpapillary gallbladder drainage

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Kawakubo K, Isayama H, Sasahira N, Nakai Y, Kogure H, Sasaki T, Hirano K, Tada M, Koike K. Endoscopic transpapillary gallbladder drainage with replacement of a covered self-ex pandable metal stent. *World J Gastrointest Endosc* 2011; 3(2): 46-48 Available from: URL: http://www.wjgnet.com/1948-5190/full/v3/i2/46.htm DOI: http://dx.doi.org/10.4253/wjge.v3.i2.46

INTRODUCTION

Endoscopic self-expandable metal stent (SEMS) placement has become a standard palliative therapy for patients with malignant biliary obstruction[1]. There is, however, a need to prevent and manage stent-related complications. Acute cholecystitis after SEMS placement is a serious complication, and tumor involvement at the orifice of the cystic duct (CD) is a risk factor[2,3]. Some patients with cholecystitis improve with conservative therapy, while others require percutaneous drainage. We report a patient with acute cholecystitis after covered SEMS placement, who was managed successfully with endoscopic transpapillary gallbladder stenting and replacement of the covered SEMS.

CASE REPORT

An 85-year-old man with malignant biliary obstruction

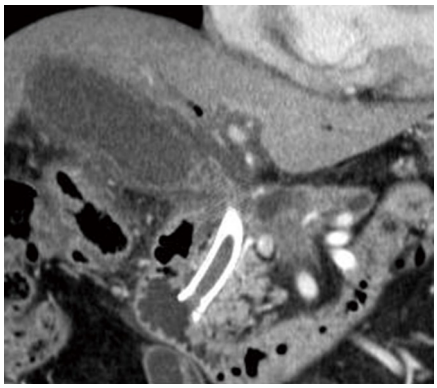

Figure 1 Computed tomography of the abdomen shows swelling of the gallbladder, wall thickening, and the previously placed covered metal stent.

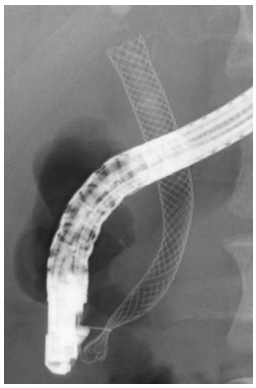

Figure 2 Fluoroscopic image showing the covered self-expandable metal stent grasped with a snare.

due to pancreatic cancer underwent endoscopic covered SEMS (diameter 10 mm, length 8 cm, partially covered Wallflex, Boston Scientific, Natick, MA, USA) placement. There was a tumor at the orifice of the CD, as demonstrated by cholangiography and intraductal ultrasound. After successful biliary drainage, he was given gemcitabine chemotherapy as an outpatient. 25 d after SEMS placement, he presented to the emergency unit with a fever and right upper abdominal pain. Computed tomography revealed acute cholecystitis, which did not resolve with conservative therapy (Figure 1). Due to the lack of a window for percutaneous transhepatic gallbladder drainage, endoscopic drainage was performed.

The orifice of the CD overlapped the previously placed covered SEMS, so we needed to remove the covered SEMS to gain access to the gallbladder. First, a duodenoscope was passed into the duodenum, and the covered SEMS was removed with a snare through the duodenoscope (Figure 2). Then, the orifice of the CD was negotiated with a sphincterotome (Clevercut; Olympus, Tokyo, Japan) and a 0.035-inch × 260-cm hydrophilic guidewire (Radifocus; Terumo, Tokyo, Japan). Following the approach to the gallbladder, the hydrophilic guidewire was replaced with a 0.035-inch × 460-cm stiff guidewire (Revowave; Piolax Medical Devices, Kanagawa, Japan; Figure 3). After withdrawing the sphincterotome, a 7Fr double pigtail stent (Zimmon Biliary Stent; Wilson-Cook Medical, Winston-Salem, NC, USA) was placed between the gallbladder and duodenum. Finally, another covered SEMS (diameter 10 mm, length 6 cm, partially covered WallFlex; Boston Scientific, Natick, MA, USA) was inserted into the common bile duct beside the gallbladder stent

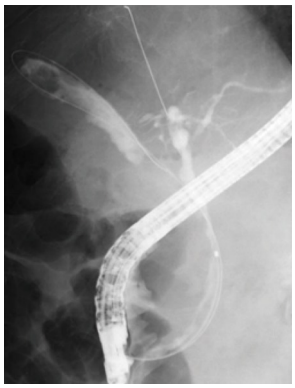

Figure 3 Cholangiogram showing the guidewire being placed in the gallbladder and intrahepatic duct.

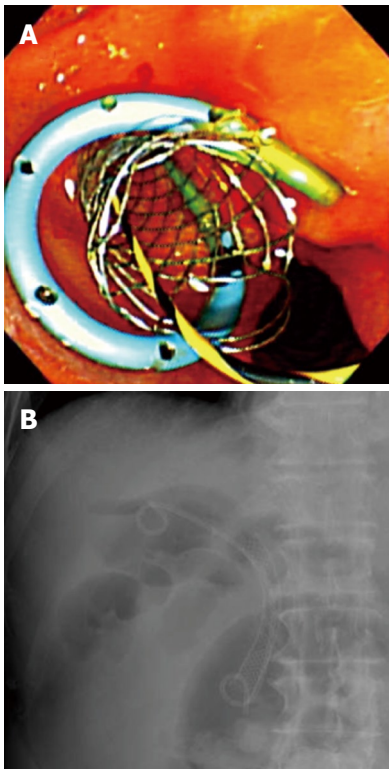

Figure 4 The transpapillary gallbladder stent and covered metal stent. A: Endoscopic image; B: Fluoroscopic image.

(Figure 4). Immediately after the endoscopic gallbladder drainage, the cholecystitis improved. At follow-up, the cholecystitis had not recurred and the patient resumed chemotherapy. Both gallbladder stent and SEMS were patent until death.

DISCUSSION

Acute cholecystitis is a serious complication following SEMS insertion, with a reported incidence of 4.3%-9.7%. Tumor involvement at the orifice of the CD, as in our case, is a risk factor for cholecystitis[2,3]. In patients in whom the cholecystitis does not resolve with conservative therapy, percutaneous cholecystostomy may be necessary[3]. In our patient, however, there was no window for percutaneous transhepatic drainage. Furthermore, percutaneous transhepatic drainage is contraindicated in patients with coagulopathy, anticoagulants, or abundant ascites. Endoscopic transpapillary gallbladder drainage has been recognized as an effective procedure[4]. To our knowledge,

there is no report of post-SEMS acute cholecystitis having been managed successfully by endoscopic transpapillary gallbladder stenting, with replacement of the covered SEMS. It is difficult to negotiate the orifice of the CD after removing a covered SEMS in patients with malignant biliary obstruction, because most of them have tumor involvement at the orifice of the CD. Intraductal ultrasonography or per-oral cholangioscopy may be useful for detecting the orifice of the CD in such patients. Removability is one of the important features of covered SEMScompared with uncovered SEMS[5]. For patients with acute cholecystitis after uncovered SEMS placement, in whom transhepatic puncture is not anatomically possible, endoscopic ultrasonography-guided transmural gallbladder stenting is a reasonable alternative to percutaneous cholecystostomy[6].

Endoscopic transpapillary gallbladder stenting with replacement of the covered SEMS has thus been proved to be safe and effective for treating patients with acute cholecystitis after covered SEMS placement, especially in patients with contraindications for percutaneous gallbladder drainage.

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Majid Abdulrahman Al Madi, MBBS, FRCPC, Gastroenterology Division, McGill University Health Center, McGill University, Royal Victoria Hospital, 687 Pine Ave West, Montreal QC H3A 1A1, Canada

Wai-Keung Chow, Visiting Staff, Division of Gastroenterology, Department of Internal Medicine, China Medical University Hospital, Taichung 407, Taiwan, China

Viktor Ernst Eysselein, MD, Professor of Medicine, Division of Gastroenterology, Harbor-UCLA Medical Center, Torrance, CA 90509, United States

Lesur Gilles, MD, Hopital Ambroise Paré, 9 avenue Charles de Gaulle, Boulogne 92100, France

Carlo M Girelli, MD, 1st Department of Internal Medicine, Service of Gastroenterology and Digestive Endoscopy, Hospital of Busto Arsizio, Via Arnaldo da Brescia, Busto Arsizio, VA 121052, Italy

Dimitrios Kapetanos, MD, Gastroenterology Department, George Papanikolaou Hospital, Exohi, Thessaloniki 57010, Greece

Ka Ho Lok, MBChB, Associate Consultant, Department of Medicine and Geriatrics, Tuen Mun Hospital, Tsing Chung Koon Road, Tuen Mun, Hong Kong, China

Jong Ho Moon, MD, PhD, Professor of Medicine, Soon Chun Hyang University School of Medicine; Digestive Disease Center, Soon Chun Hyang University Bucheon Hospital, Bucheon 420-767, South Korea

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

Robert J Richards, MD, Gastroenterology/Hepatology, Stony Brook University HSC, Stony Brook, NY 11793, United States

Reena Sidhu, MRCP, MD, Department of Gastroenterology, Royal Hallamshire Hospital, 15 Barncliffe Road, Fulwood, Sheffield S10 4DF, United Kingdom

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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

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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
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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

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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
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December 01-04, 2011
2011 Advances in Inflammatory Bowel Diseases/Crohn's & Colitis Foundation's Clinical & Research Conference
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Instructions to authors

GENERAL INFORMATION

World Journal of Gastrointestinal Endoscopy (*World J Gastrointest Endosc*, *WJGE*, online ISSN 1948-5190, DOI: 10.4253), is a monthly, open-access (OA), peer-reviewed online journal supported by an editorial board of 400 experts in gastrointestinal endoscopy from 45 countries.

The biggest advantage of the OA model is that it provides free, full-text articles in PDF and other formats for experts and the public without registration, which eliminates the obstacle that traditional journals possess and usually delays the speed of the propagation and communication of scientific research results.

Maximization of personal benefits

The role of academic journals is to exhibit the scientific levels of a country, a university, a center, a department, and even a scientist, and build an important bridge for communication between scientists and the public. As we all know, the significance of the publication of scientific articles lies not only in disseminating and communicating innovative scientific achievements and academic views, as well as promoting the application of scientific achievements, but also in formally recognizing the "priority" and "copyright" of innovative achievements published, as well as evaluating research performance and academic levels. So, to realize these desired attributes of *WJGE* and create a well-recognized journal, the following four types of personal benefits should be maximized. The maximization of personal benefits refers to the pursuit of the maximum personal benefits in a well-considered optimal manner without violation of the laws, ethical rules and the benefits of others. (1) Maximization of the benefits of editorial board members: The primary task of editorial board members is to give a peer review of an unpublished scientific article via online office system to evaluate its innovativeness, scientific and practical values and determine whether it should be published or not. During peer review, editorial board members can also obtain cutting-edge information in that field at first hand. As leaders in their field, they have priority to be invited to write articles and publish commentary articles. We will put peer reviewers' names and affiliations along with the article they reviewed in the journal to acknowledge their contribution; (2) Maximization of the benefits of authors: Since *WJGE* is an open-access journal, readers around the world can immediately download and read, free of charge, high-quality, peer-reviewed articles from *WJGE* official website, thereby realizing the goals and significance of the communication between authors and peers as well as public reading; (3) Maximization of the benefits of readers: Readers can read or use, free of charge, high-quality peer-reviewed articles without any limits, and cite the arguments, viewpoints, concepts, theories, methods, results, conclusion or facts and data of pertinent literature so as to validate the innovativeness, scientific and practical values of their own research achievements, thus ensuring that their articles have novel arguments or viewpoints, solid evidence and correct conclusion; and (4) Maximization of the benefits of employees: It is an iron law that a first-class journal is unable to exist without first-class editors, and only first-class editors can create a first-class academic journal. We insist on strengthening our team cultivation and construction so that every employee, in an open, fair and transparent environment, could contribute their wisdom to edit and publish high-quality articles, thereby realizing the maximization of the personal benefits of editorial board members, authors and readers, and yielding the greatest social and economic benefits.

Aims and scope

The major task of *WJGE* is to report rapidly the most recent results in basic and clinical research on gastrointestinal endoscopy including: gastroscopy, intestinal endoscopy, colonoscopy, capsule endoscopy, laparoscopy, interventional diagnosis and therapy, as well as advances in technology. Emphasis is placed on the clinical practice of treating gastrointestinal diseases with or under endoscopy. Papers on advances and application of endoscopy-associated techniques, such as endoscopic ultrasonography, endoscopic retrograde cholangiopancreatography, endoscopic submucosal dissection and endoscopic balloon dilation are also welcome.

Columns

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In press

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

Organization as author

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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No author given

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]

Volume with supplement

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9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

Books

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12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

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13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference paper

14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

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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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