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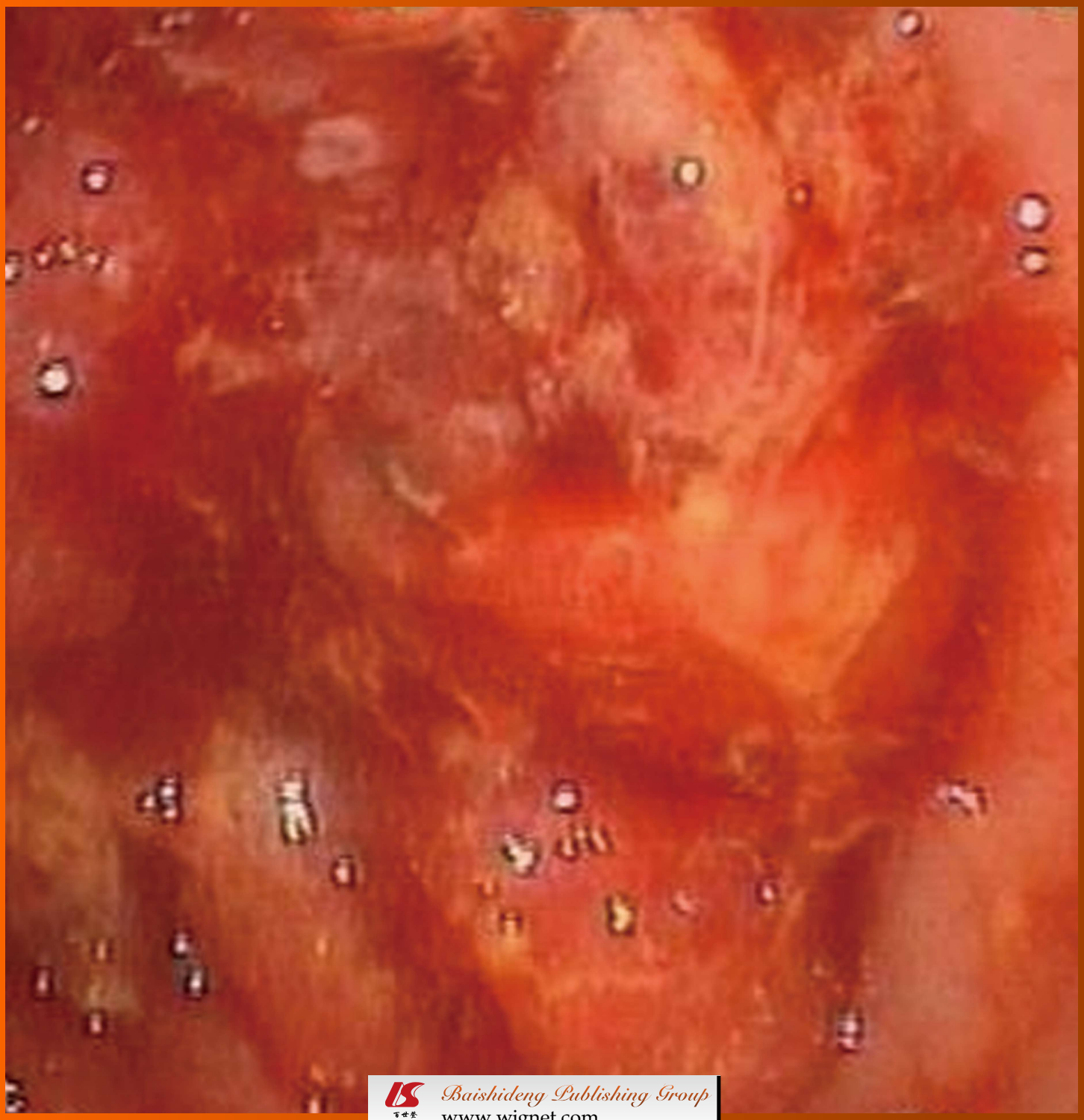

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WJGE covers topics concerning gastroscopy, intestinal endoscopy, colonoscopy, capsule endoscopy, laparoscopy, interventional diagnosis and therapy, as well as advances in technology. Emphasis is placed on the clinical practice of treating gastrointestinal diseases with or under endoscopy.

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EDITORIAL

How we can measure quality in colonoscopy?

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Abstract

Measuring quality is a current need of medical services either to assess their cost-effectiveness or to identify discrepancies requiring refinement. With the advent of bowel cancer screening and increasing patient awareness of bowel symptoms, there has been an unprecedented increase in demand for colonoscopy. Consequently, there is an expanding open-discussion on missed rates of cancer or precancerous polyps during diagnostic/screening colonoscopy and on the rate of adverse events related to therapeutic colonoscopy. Delivering a quality colonoscopy service is therefore a healthcare priority. Colonoscopy is a multi-step process and therefore assessment of all aspects of the procedure must be addressed. Quality in colonoscopy refers to a combination of many patient-centered technical and non-technical skills and knowledge aiming to patient's safety and satisfaction through a continuous effort for improvement. The benefits of this endless process are hiding behind small details which can eventually make the difference in colonoscopy. Identifying specific quality metrics help to define and shape an optimal service and forms a secure basis of improvement. This paper does not aim to give technical details on how to perform colonoscopy but to summarize what to measure and when, in accordance with the current identified quality indicators and standards for colonoscopy.

Key words: Colonoscopy; Quality assurance; Metrics; Standards; Outcome

Core tip: With the advent of bowel cancer screening and increasing patient awareness of bowel symptoms, there has been an unprecedented increase in demand for colonoscopy. Delivering a quality colonoscopy service is therefore a healthcare priority. Colonoscopy is a multi-step process and therefore assessment of all aspects of the procedure must be addressed. Quality in colonoscopy refers to a combination of many patient-centered technical and non-technical skills. Identifying specific quality metrics help to define and shape an optimal service.

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INTRODUCTION

Colonoscopy is the cornerstone in diagnosis and management of colorectal disease allowing direct optical diagnosis, tissue sampling for histological analysis and therapy of colonic lesions[1]. Quality of colonoscopy practice is highly variable and there is increasing public awareness of missed cancers, incomplete procedures and

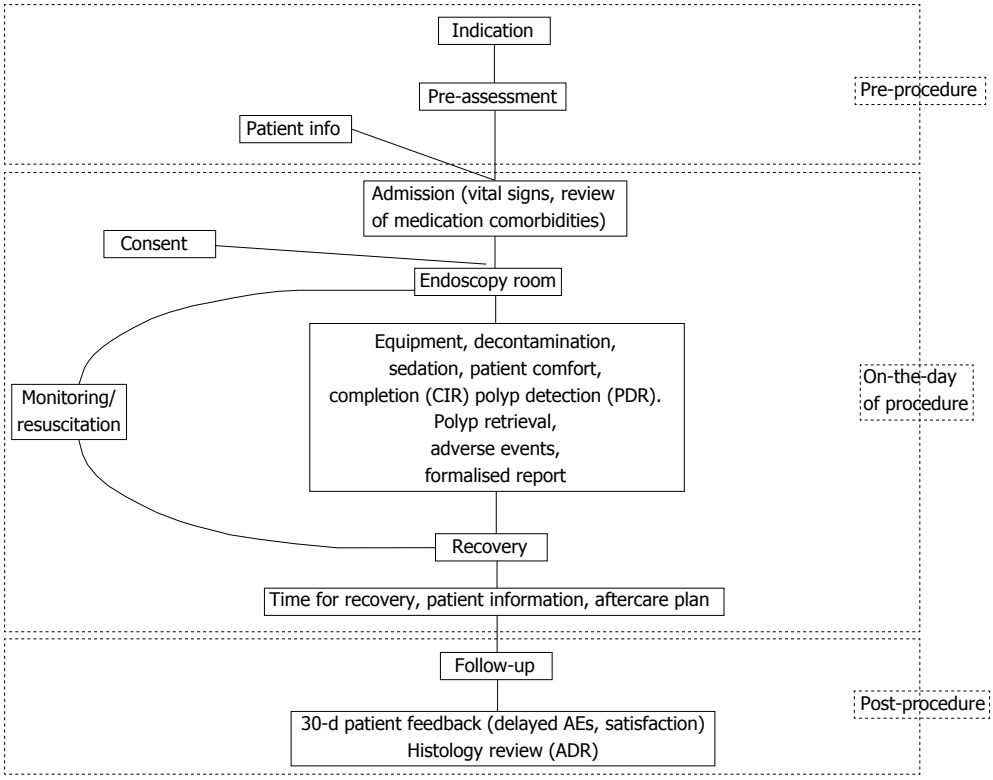

Figure 1 The cascade of colonoscopy. AE: Adverse event; ADR: Adenoma detection rate.

of adverse events related to colonoscopy which are potentially preventable[2,3]. The establishment of important, measurable quality indicators (metrics) and minimum quality standards is essential to define and shape a quality colonoscopy service.

The current quality indicators and standards for colonoscopy are based on varying levels of evidence, ranging from local perceptions and expert consensus to evidence from randomized controlled trials. The terms "auditable outcome" (an important indicator for which no clear evidence base exists) and "quality standard" (an auditable outcome for which there is an evidence base that can support a minimum standard) have been introduced to help define quality in endoscopy[4]. This paper does not aim to give technical details on how to perform colonoscopy but rather summarizes what to measure and when, in accordance with the current identified quality indicators and standards for colonoscopy.

HOW WE CAN MEASURE QUALITY

A colonoscopy service can be broken down into three main steps: pre-procedure, on the day of procedure and post-procedure (Figure 1). A high quality colonoscopy service should be patient-centered, evidence-based, cost-effective and adhering to best practice. Quality indicators and standards for each step of the colonoscopy service should be as simple and easy to audit as possible (Table 1).

Pre-procedure

An appropriate indication for colonoscopy should be determined in 100% of cases. Guidelines for indications and contraindications for colonoscopy should be used as a filter to avoid unnecessary and potentially hazardous procedures[5,6]. Time-scheduling should be based on priority (surveillance *vs* symptoms suggestive of CRC) and urgent referrals should be seen more rapidly. In our opinion a 6-wk time limit should be the maximum waiting time for a routine colonoscopy and $\geqslant$ 85% of individuals initially offered a colonoscopy should finally undergo a colonoscopy[4].

We recommend nurse-led patient pre-assessment either in a dedicated clinic or by telephone consultation especially when this has not been done by the vetting gastroenterologist. The endoscopist needs to have complete information of patient's medical history prior to colonoscopy; comorbidities such as clotting disorders, use of anticoagulants or anti-platelet agents, diabetes, allergies, renal function impairment, glaucoma, heart failure and factors related to the risk of endocarditis should be recognised prior to colonoscopy and instructions given to each patient should be driven by current recommendations and local policy[7-10]. The American Society of Anaesthesiologists (ASA) status and factors which could increase the risk and technical difficulty of colonoscopy, such as previous abdominal surgery (*i.e.*, hysterectomy) or diverticular disease should be recorded[7,11].

Patient information leaflets should be available and sent out to patients as a routine, along with a copy of the consent form. Patients must be aware of why the procedure is being organised, what is involved and of the risks related to colonoscopy. They should be informed about

Table 1 Quality metrics for colonoscopy as proposed by ESGE's guidelines and BCSP in United Kingdom

When to measure	Outcome to measure	Standard
Pre-procedure	Appropriateness	100% indicated
	Pre-assessment–bowel prep to use	100% of cases
	Patient information	100% of cases
	Awaiting time when positive test	< 4 wk (< 2 wk desirable)
On the day of procedure	Review of comorbidities, check of vital signs	100% on admission
	Informed consent	100% signed
	Decontamination of endoscopes	100% agreement with local policy
	Appropriate function and availability of endoscopes/equipment	100% checked by competent staff
	Equipment for resuscitation and monitoring	100% regular checks
	CO_2 insufflation	100% availability
	CIR	> 90% unadjusted
	Use of reversal agents	< 1/500 cases
	Bowel cleansing	good/excellent > 90%
	Patient comfort	NA
	Polyp detection rate	Dependent on case mix
	Polyp retrieval rate	> 90%
	Time of scope withdrawal	> 6 min
	Complication rates	Bleeding < 1/100 Perforation < 1/1000 (diagnostic) < 1/500 (therapeutic)
	Electronically based endoscopy report	100% attached to histology request
	Aftercare plan	100% provided at recovery area
	Time for recovery	NA
Post-procedure	Annual number of procedures/endoscopist	> 150 (> 300 desirable)
	Adenoma detection rate	> 15% unadjusted to race or gender
	Time of histopathology report	< 15 d post-colonoscopy
	Patient feedback/delayed AEs	100% at 30 d
	Endoscopic Surveillance needed	100% agreement with guidelines

CIR: Caecal intubation rate; AEs: Adverse events; NA: Not available.

Table 2 Groups of patients in whom polyethylene glycol bowel-preparation is considered as safer and thus should be preferred

Candidates for polyethylene glycol bowel preparation for colonoscopy
[1]GFR < 60 mL/min per 1.73 m^2
Electrolyte imbalance
Cardiac failure
Liver cirrhosis
Hypertension with arteriosclerosis
Patients on diuretics
(when cannot be stopped 24 h prior to colonoscopy)
Patients on ACE inhibitors
(when cannot be stopped 72 h prior to colonoscopy)
Patients on NSAIDs
(when cannot be stopped 72 h prior to colonoscopy)

[1]Estimated glomular filtration rate (GFR) from serum creatinine concentration. NSAIDs: Nonsteroidal antiinflammatory drugs; ACE: Angiotensin-converting enzyme.

the options for sedation in advance and the associated restrictions on travelling home[7].

A clean bowel is a prerequisite for a reliable and efficient examination[12,13]. Clear patient information, reduced fiber diet, regardless of type of bowel preparation used, help to maximise bowel cleansing[14]. PEG-electrolyte is the preparation of choice in patients with renal impairment although it does not eliminate the risk of acute renal failure and it is considered safer for patients with cardiac failure[15,16]. Adequate hydration is vital to protect against adverse events of bowel preparation while timing and in particular PM/AM splitting of administration of the recommended dose and assurance of patient's understanding of the process also appear to be important[14,17]. Table 2 outlines patients at risk of electrolyte imbalance and documents those who of when should have an assessment of renal function prior to bowel preparation. Those with established renal disease, stage Ⅲ or greater, should have PEG-electrolyte bowel preparation[18-22]. In our institution we use a combination of 10 senna tablets and 2 doses of sodium picosulfate the day before colonoscopy for morning appointments, while the second dose of sodium picosulfate is taken in the morning of the same day for afternoon colonoscopies. The patient is encouraged to drink at least 2 L of clear fluids daily for 2 d before the procedure and to avoid fiber 2 d before scheduled colonoscopy. We usually use a 2lt PEG solution (MOVIPREP) when needed. Although hospitalisation has been related with poorer bowel cleansing and should be routinely avoided, hospital admission prior to colonoscopy may be required in some cases, especially for patients in whom reduced absorption of regular medications may prove problematic and may need intravenous administration. Fragile patients with multiple comorbidities which are at risk of cardiac or renal failure and should be monitored during bowel prep are often admitted to hospital prior to colonoscopy[23]. Selection of these patients is a matter of careful clinical pre-assesment.

Colonoscopy in obese patients may prove technically demanding in some cases however, in our practice and according to previous reports, routine colonoscopy is the screening test of choice and can be performed adequately in obese patients when optimal standards are fulfilled[23]. Patients with previous incomplete procedures, multiple comorbidities or on anticoagulant treatment in whom discontinuation can prove catastrophic should be offered a virtual colonoscopy (CT colonography) as an alternative. In these cases virtual colonoscopy may prove an important pre-assessment tool regarding the cost, tolerability and reduced time of the procedure compared with conventional colonoscopy[24,25].

On the day of the procedure

A brief review of the cardiorespiratory function including blood pressure, pulse rate and oxygen saturation in addition to documentation of adverse events related to bowel preparation or any medication given prior to colonoscopy (*i.e.*, antibiotic prophylaxis) should be performed on the day of the procedure and before the patient's entrance into the endoscopy room.

A signed informed consent should be obtained by 100% of patients prior to colonoscopy, ideally in a separate area rather than the endoscopy room where a patient's privacy can be assured. Consent for colonoscopy must include a clear and realistic explanation of the procedure, possible attendant discomfort, the benefits and a clear discussion of risks and potential adverse events including sedation reactions, bleeding (immediate and delayed), perforation and missed pathology. Patient's right to withdraw consent at any stage of the colonoscopy process should be understood by all members of the team[4,26]. Some institutions having the patient consented in clinic by the requesting consultant as well as giving the prescription for bowel preparation and patient leaflets and thus alleviating the need for postal issue for the same. This practice can prove beneficial acting as an indirect vetting as well of high risk patients.

Endoscopy room

The appropriateness, availability and functionality of the endoscopy room and equipment used during colonoscopy (including equipment used for patient monitoring) should be ensured through regular checks. Cleansing and decontamination of endoscopes should conform to current National or International guidelines[27].

Monitoring of vital signs (blood pressure, pulse and oxygen saturation) and regular checks of patient's comfort and ability for verbal communication should be routinely used during colonoscopy. The use of CO_2 capnography is recommended to identify hypoventilation and hypoxia if heavy sedation required[28].

Patient's comfort during colonoscopy is a critical quality outcome which refers to public acceptance rate of the procedure as a screening tool[29]. Levels of patient discomfort (no or minimal, mild, moderate, severe) should be recorded during colonoscopy.

The use of CO_2 insufflation, instead of air, is currently a quality standard to maximize comfort during unsedated colonoscopy and flexible sigmoidoscopy and permits reliable radiologic examination at the same day following colonoscopy[7,30]. Moreover, since carbon dioxide is an inert gas that cannot form a combustible mixture with hydrogen and methane, CO_2 insufflation avoids the very rare risk of explosion during colonoscopy with electrocautery and reduces post-polypectomy admissions after removal of large polyps[31,32]. Insufflation of CO_2 should be avoided in patients with COPD, known CO_2 retention or severely reduced pulmonary function.

The use of sedation improves patient tolerance of colonoscopy. A "titrated" (administrated gradually during procedure) low dose of an anxiolytic, such as midazolam (1.25-5 mg), given alone or combined with an opiate like pethidine (12.5-100 mg) or fentanyl (25-100 μg) are usually sufficient to achieve conscious sedation during colonoscopy[33], however, thresholds of pain and over-sedation remain undistinguishable and variable between individuals. Dosage reduction should be considered for older patients (> 70)[33-35]. Nitrous oxide/oxygen inhalation (Entonox) should be an alternative for people that cannot have intravenous sedation[36]. The type and dose of medications used the level of sedation (minimal-anxiolysis, moderate-conscious, deep or general anaesthesia) and the use of reversal drugs should be recorded at every colonoscopy and should be an auditable safety outcome.

The adequacy of colonic cleansing is an important outcome related to the reliability and completion rates of colonoscopy and should be reported at each procedure. Valid scales for assessment of quality bowel preparation have been made according to the presence of solid or semisolid stool and the relative limitation to achieving adequate visualization[37,38]. Excellent or adequate bowel preparation documented in > 90% of cases has been considered as a standard of bowel preparation efficacy[4,7].

Intubation of the most proximal part of the colon is a prerequisite to achieving complete examination. Intubation of the terminal ileum (TI) is not required if there is not specific indication while obtaining biopsies from normal TI is discouraged secondary to the relative concern of variant Creutzfeldt - Jakob disease's transmission[39]. Caecal intubation rate (CIR) is a key quality indicator that reflects the performance skills of each colonoscopist, but can be affected by a variety of factors that can make the insertion of the scope difficult or impossible[40]. The main conflict in measuring the CIR of each colonoscopist is whether it should be adjusted for bowel preparation, obstructive lesions or for symptomatic patients. Overall, an unadjusted CIR > 90% can be used as the quality standard of colonoscopy, regardless of case[7].

The routine use of photodocumentation or videorecording is an emerging necessity in relation to the medicolegal risks of missed pathology or adverse events

(AEs) following colonoscopy[41]. Photographic evidence of the appendix orifice and/or the ileocaecal valve has been considered as a standard practice to achieve completion[7]. Unarguably, additional pictures of the ileal mucosa provide strong evidence of completion[42]. Rectal retroversion has been considered as an established diagnostic technique to improve detection of lesions abutting the dental line[43,44] however an adequate examination can also be performed by tip manipulation in the forward view.

The incidence of colorectal cancer (CRC) can be significantly reduced through detection and appropriate removal of adenomatous polyps during colonoscopy[1]. The polyp detection rate (PDR) is defined as the number of colonoscopies at which one or more polyps were found (regardless of histological type) divided by the total number of colonoscopies performed (in the same time period). Counting polyps or polypectomy rates is easy during colonoscopy but is not as important parameter as adenoma detection rate (see later). A high retrieval rate (> 90%) of polyps removed is a recognized quality standard in the United Kingdom BCS program and can be affected by polyp size and cold snare technique of polypectomy[45]. The number and size of adenomatous polyps removed at colonoscopy should be recorded as this defines the risk of CRC and determines endoscopic surveillance[4,46,47].

Time spent on withdrawal (WT) is an important quality outcome and should be recorded during colonoscopy. A time for scope withdrawal of more than 6 min has been well-correlated with increased detection of adenomas and thus is considered as an important quality standard to be followed by each endoscopist[48]. Longer WT has been related with increased detection of proximal and serrated polyps[49,50]. Probably adequate withdraw technique and high technical endoscopist's skills are more important to increase detection rate when appropriate WT (> 6 min) has been spent, but this is a matter of proper training and accreditation in colonoscopy that exceeds the purposes of this paper[51,52].

AEs in colonoscopy are uncommon but can be life threatening. Appropriate documentation of AEs related to colonoscopy is a substantial outcome of safety of the procedure. A Lexicon has been previously developed to provide clear definitions for AEs and levels of severity, including the minimum threshold at which an AE should be documented and reported[53]. Early AEs (bleeding, perforation, oversedation, vasovagal attacks), whether they have been adequately resolved during the procedure (*i.e.*, use of haemostatic equipment or reversal drugs, hydration) or whether further actions are required, have to be clearly documented.

The endoscopist should be competent with the function of all supplementary equipment used during the procedure. Therapeutic colonoscopists should be technically competent to identify and safely remove high-risk lesions and be comfortable with techniques of endoscopic haemostasis[54,55]. Around 90% of post-polypectomy bleeding should be amenable to conservative management without the need for surgical intervention. According to current recommendations based on data from retrospective studies, the incidence of bleeding for colonoscopies where polypectomy is performed should not exceed 1/100[4]. However, this is a cut -off point that needs to be adjusted according to the time (immediate or delayed) and severity of bleeding, patients' comorbidities and complexity of the procedure (*i.e.*, EMR or simple polypectomy). Future analysis of risk factors for delayed bleeding should be possible and would optimally permit individualization of the risk of bleeding between patients. Risk of perforation should not exceed 1/1000 procedures, but may have to be adjusted to 1/500 for therapeutic colonoscopies with polypectomy[4]. In cases of therapeutic colonoscopy, the final report should include a clear description of "alarm post procedural symptoms" symptoms such as rectal bleeding, fever or abdominal pain that can be associated with delayed AEs requiring immediate medical support[4,56,57].

An increased number of AEs (ie bleeding or perforation) during therapeutic procedures always raise issues about the adequacy of therapeutic skills of each endoscopist. The European guidelines for quality assurance in colorectal cancer screening and diagnosis have proposed 5 levels of competency in colonoscopy related to the interventional armamentarium of each colonoscopist. According to this consensus colonoscopists should be able at least to remove lesions < 10 mm in order to avoid additional endoscopic procedures. We recommend that basic EMR technique for sessile polyps 1-2 cm in size, or for small flat adenomas smaller than 1 cm, should be within the armamentarium of all colonoscopists.

Recovery area

Standard protocols for monitoring and for emergencies should be available in the recovery area. Checks of availability and proper function of resuscitation and monitoring equipment should be regularly updated. Time of recovery is an important auditable outcome and should be recorded. After recovering from sedation and before leaving the endoscopy unit, patients need to be told about the outcome of their procedure in a simple and comprehensive way. Breaking bad news regarding suspicion of cancer should be done according to the established local policy. The average waiting time for the histopathology report and the aftercare plan should be provided and supported by a detailed written report of the procedure that includes a contact telephone number (24 h/d, 7 d/wk) in case of a procedure-related complication. An electronically based and formalized endoscopy report is essential for further interpretation of outcomes.

A copy of the endoscopy report should be attached to any histology request and should be as detailed as possible to provide accurate description of suspicious lesions including their location, their estimated size, their nature according to accredited classification systems (*i.e.*,

Paris or Lateral Spreading Tumors - LST - classification)[58], whether they are ulcerated and in case of excision whether this was completed or not.

Post-procedure

Adenoma detection rate (ADR) is currently the benchmark of quality in colonoscopy and represents the number of colonoscopies at which one or more histologically confirmed adenomas were found divided by the total number of colonoscopies performed in the same time period[59]. ADR reflects a colonoscopist's technical skills and care to achieve visualization of the entire colon during the procedure. High ADRs reduce the probability of interval cancer by correctly identify surveillance intervals[60]. The overall prevalence of CRC, polyps and adenomas may differ between patient populations according to gender, race, diet or environmental factors and subsequently ADRs may vary[61]. Measurement of ADR is greatly assisted by a direct link between the databases of the endoscopy and pathology departments, but this is not available everywhere[62]. Polypectomy rates can potentially provide an ADR estimate based on previous ADRs but polyp detection rate (PDR) should be used cautiously for polyps of the left colon[63-66]. Previous reports argue that reliability of ADR is much higher when refers to a sufficient volume of colonoscopies (> 150/year in our BCSP) while the number and features (size, histology or grade of dysplasia) of adenomas detected per procedure is not included when counting ADR[67,68]. The mean number of adenomas per procedure (MAP) (defined as the total number of adenomas detected divided by the number of procedures) and the mean number of adenomas per positive procedure (MAP +) (defined as the total number of adenomas detected divided by the number of procedures in which one or more adenomas were detected) can provide additional information for endoscopist's performance[44,69,70]. We recommend an ADR > 15% as the minimum outcome unadjusted for gender or race.

The reliability of a colonoscopy service is dependent on a well-organized aftercare system. This should provide patients with easy-access to further care pathways deemed necessary by colonoscopy such as appropriate time for follow-up colonoscopy (indicated by current guidelines) need for radiological or surgical examination or referral to local Multi-Disciplinary-Team (MDT) meeting. This network should ensure that no patient is lost to follow-up and it requires good communication between relevant departments (Gastroenterology, Radiology, Histopathology and Surgery).

A routine policy of contacting patients within a defined period of time (30 d) following colonoscopy is recommended to check for delayed adverse events related to the procedure and to obtain the overall patient's feedback for the service. A simple quality questionnaire for each part of colonoscopy service is useful to detect problems with the service. We recommend a routine 30-d check for every patient having a colonoscopy while patients should also be encouraged to report any AE in the meantime. Regular reviews of complications and 30-d mortality is an essential part of quality assurance. Records of adverse events should be kept active. Clusters of AEs should instigate a formal review of individual cases.

CONCLUSION

Quality in colonoscopy encompasses optimal collaboration of various professionals with clearly defined processes. Quality assurance in colononoscopy should be based on measurement of simple and reproducible outcomes which permit regular checks on each step of the colonoscopy service. CIR and ADR are the key elements of personal endoscopic performance and their value is maximized when standards of patient's safety, comfort and satisfaction are adequately monitored and reviewed.

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REVIEW

Enteroscopy in small bowel Crohn's disease: A review

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Abstract

Crohn's disease (CD) is a chronic inflammatory condition of the gastrointestinal tract resulting in inflammation, stricturing and fistulae secondary to transmural inflammation. Diagnosis relies on clinical history, abnormal laboratory parameters, characteristic radiologic and endoscopic changes within the gastrointestinal tract and most importantly a supportive histology. The article is intended mainly for the general gastroenterologist and for other interested physicians. Management of small bowel CD has been suboptimal and limited due to the inaccessibility of the small bowel. Enteroscopy has had a significant renaissance recently, thereby extending the reach of the endoscopist, aiding diagnosis and enabling therapeutic interventions in the small bowel. Radiologic imaging is used as the first line modality to visualise the small bowel. If the clinical suspicion is high, wireless capsule endoscopy (WCE) is used to rule out superficial and early disease, despite the above investigations being normal. This is followed by push enteroscopy or device assisted enteroscopy (DAE) as is appropriate. This approach has been found to be the most cost effective and least invasive. DAE includes balloon-assisted enteroscopy, [double balloon enteroscopy (DBE), single balloon enteroscopy (SBE) and more recently spiral enteroscopy (SE)]. This review is not going to cover the various other indications of enteroscopy, radiological small bowel investigations nor WCE and limited only to enteroscopy in small bowel Crohn's. These excluded topics already have comprehensive reviews. Evidence available from randomized controlled trials comparing the various modalities is limited and at best regarded as Grade C or D (based on expert opinion). The evidence suggests that all three DAE modalities have comparable insertion depths, diagnostic and therapeutic efficacies and complication rates, though most favour DBE due to higher rates of total enteroscopy. SE is quicker than DBE, but lower complete enteroscopy rates. SBE has quicker procedural times and is evolving but the least available DAE today. Larger prospective randomised controlled trial's in the future could help us understand some unanswered areas including the role of BAE in small bowel screening and comparative studies between the main types of enteroscopy in small bowel CD.

Key words: Crohn's disease; Enteroscopy; Ileoscopy; Balloon-assisted; Device-assisted; Spiral device; Overtube; Stricture; Dilatation

Core tip: Management of small bowel Crohn's disease has reached new frontiers with the recent renaissance of enteroscopy, that has improved diagnosis and enabled therapeutic interventions. The use of magnetic resonance enteroclysis or wireless capsule endoscopy as the first line modality followed by enteroscopy is the most cost effective. Enteroscopy could be achieved using either a push enteroscope or device-assisted enteroscope (DAE). The latter includes double balloon enteroscopy (DBE), single balloon enteroscopy and more recently spiral enteroscopy. All three DAE modalities are comparable, though most favour DBE due to higher rates of total enteroscopy. The article

is intended for the general gastroenterologists, non-gastroenterologists and general practitioners

Tharian B, Caddy G, Tham TCK. Enteroscopy in small bowel Crohn's disease: A review. *World J Gastrointest Endosc* 2013; 5(10): 476-486 Available from: URL: http://www.wjgnet.com/1948-5190/full/v5/i10/476.htm DOI: http://dx.doi.org/10.4253/wjge.v5.i10.476

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory condition of the gastrointestinal tract resulting in inflammation, stricturing and fistulae secondary to transmural inflammation[1,2]. Diagnosis relies on clinical history, abnormal laboratory parameters characteristic radiologic and endoscopic changes within the gastrointestinal tract and most importantly histology for confirmation and grading of severity[2]. CD can affect the entire gastrointestinal tract from mouth to anus, in addition to being a multisystem disease. It affects only the small intestine in 30%, ileo-colonic in 50%, colonic disease alone in 30% and upper GI tract in approximately in 5%[3,4]. CD may have characteristic endoscopic features like aphthous ulcers, longitudinal erosions, cobble stone appearance and fissures[4,5] (Figure 1).

The detection of small bowel CD and its management presents its own challenges, especially when the disease is present beyond the reach of the gastroscope and colonoscope. This is mainly due to length of the small bowel but also the tortuous anatomy and the floppy mesentery that leads to looping when a scope is advanced beyond the duodenum[6-13]. The distal 10-20 cm of the ileum can often be accessible with ileo-colonoscopy but more proximal visualisation is often limited by looping. In addition, disease of the ileo-caecal valve can prevent intubation of the ileum. Enteroscopy helps in assessing mucosal disease while cross sectional imaging is better for transmural involvement including fistulae. Small bowel radiological investigations include barium follow through, computed tomography (CT) enteroclysis or enterography, magnetic resonance enteroclysis or enterography and small bowel ultrasound (USS)[7,9-13]. The latter is not widely used since the ultrasound waves have limited penetration through air. However it is useful in assessing thickness of the small bowel and vascularity with Doppler and correlates with active disease. Wireless capsule endoscopy (WCE) is a sensitive test for small bowel disease and is often used to investigate small bowel CD, prior to any invasive deep bowel enteroscopy, once small bowel strictures have been excluded[1,14-19]. Dionissio *et al*[20] had shown in their meta-analysis comparing 18 prospective studies that WCE was best in evaluation of non-stricturing small bowel CD and magnetic resonance enteroclysis (MRE) had the highest diagnostic yield in known CD. This review is not going to cover the various radiological investigations or WCE[20,21].

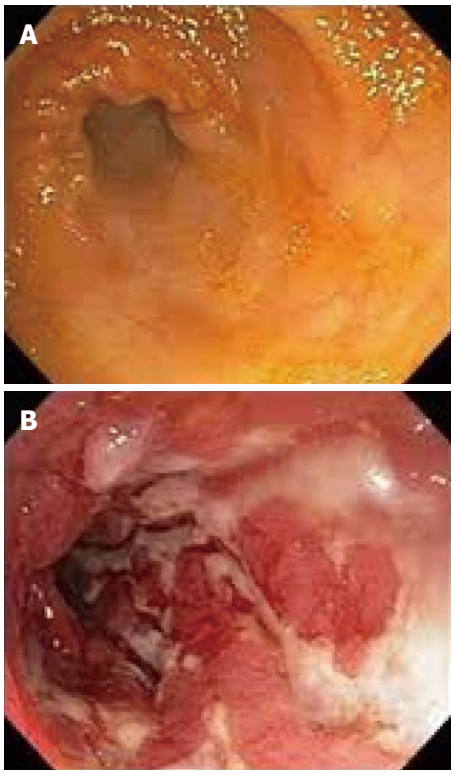

Figure 1 Normal (A) *vs* small bowel Crohn's (B).

Technological advances have extended the reach of the gastroenterologist, enabling access to the entire gut using flexible fibre optic scopes, with a combination of pushing, pulling and torquing to pleat the long and tortuous small bowel. Enteroscopy has improved the field of small bowel CD, in which radiological investigations previously predominated. Despite all these tools to empower the gastroenterologist and radiologist, the assessment of small bowel damage in CD is still far from sufficient. Evidence available from randomised controlled trials comparing the various modalities is limited and at best regarded as Grade C or D (based on expert opinion). Most of the studies performed to date are single centre experiences (retrospective studies) or multicentre trials involving small numbers. Thus a main limitation of this article is lack of comparative data specifically on CD.

The advantages of enteroscopy include the ability for real-time viewing of the small bowel, to biopsy abnormal mucosa and to undertake therapy such as pneumatic dilatation using the through-the-scope (TTS) balloons, achieving hemostasis, polypectomy, local injection of triamcinolone and immunomodulatory drugs and more recently metallic and biodegradable stent insertion[18,22-25]. Endoscopic dilatation (ED), the commonest therapeutic use of deep enteroscopy in CD, has been used when medical therapy fails to relieve obstruction. These are often done using centre based and regional guidelines, which are often tailored depending on the availability of local expertise, financial constraints and patient preference. The scope of an enteroscope is much wider, including comple-

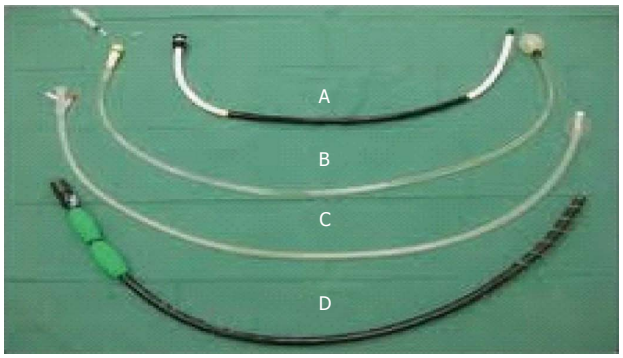

Figure 2 Device assisted enteroscopes. A: Conventional semi-rigid overtube (Olympus); B: Double-balloon overtube (Fujinon); C: Single-balloon overtube (Olympus); D: Spiral overtube (Spirus Medical). Available from: URL: www.annalsgastro.gr.

tion colonoscopy and for endoscopic retrograde cholangiopancreatography in surgically altered anatomy[24,25]. The various methods currently available worldwide can be either a push enteroscopy (PE) or device-assisted enteroscopy (DAE) using overtubes (Figure 2). The latter includes balloon-assisted enteroscopes (BAE) [double balloon enteroscopy (DBE) and single balloon enteroscopy (SBE)] and more recently spiral enteroscopy (SE). The complimentary use of cross sectional imaging and endoscopy is invaluable in the diagnosis and management of small bowel CD (Table 1).

PUSH ENTEROSCOPY

Traditional push enteroscope was developed in the 1980's. PE has a working length between 220 and 250 cm and is inserted per orally directly into the proximal jejunum[26]. The alternative is to use an adult or paediatric colonoscope for the same purpose. It can be used for both diagnostic and therapeutic purposes[26-29]. The push enteroscope may be used with or without an overtube (Figure 3). There have been several studies comparing the use of an overtube in push enteroscopy but not specifically in CD. Taylor and colleagues studied a small group of 38 patients (19 with an overtube and 19 without) and compared the depth of insertion as measured by the distance of insertion with the scope in a shortened position[29]. The median total straightened scope length of insertion just reached significance (125 cm *vs* 110 cm). From the pylorus the depth of insertion was also significant (70 cm *vs* 50 cm). However, there was no significant difference in the detection of small bowel pathology[29]. Overall complication rate of this widely available procedure in this study was 1%.

This technique is still commonly used to assess and treat proximal small bowel pathology due to its ease of use. Benz and colleagues studied enteroscopy in a group of 80 patients randomly assigned to enteroscopy with an overtube *vs* enteroscopy without an overtube[27]. The authors found that depth of insertion as measured by distance in a straightened position from the pylorus and

Table 1 Ranking of enteroscopic techniques for small bowel Crohn's disease

Modality tested	PE	DBE	SBE	SE
Availability	1	2	3	4
Ease of use	1	4	3	2
Platform used	Any	Fujinon	Olympus	Any
No of operators	1	1[2]	1	2[1]
Depth achieved	4	1	2	3
Speed	1	4	3	2
Therapeutic	4	2	2	1[1]
Safety	1	2	2	2
Cost	1	3	3	2

The numbers 1 to 4 refer to the authors ranking, with 1 being the highest and 4 being the lowest. [1]Once motorised might need only one operator. Best for stent insertion due to the stability achieved due to the overtube stabilization, though completion rates better for DBE/SBE; [2]Needs two operators in the early phase of the learning curve. PE: Push enteroscope; DBE: Double balloon enteroscope; SBE: Single balloon enteroscope; SE: Spiral enteroscope.

number of counted folds was significantly increased by using an overtube. A further study by the same author compared 2 working lengths of endoscope (250 cm *vs* 220 cm) to compare the depth of insertion in 28 patients[28]. An overtube was used in all cases. The median insertion from the pylorus was 72.5 cm *vs* 70.0 cm but no significant difference was demonstrated in depth of small bowel insertion using a longer endoscope[28].

Another method of improving depth of insertion into the small bowel is by using a variable stiffness scope in an attempt to reduce excess looping of the scope within the stomach[30]. Harewood and colleagues prospectively studied enteroscopy in 3 groups of patients (one with standard enteroscope with overtube, one without overtube and a third one with variable stiffness)[31]. Depth of insertion beyond the ligament of Treitz was significantly greater using a variable stiffness enteroscope (89 cm) compared to a standard enteroscope (68 cm) and was over twice that without an overtube (41 cm) (P = 0.03). In this study, patients in the overtube group required significantly more sedation than the other groups, although the overall patient tolerance and procedure duration showed no significant difference. Again, no additional yield of pathological findings was observed with the greater depth of insertion[32]. In a small study by Perez-Cuadrado *et al*[33], 50% (4 of 8) of this patient group with suspected CD had detectable macroscopic and/or microscopic evidence of small bowel CD not detected by other endoscopic or radiological methods. The same author demonstrated the therapeutic role of PE in small bowel Crohn's for jejunal stricture dilatation[32]. In a recent study by Darbari *et al*[34], it was shown that PE was useful and safe in proximal small bowel disease, predominantly CD, leading on to definite change in management. In this study, proximal small bowel CD was detected in 23 out of 44 suspected cases. ED is often considered successful if the scope could be passed through the stricture once dilated. ED should ideally be limited to accessible linear fibrotic strictures under 4 cm

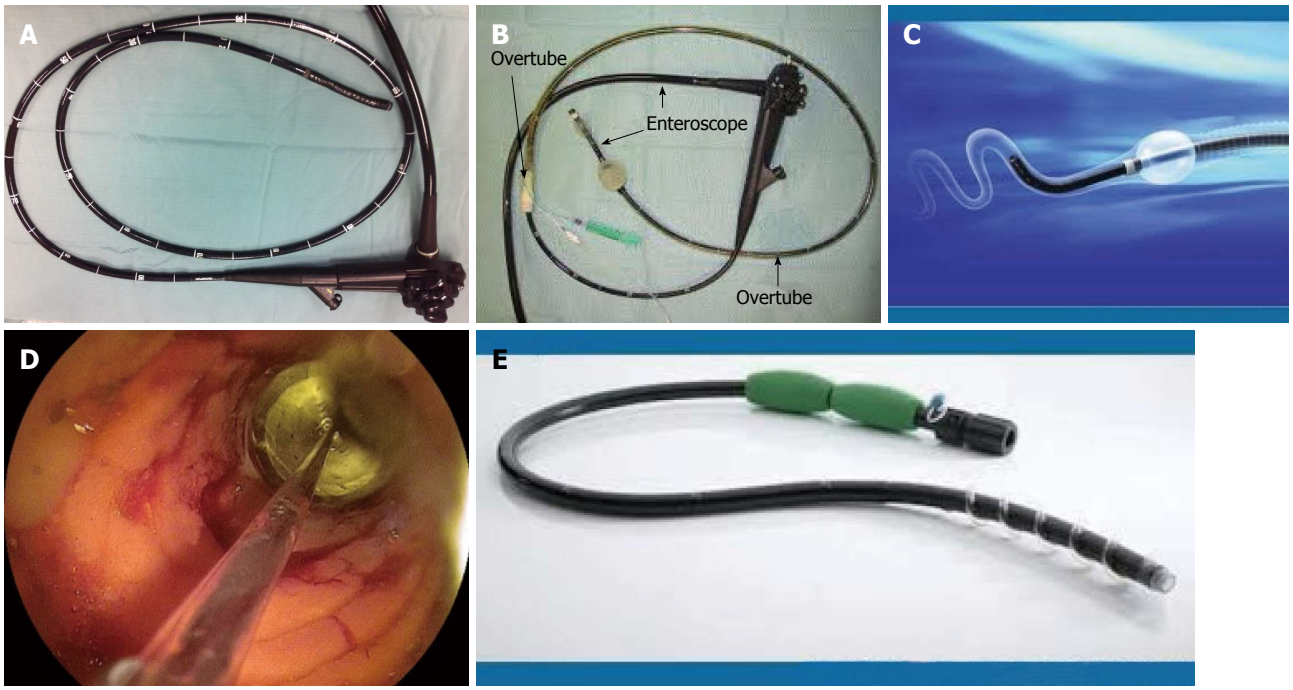

Figure 3 Enteroscope. A: Push enteroscope; B: Double balloon enteroscope (www.sciencedirect.com); C: Single balloon enteroscope (www.medscape.com); D: Balloon dilatation of jejunal stricture (www.kcvl.cz); E: Spiral enteroscope (www.medscape.com).

length to minimise risk of perforation[35,36].

DBE

DBE, originally developed in 2001 by Prof Hironori Yamamoto, is useful in the diagnosis of small bowel diseases including (CD)[9,23,37-39] (Figure 3B). DBE is often used following WCE due to potential miss rate of the latter and to guide the approach of insertion of DBE (antegrade or retrograde). The standard system has an endoscope with an outer diameter of 8.5 mm and a working length of 200 cm[38-40]. It is also provided with a 145 cm soft overtube with 12.2 mm outer diameter and a dedicated pump. One balloon is attached to the tip of the scope, after back loading the overtube (which has an additional balloon attached to the tip of the overtube)[6,25,32,39,41,42]. DBE can be performed with an anterograde (oral) followed by a retrograde (anal) approach or vice versa, with conscious sedation, deep sedation or general anaesthesia. Either air or carbon dioxide can be used, the latter recommended due to better patient tolerance, especially for therapeutic procedures and less post procedural discomfort, when a prolonged procedure is anticipated. Fluoroscopic guidance could be used till competence is achieved, but is not essential[39-41,43].

The overall yield of DBE was better than push enteroscopy and similar to capsule. Oshitani *et al*[6] showed that, in their study of 30 patients with CD, small bowel ulcers and aphthae were picked up in 9 patients who underwent DBE who had normal small bowel follow through. WCE done in 8 of these patients without symptoms of strictures showed additional finding of small bowel scarring in only one of the patients, though one of the eight developed capsule retention, that was retrieved using DBE. Nine ileal strictures were picked up with barium compared to only 6 with DBE[6].

The scope is inserted as far as possible into the bowel. Then the overtube balloon is inflated to anchor the tip in place and the scope is gently pulled backward to pleat the small bowel behind the balloon. The scope is further advanced into the lumen, followed by inflation of the scope balloon to anchor its tip. Thus by repetitive cycles of balloon inflation/deflation, the scope is advanced. In the early stages of training, this needs two operators, though once experienced one would be sufficient (Figure 4)[39]. A practical tip that is often advocated by Professor Yamamoto to advance an enteroscope is, slight "jiggling" of the scope, with alternating small "in-out" and "right-left" movements, that enables the tip to move forward. The distal most point is tattooed with India ink in the anterograde approach, to be visualised *via* the retrograde approach for total enteroscopy[24,37,44,45]. The procedure time can vary between 70 to 120 min for the ante-grade procedure and about 15-20 min longer for the retrograde approach, with ileal intubation rates in the latter being over 90% in high volume centre[43]. DBE has a steep learning curve[39,46]. Zhang *et al*[47] rightly commented that the combined analysis of imaging and gastro endoscopic findings in addition to a diligent clinical history and examination is essential to enhance the diagnostic efficiency of DBE .

In a study of 37 patients with CD who underwent DBE diagnostic yield was 60%. Yield levels increased if direction of insertion (ante-grade or retrograde) was aided by prior investigations[9]. The retrograde approach is useful for lesions noted in the distal 40% of

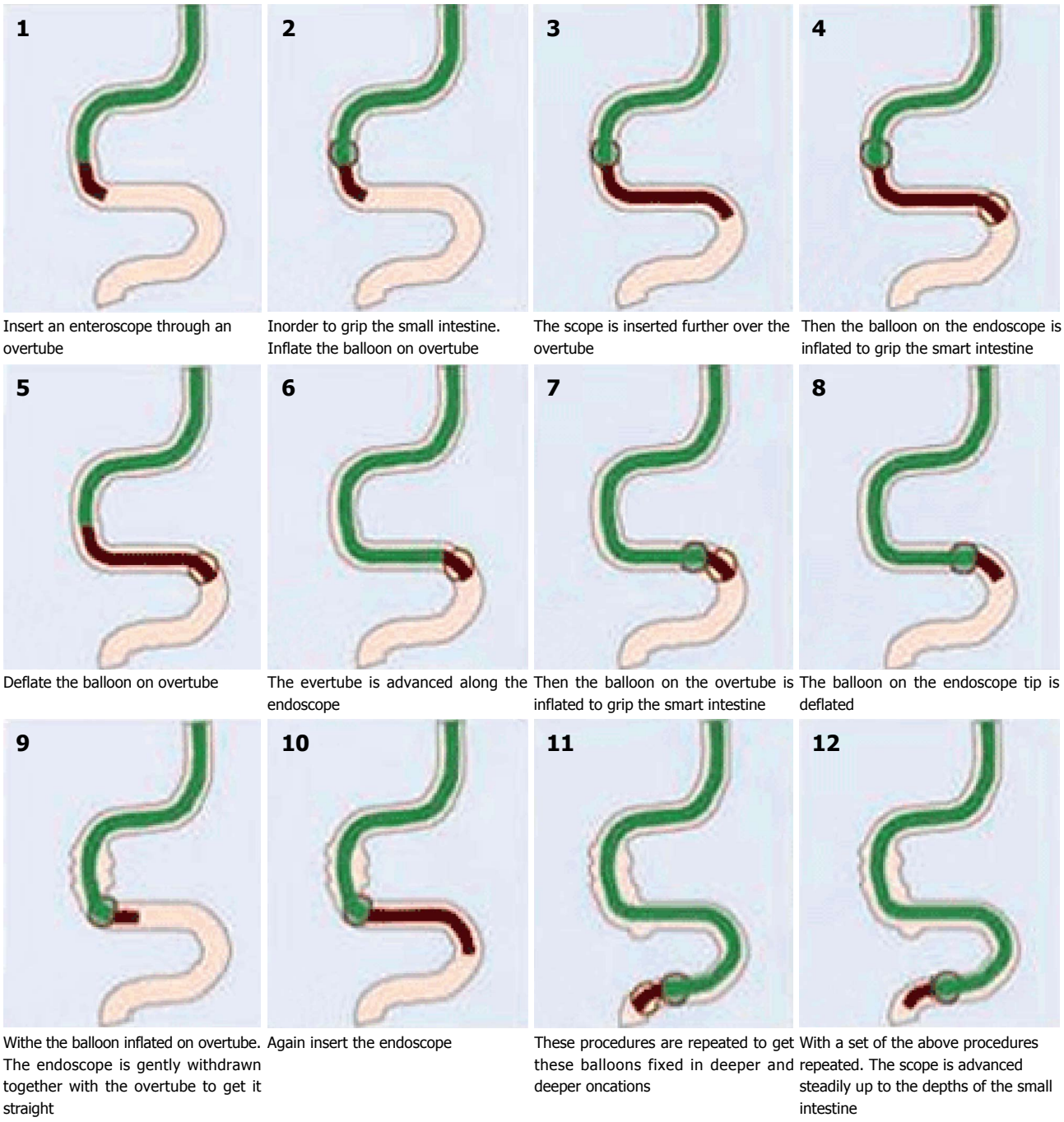

Figure 4 Push and pull technique with double balloon enteroscopy. Available from: URL: www.wlsvitagarten.com.

the WCE[48]. In an early retrospective study, the role of DBE in evaluation of 40 patients with CD was found to be superior to radiological studies in detecting mucosal ulcers and strictures[6]. Moreover endoscopic findings often precede radiologic findings that often delay the diagnosis by 1 to 7 years, and hence earlier diagnosis with DBE may lead on to earlier mucosal healing that is the corner stone in management of CD[8,45,49,50]. The ability of therapeutic potential of DBE remains a significant advantage over capsule endoscopy. In a study of 19 patients (10 amenable to endoscopic therapy), Pohl *et al*[51] demonstrated that dilatation under fluoroscopy yielded a clinical improvement in 80% and avoidance of surgery in 60% albeit over a mean short term follow up period of 10 mo, with no reported complications. The technique is also useful for retrieval of retained capsules[2,38,43,52].

In a similar study, 8 of 9 patients with Crohn's strictures underwent successful endoscopic dilatation (1 patient had a perforation). Clinical improvement occurred in these 8 patients with no surgical requirement over a follow up of 20 mo. Twenty five percent of patients did require a second dilation[53]. DBE has been shown to alter medical management in patients with established and suspected CD. Mensink and colleagues identified 24 patients with active CD (60% of study population)

resulting in a change in management in 75% through a step up approach in these patients medical management. Over 80% of these patients had a clinical improvement with a reduction in CDAI[54,55]. In a further study by the same author a small population of Crohn's patients with suspected proximal small intestinal Crohn's underwent DBE. Approximately three quarters of patients had proximal small bowel Crohn's features, and approximately 50% were beyond reach of standard enteroscopy. There was a change in management in three quarters of those patients with detectable disease by DBE[55]. DBE can also help in assessment of radiologic abnormalities and thus to avoid unnecessary exploratory surgery[8,49,54,56].

The procedure hence is very valuable with a high success rate, but not preferred for those with difficult anatomy due to previous surgery, pathology or acute angle at the stoma due to higher perforation rate (0.4% of procedures and up to 3% when dilated)[43,57-59]. It should also be avoided in those with latex allergy since the balloons are made of latex[8]. The other complications include small risk of pancreatitis (0.3% of procedures), bleeding (0.2% of procedures) and aspiration pneumonia[60-62]. ED should be postponed till the ulcer heals due to higher risk of perforation and is discouraged if over 6 cm long[63].

SBE

SBE was introduced in 2007. It uses an enteroscope with 200 cm working length and 2.8 mm channel diameter, an overtube with a silicone balloon that has an outer diameter of 13.2 mm and a balloon controller pump[57,64,65]. The technique is similar to DBE, with the only difference being that the tip of the flexible scope is used to anchor the endoscope, avoiding need of a second balloon[65] (Figure 3C). The depth of insertion ranges from 133 to 270 cm and 73 to 199 cm for the retrograde examination, with a therapeutic yield between 7% to 50%. Total enteroscopy rate is lower than DBE, but is a safe, effective and useful technique for deep small bowel endoscopy[64,66-68]. The main advantage of SBE is the ease of assembling the apparatus taking 5 min compared to 15 min for DBE and overall shorter procedure duration of 55 min compared to 95 for DBE. Secondly it has variable stiffness, thus eliminating the need for a stiffening wire[67,69-73]. Thirdly SBE can be used in patients with latex allergy unlike DBE. Dr. Reddy's group from Hyderabad, initially described use of "power suction" during straightening of the scope, that can be used instead of inversion of the tip, to minimise the perforation rate that is around 2%[74].

In a small study in children between 8 and 18 years old by de Ridder *et al*[68], it was shown that SBE is a safe technique and picks up active small bowel Crohn's that has been missed by magnetic resonance imaging and USS. Similarly, Di Nardo *et al*[69], showed the safety, yield and therapeutic efficacy of SBE in their study of 16 children with suspected and 14 with known Crohn's with atypical presentation, who had negative radiologic and conventional upper and lower gastrointestinal endoscopy. In a recent randomised multicenter trial, Domagk *et al*[66] showed the non-inferiority of SBE over DBE in evaluation of small bowel pathology[71]. Takano *et al*[70] showed in their randomised controlled trial that, total enteroscopy was much better accomplished with DBE than SBE, though it was a single centre study involving only small numbers. Bortlik *et al*[75] showed that in their experience of SBE in 35 patients, it provided an evaluation of mucosal healing after treatment and revealed severe inflammatory changes in one third. Therapeutic procedures especially dilation using TTS balloon were done in approximately a third (Figure 3D). SBE is cheaper, easier to perform, has a shorter learning curve than DBE and is a less complex method of balloon assisted enteroscopy[65,66,68,71,73,76]. Current results are conflicting if the SBE and DBE have comparable performance and diagnostic yield. However, more studies favour use of DBE for total small bowel enteroscopy[70].

SE

This is the latest of the armamentarium, available since 2008 to gastroenterologists, to examine the small bowel and is simpler and faster than the predecessors[71,77,78]. The current second generation device uses an FDA approved 118 cm Endo-Ease Discovery™ SB overtube with a soft raised helix, a coupling device to fix the lubricated overtube to the enteroscope 25 cm from its tip, two handles for manual rotation and an injection port for lubrication (C 8)[74,79-82]. The distal end of the device has an external diameter of 16 mm and the internal diameter of the overtube is 9.8 mm. Clockwise rotation pleats the small bowel onto the scope, once engaged and advances the same thus transforming the torquing force into a linear one, the concept developed by Spirus Medical, Inc. and proposed for use in enteroscopy by Dr. Akerman *et al*[77,81,82] in 2006. Push and rotation technique is used until the scope gets beyond the Ligament of Trietz, followed by only rotation. The small bowel does not get twisted as it is held by the mesentery. It can be performed under conscious sedation or general anaesthetic, preferably the latter. In an intubated patient, the cuff on the endotracheal tube has to be deflated before introducing the spiral enteroscope to prevent oesophageal trauma, until it enters the stomach[77,83,84] (Figure 3E).

The major advantage of SE is the rapid advancement and stable controlled withdrawal enabling therapeutics to be delivered effectively[42,71,77,84]. The overtube can be disengaged from the coupler enabling complete withdrawal of the endoscope and reintroduction (often needed for removal of multiple polyps), without losing the position in the small bowel[42,71,84-86]. The other major advantage is that no dedicated enteroscopy system needs to be purchased and the Endo-Ease spiral overtube could transform an ordinary enteroscope or a paediatric colono-

scope to a SE device[40,77,78,81]. Spiral enteroscopy is very useful for proximal small bowel pathology, especially for therapeutic interventions, due to the stability achieved with the overtube.

This procedure requires two operators, one operator handling the scope and the other rotating the overtube. The enteroscope is unlocked from the overtube, advanced and then withdrawn using the hook and suction technique. Anticlockwise rotation of the handle of the overtube is used to withdraw the system allowing visualisation of the mucosa in a controlled fashion. The depth of insertion of SE is usually calculated on the way out. It has not yet been safely demonstrated for retrograde approach, unlike DBE. A promising motorised overtube is in its early stages of development, which could make it single operator dependent. Sore throat and transient difficulty in swallowing are described by around a quarter of the patients, though tiny asymptomatic mucosal disruptions are similar to the balloon assisted devices.

In a study by Buscaglia *et al*[83] the mean procedure length was around 34 min with a mean insertion depth of 262 cm. One of the early studies by Frieling *et al*[87] showed that the diagnostic yield of DBE was superior to that of SE. But as the authors commented, one of the main drawbacks was that it involved only small numbers of 17 and 18 subjects respectively. In yet another small cross over study involving 10 patients, May *et al*[42] showed that SE had a shorter procedure duration by a mean of 22 min, though the depth of insertion was greater by about 60 cm with DBE. Khashab *et al*[86] in their first comparative study on SE *vs* SBE, showed greater depth of maximal insertion with the former, although the yield and procedure length were comparable. Akerman *et al*[77,81] showed an overall severe complication rate less than 0.3% in their review of 2950 patients treated with SE, with perforation occurring in 0.4% of the first 1750 patients and no reported cases of pancreatitis. However Teshima *et al*[88] showed that asymptomatic hyperamylasemia occurred in up to 20% of patients undergoing SE. Data is limited especially with regards to comparative studies specifically related to use of SE in CD. But overall it is considered to be a safe and quick procedure and compares favourably with other DAE for assessing the small bowel and for delivering therapies in the midgut[71,77,79,80,83-86,89,90].

OTHER METHODS OF DEEP SMALL BOWEL ENTEROSCOPY

Intraoperative enteroscopy (IOE) developed over 35 years ago enables the entire gut to be viewed without making an incision on the intestine, by the cooperation of the operating surgeon and the endoscopist[91]. It was done using rigid sigmoidoscopes in the 50's, until fibre optic scopes became available in the 70's[92]. Once the surgeon has completed exploring the small bowel laparoscopically and freed the bowel from any adhesions, small bowel loops can be pleated over the orally inserted PE. The current role of IOE is in difficult mid gut pathology, in guiding the surgeon intraoperatively and in marking the lesion with a suture to be dealt with on removing the scope[92-96]. There have not been many studies evaluating role of IOE in CD[94,97]. Complications include standard ones associated with laparoscopy and endoscopy, prolonged post operative ileus, air embolism and multiorgan failure. IOE once regarded as the gold standard for small bowel evaluation has been relegated a "last resort" in the era of less invasive therapeutic total enteroscopy with DAE[91,95-98].

CONCLUSION

Novel biologic agents and progress in our assessment and management of small bowel CD, which is currently far from sufficient, might help alter the natural history and predict outcomes in Crohn's disease. However enteroscopy, which is a rapidly evolving field, has had a significant renaissance recently and the small bowel is no longer the black box for the endoscopist or the final frontier. The lack of randomised controlled trial's (RCT's) and meta-analysis on enteroscopy in small bowel Crohn's limits more detailed comparative data between various techniques. PE is still a useful tool in centres that do not have WCE, BAE or SE. An algorithm that we suggest for investigation of small bowel CD would be gastroscopy and colonoscopy (with terminal ileal assessment). This might be followed by either a barium small bowel follow through or CT enteroclysis and increasingly by using MRE, considering the lack of radiation and possibility of repeated studies, considering the fact that the age group affected is often young or middle aged people of child bearing age, to limit radiation exposure. If MRE is normal one could consider WCE, if there is a high index of suspicion of early mucosal disease or malabsorption, which may not show up in MRE. If there is evidence of active small bowel Crohn's especially strictures or fistulae, then ideally aggressive treatment with anti tumour necrosis factor from the outset. If any complications of CD are seen, such as strictures or bleeding, then DBE/SBE or SE, depending on availability of local expertise, to assess the pathology and consider local treatment-biopsy, diathermy, balloon dilatation or injection of various drugs as might be appropriate to the setting. If initial small bowel imaging at time of first diagnosis is normal, then currently no recommendations are available regarding surveillance intervals or its clinical relevance. There may be multi centre studies in the future can look into appropriate screening intervals and on a more tailored approach for enteroscopy in CD.

A comparison of the various enteroscopy techniques is summarised in the table below. The evidence suggests that all three DAE modalities have comparable insertion depths, diagnostic and therapeutic efficacies and complication rates and can be used as complementary tools. However, most gastroenterologists including the authors, favour DBE due to higher rates of total enter-

oscopy. Larger prospective RCT's in the future could help us understand some unanswered areas including the role of BAE in small bowel screening, comparative studies between the main types of BAE in the field of small bowel CD and strengthen the available evidence, especially with regards to their potential roles and clinical impact. Further studies are needed for device refinement and development to make them more cost effective.

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REVIEW

Which endoscopic treatment is the best for small rectal carcinoid tumors?

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Abstract

The incidence of rectal carcinoids is rising because of the widespread use of screening colonoscopy. Rectal carcinoids detected incidentally are usually in earlier stages at diagnosis. Rectal carcinoids estimated endoscopically as < 10 mm in diameter without atypical features and confined to the submucosal layer can be removed endoscopically. Here, we review the efficacy and safety of various endoscopic treatments for small rectal carcinoid tumors, including conventional polypectomy, endoscopic mucosal resection (EMR), cap-assisted EMR (or aspiration lumpectomy), endoscopic submucosal resection with ligating device, endoscopic submucosal dissection, and transanal endoscopic microsurgery. It is necessary to carefully choose an effective and safe primary resection method for complete histological resection.

Key words: Carcinoid tumor; Rectum; Polypectomy; Endoscopic mucosal resection; Endoscopic submucosal dissection

Core tip: Rectal carcinoids less than 10 mm in diameter can be resected by various endoscopic techniques, such as conventional polypectomy, endoscopic mucosal resection (EMR), cap-assisted EMR (EMR-C), endoscopic submucosal dissection (ESD), or transanal endoscopic microsurgery (TEM). There are currently limited comparative data to recommend a specific endoscopic treatment. Therefore, the choice of treatment modalities for small rectal carcinoids depends on the degree of endoscopic or surgical expertise at a given facility. Furthermore, any one of the above treatment methods could have a favorable clinical outcome if performed by gastroenterologists or surgeons with special techniques. EMR-C and TEM can be used as a salvage treatment after incomplete resection by endoscopic polypectomy. The efficacy of endoscopic submucosal resection with ligating device and ESD for salvage treatment requires further investigation.

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INTRODUCTION

Carcinoids, also termed well-differentiated neuroendocrine tumors (NETs), are the most common neu-

roendocrine tumor of the gastrointestinal tract[1]. The incidence and prevalence of carcinoid tumors have increased quickly and steadily worldwide over the past few decades[2]. Rectal carcinoids are typically small, localized, nonfunctioning tumors that rarely metastasize[2]. The Surveillance, Epidemiology, and End Results registry database of the National Cancer Institute showed that the age-adjusted incidence of rectal carcinoids has increased from approximately 0.2 per 100000 in 1973 to 0.86 per 100000 in 2004[2,3]. The increased incidence can be partially explained by widespread colorectal cancer screening, heightened awareness, and improved diagnostic modalities. Rectal carcinoids comprise 12.6% of all carcinoid tumors and represent the third largest group of the gastrointestinal carcinoids in Western countries[1]. The frequency of rectal carcinoids is higher in studies from South Korea (48%) and Taiwan (25%) compared to Western countries[4,5]. The causes of racial/ethnic differences in NETs by site are unclear and require further investigation.

The treatment of rectal carcinoids depends on the tumor size (Figure 1). Recent consensus guidelines on the management of rectal carcinoids suggests that small tumors (< 1-2 cm) confined to the mucosa or submucosa can be managed with endoscopic resection due to their low risk of metastatic spread[6]. Rectal carcinoids estimated endoscopically as < 10 mm in diameter without atypical features and confined to the submucosal layer without lymphovascular invasion rarely metastasize. Therefore, these tumors are considered good candidates for local excision, including endoscopic resection. A variety of endoscopic techniques are used to treat rectal carcinoids. Those techniques include conventional polypectomy, endoscopic mucosal resection (EMR), cap-assisted EMR (EMR-C or aspiration lumpectomy), endoscopic submucosal resection with ligating device (ESMR-L), endoscopic submucosal dissection (ESD), and transanal endoscopic microsurgery (TEM). Due to a lack of controlled prospective studies, the management of small rectal carcinoid tumors has been a matter of debate. In this Technical Advances article, we review the efficacy and safety of various endoscopic treatments for small rectal carcinoid tumors.

CONVENTIONAL POLYPECTOMY OR EMR

Endoscopic resection of rectal carcinoids with conventional polypectomy or EMR is a simple procedure (Figure 2)[7-9]. However, it is difficult to achieve histologically complete resection with these techniques because 76% of rectal carcinoids extend into the submucosal layer[9,10]. In addition, crush injury of resected specimens could lead to difficulty in pathologic evaluation[7]. The histologically complete resection rate of conventional polypectomy varies from 28.6% to 100% according to previous studies[11]. Incomplete resection of the tumors often requires additional surgical intervention.

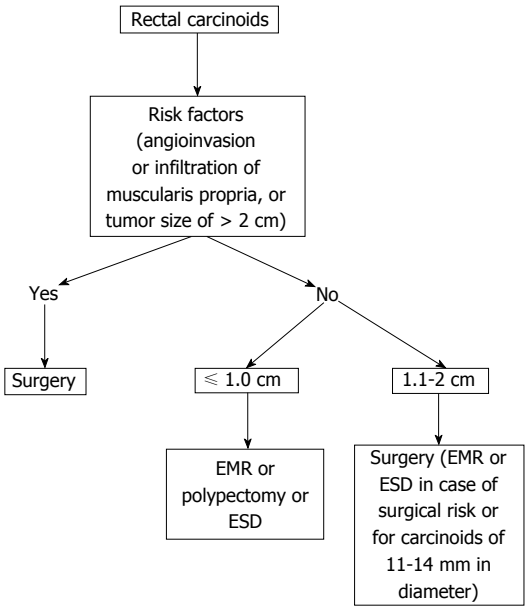

Figure 1 Treatment of rectal carcinoids. EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosal dissection.

POLYPECTOMY OR EMR USING TWO-CHANNEL COLONOSCOPY

Using a two-channel colonoscope, both grasping forceps and a polypectomy snare can be inserted into the gastrointestina lumen simultaneously. Therefore, rectal carcinoids can be pulled toward the center of the lumen and resected by electrocoagulation (Figure 3). Iishi *et al*[12] demonstrated that the complete resection rate of rectal carcinoids with a two-channel colonoscopy (9 of 10 tumors, 90%) was significantly higher than with a one-channel colonoscopy (2 of 7 tumors, 29%). In addition, there were no complications during or after endoscopic treatment. Polypectomy or EMR using the two-channel method are expected to have a deeper vertical resection margin and lead to a curative resection. However, a recent study showed a positive resection margin in 11 (26%) of 58 EMR samples collected using the two-channel method. Furthermore, the complete resection rate of this method was not different from conventional EMR[13]. Another limitation is that the mucosa can be torn before the tumor is adequately elevated with the grasping forceps[14].

EMR-C OR ASPIRATION LUMPECTOMY

Aspiration lumpectomy is an endoscopic approach for a tumor that can be easily resected by lifting the mucosa away from the submucosa with saline injection, followed by aspirating the lesion into a transparent cap or cylinder[15]. In 1996, Imada-Shirakat *et al*[16] reported that histologically complete resection was achieved in eight patients with rectal carcinoids less than 10 mm and located within the submucosal layer using this technique. There were no recurrences or distant metastasis found during the mean observation period of 13.3 mo. Nagai

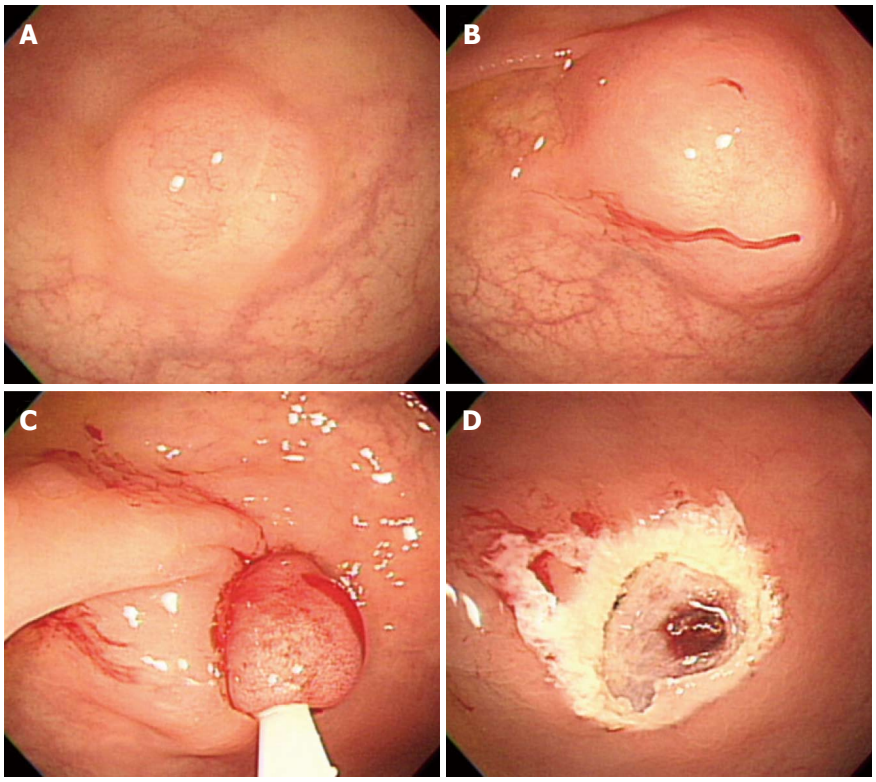

Figure 2 Endoscopic mucosal resection. A: An approximately 6 mm rectal carcinoid tumor; B: Injection of submucosal saline solution; C: Endoscopic mucosal resection (EMR) procedure; D: A clear, post-EMR ulcer.

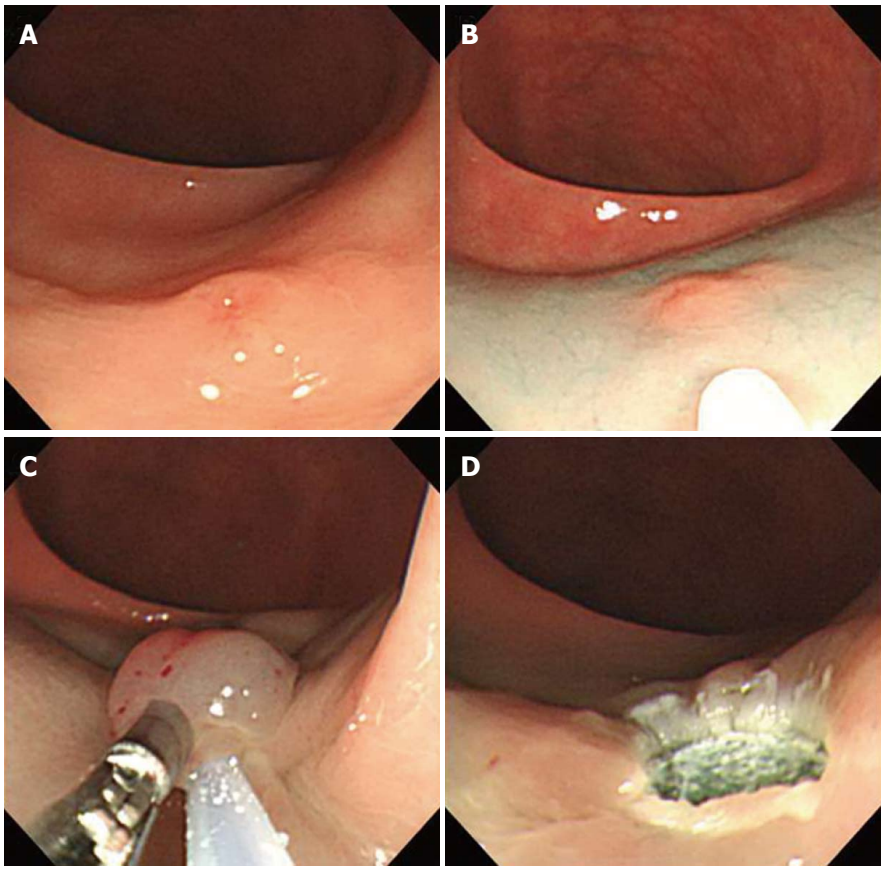

Figure 3 Endoscopic mucosal resection using two-channel colonoscopy. A: An approximately 5 mm rectal carcinoid tumor; B: Injection of submucosal saline solution into the base of the lesion using needle forcep; C: Pulling the lesion with grasping forcep and snare resection; D: A clear, post-endoscopic mucosal resection ulcer.

et al[14] demonstrated that the rate of complete resection with aspiration lumpectomy (100%) was significantly higher ($P < 0.05$) than with saline assisted snare resection (termed 'strip biopsy') in a small series of consecutive patients with rectal carcinoids. Jeon *et al*[17] used this technique for secondary endoscopic treatment to remove the remnant tumor after primary EMR or polypectomy, which is technically difficult due to submucosal fibrosis

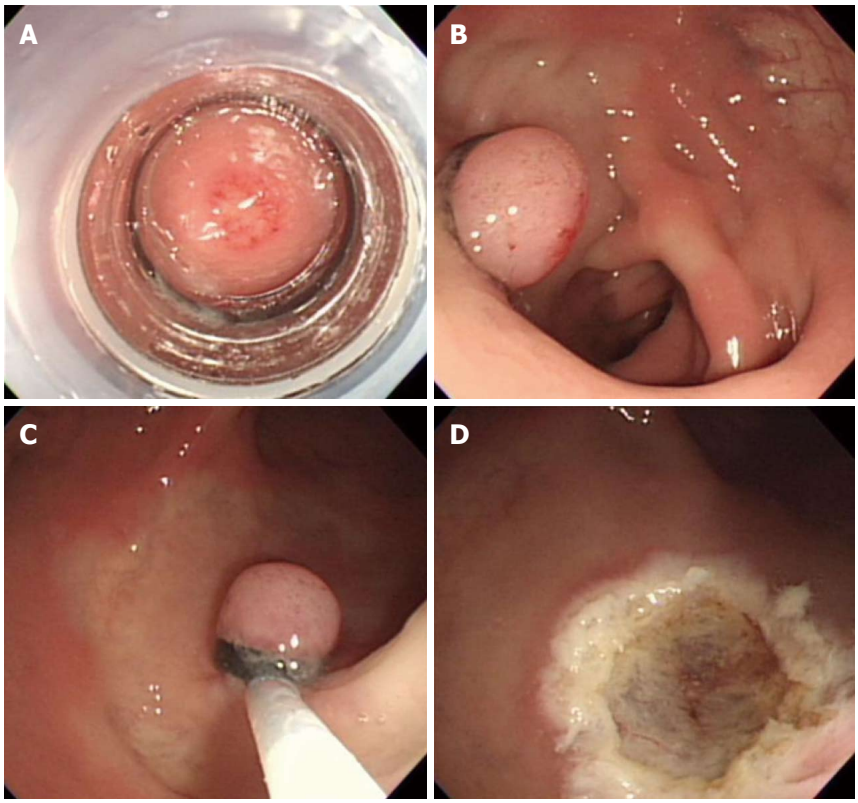

Figure 4 Endoscopic submucosal resection with ligating device. A: Aspiration of a carcinoid tumor into the ligating device; B: Deployed elastic band; C: Snare resection performed below the band; D: A clear, post-endoscopic submucosal resection with ligating device ulcer.

of residual tissue. This study demonstrated that EMR-C is a useful method for salvage treatment of a failed *en bloc* resection of rectal carcinoids after primary EMR or polypectomy. One of the interesting findings of this study is that all 7 patients had positive microscopic margins after primary EMR but negative endoscopic and histological findings based on a biopsy of the scarred tissue. The pathologic findings from all tissue obtained by salvage resection showed the existence of remnant tumor. This result suggests that a negative biopsy in a surveillance examination does not prove the absence of a remnant tumor and that false negative results might be due to embedding or the residual remnant tumor during tissue healing after the primary resection

ENDOSCOPIC SUBMUCOSAL RESECTION WITH LIGATING DEVICE

In 1999, Berkelhammer *et al*[18] first introduced the band-snare resection as a method of EMR for small rectal carcinods. This method may provide a more appropriate resection margin compared to standard polypectomy (Figure 4). A randomized controlled study comparing ESMR-L to EMR showed that the complete resection rate of ESMR-L (100%, 8/8) was significantly higher than EMR (57.1%, 4/7), and all patients were followed-up for 3 years without any recurrence[19]. In a large case series including 61 patients, the complete resection rate of ESMR-L was 95.2% (60 out of 63 lesions)[20]. The complete resection rate for lesions located in the lower rectum was 98.3%, which was significantly higher than lesions in the upper rectum and rectosigmoid colon (50%). In a large-scale study comparing ESMR-L (45 lesions) and EMR (55 lesions) including 100 cases, the overall ESMR-L complete resection rate was higher than EMR (93.3% *vs* 65.5%, respectively, $P = 0.001$)[21]. In addition, this study demonstrated that the location of the tumors had no influence on the complete resection rate when ESMR-L was performed, in contrast to the results of EMR. Recently, Moon *et al*[22] introduced EMR using a double ligation technique (ESMR-DL) to treat 11 patients with small rectal carcinoids. The lesion was aspirated into the ligating device, and an elastic band was placed around the base. Then, a detachable snare was used to perform a ligation below the elastic band, and the lesion was removed with snare resection above the band. After ESMR-DL, there were no immediate or delayed complications such as bleeding or perforation.

ESD

Endoscopic submucosal dissection is considered a valuable endoscopic treatment for early gastric cancer and large superficial gastric neoplasms. This technique provides a higher *en bloc* and histologically complete resection rate than EMR, enables accurate pathologic diagnoses, and is less invasive than surgery (Figure 5)[23]. Recently, ESD has been applied to the treatment of large colorectal neoplasms and has been reported to be more effective than either EMR or EMR-precutting[24]. However, ESD has the disadvantage of a considerably higher risk for perforation because the technique involves dissection of the submucosal tissue beneath the lesion. In addition, highly trained endoscopists are required. Thus,

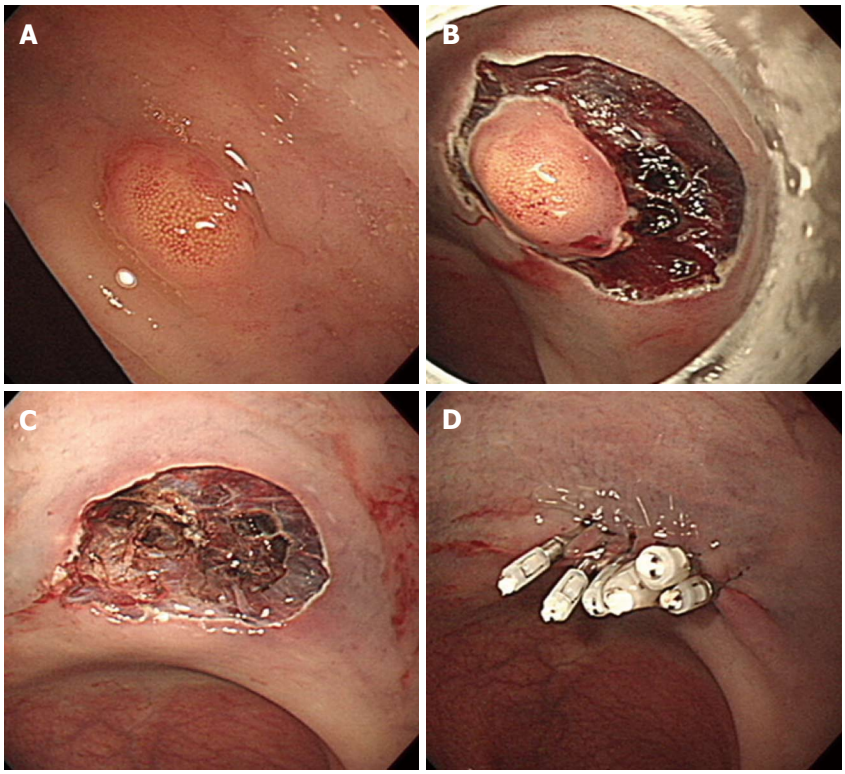

Figure 5 Endoscopic submucosal dissection. A: An approximately 5 mm rectal carcinoid tumor; B: Mucosal incision and submucosal dissection; C: A clear, post-endoscopic submucosal dissection ulcer; D: Endoscopic closure of the ulcer floor with endoclips.

the safety issues associated with this technique must be solved. As a result, ESD is not yet widely accepted for the treatment of colorectal neoplasms[25].

There have been few studies reporting the efficacy and safety of ESD for the resection of rectal carcinoids. Recently, Onozato *et al*[26] reported that ESD was technically feasible in five cases with rectal carcinoids less than 10 mm. In addition, no complications were observed, and all lesions were completely resected histologically. In a meta-analysis including four studies[27-30], ESD was a more effective procedure for the treatment of rectal carcinoids and had a higher complete resection rate than EMR[31]. ESD was more effective than EMR in complete histological resection [odds ratio, 0.29; 95%CI: 0.14-0.58; P = 0.000]. Additionally, ESD was as safe as EMR (rate difference, -0.01; 95%CI: -0.07 - 0.05; P = 0.675). The recurrence rate did not differ significantly between the EMR and ESD groups. The duration of ESD was longer than EMR. Because the rectum is fixed in the retroperitoneum, the risk of peritonitis following perforation is lower than in other parts of the colon. One of limitations of ESD with a knife is the inability to fix the knife to the target lesion, which leads to high complications such as bleeding and perforation. New grasping type scissor forceps, which can grasp and incise the targeted tissue using an electrosurgical current, may reduce these complications[32]. More recently, there have been a few studies comparing ESD to other endoscopic treatment modalities besides EMR. Kim *et al*[33] reported a large retrospective analysis including 115 patients, which were classified into an EMR group (n = 33), ESMR-L group (n = 40), and ESD group (n = 44). The curative resection rate in the EMR group was 77.4%, which was significantly lower than that of the ESMR-L (95%) and ESD groups (97.7%). This result suggests that ESMR-L and ESD may be superior to conventional EMR. A recent study by Choi *et al*[25] comparing ESMR-L (n = 29) with ESD (n = 31) for the endoscopic treatment of rectal carcinoids showed that the complete resection rate was 80.6% in the ESD group and 82.8% in the ESMR-L group (P = 0.833). The resection time was significantly longer in the ESD group than in the ESMR-L group. The authors concluded that ESMR-L might be considered the treatment of choice for small rectal carcinoid tumors because of reduced procedure time. A small comparative study by a Japanese group[34] also showed a similar result to the above study. A retrospective analysis of 3 types of endoscopic resection technique by Zhao *et al*[35] demonstrated that complete resection rates using the EMR, EMR-C, and ESD were 80%, 100%, and 100%, respectively. The average procedure time was the shortest in the EMR-C group. This study concluded that EMR-C might be the best endoscopic excision method, considering the clinical efficacy, surgical time, and complication rate.

TEM

Transanal endoscopic microsurgery was originally designed by Buess *et al*[36] in the 1980s. The procedure allows full thickness excisions as high as 20 cm from the anal verge to be performed using a 40-mm operating rectoscope. Although TEM is not superior to conventional transanal excision (TAE) for resecting lesions in the lower rectum, it has distinct advantages for removing lesions in the mid and upper rectum[37]. In addition to improved

access to more proximal lesions, TEM provides several advantages over TAE, including improved visualization with better exposure, higher likelihood of achieving clear resection margins, and lower recurrence rates[38]. The application of TEM for rectal carcinoids has been described in several small case series[6]. Kinoshita *et al*[39] reported clinical experience including 27 patients with rectal carcinoids treated by TEM. In this study, TEM was performed as a primary excision (n = 14) or as completion surgery after incomplete resection by endoscopic polypectomy (n = 13). Negative margins were obtained in all cases. There was no additional radical surgery performed, and patients were followed-up for 70 mo without recurrence. The largest series in the United States included 24 patients over a 12-year period[40]. There were 6 (25%) primary surgical resections, and 18 (75%) resections were performed after incomplete snare excisions during colonoscopy. This study showed all negative margins, a similar zero rate of recurrence and a similarly low morbidity rate. In addition to its usefulness in primary surgical resection of rectal carcinoids especially in the mid and upper rectum, TEM can be used as a salvage treatment after incomplete resection by endoscopic polypectomy. The possible complications of TEM include bleeding and perforation. In addition, transient soiling can occur due to the large width of the rectoscope tube[37].

FUTURE PERSPECTIVES AND CONCLUSIONS

In rectal carcinoids estimated endoscopically as < 10 mm in diameter, endoscopic treatment is a feasible option. Although endoscopic resection of rectal carcinoids with conventional polypectomy or EMR is a simple procedure, it is difficult to achieve histologically complete resection. EMR-C, ESMR-L, and ESD showed similar efficacy and safety. However, there are currently limited comparative data to recommend a specific endoscopic treatment. Therefore, the choice of treatment modalities for small rectal carcinoids depends on the degree of endoscopic or surgical expertise at a given facility. Furthermore, any one of the above treatment methods could have a favorable clinical outcome if performed by gastroenterologists or surgeons with special techniques.

Endoscopic treatment for rectal carcinoid requires special techniques for a deeper resection to achieve clear margins. For this purpose, lesions are usually lifted using submucosal injection with saline solution with or without epinephrine. In addition, adequate submucosal injection is important for the reduction of thermal damage to tissue as well as the prevention of complication such as bleeding or perforation. Although electrocauterization during endoscopic resection could destroy remnant tumor, its burning or coagulation artifact may make the pathologic examination of resection margin difficult. Therefore, to separate the margin of carcinoid tumor from the underlying muscle layer adequately could provide better pathological assessment of radial margins and the depth of invasion[41].

EMR-C and TEM can be used as a salvage treatment after incomplete resection by conventional polypectomy or EMR. However, the efficacy of ESMR-L and ESD for salvage treatment requires further investigation. Endoscopic tattooing of colonic lesions helps to localize polypectomy sites that may difficult to identify with repeat endoscopy[42]. In cases with positive resection margin after endoscopic treatment of rectal carcinoids, tattooing the area of resection will help facilitate the lesion site location for further resection.

Newly developed over-the-scope clip (OTSC) has a higher compression force and the capacity to capture a larger volume of tissue than the through-the-scope clip[43]. Recent prospective study has shown that perforations occurring after full- thickness resection of gastric subepithelial tumors less than 3 cm could be managed by OTSC closure[44]. Although further prospective clinical trial is required, this study suggests that endoscopic full-thickeness resection with OTSC closure can be applied to selected patients with colonic subepithelial lesions to have malignant potential. Finally, a prospective large-scale study is warranted for the assessment of therapeutic efficacy of various endoscopic treatments and long-term outcome.

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Colorectal stenting as first-line treatment in acute colonic obstruction

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Abstract

Tumoral obstructions in almost the entire gastrointestinal tract can be resolved with interventional digestive endoscopy techniques. Self-expanding metal stent (SEMS) insertion in the obstructed colon is a minimally invasive and relatively simple procedure providing an effective first-line treatment for relief of acute malignant obstruction symptoms and serving either as a preoperative or "bridge to surgery" procedure or as palliative definitive care. This technique was introduced in the early 1990s. Although there is still debate about its real value, a lot of reports have been published since then and the procedure is advocated by many surgical groups as the method of choice for the initial treatment of left-sided tumoral colonic obstruction. Before the procedure, colonic obstruction has to be diagnosed by abdominal radiographs, water contrast enema and/or a computed tomography scan. The greatest information is provided by the latter and it is perhaps the method of choice prior to stenting. Skills and training are mandatory, as in all interventional procedures. The key step for success is to cross the malignant stricture with a guidewire. Care must be taken not to over insufflate an obstructed colon during the procedure. SEMS slide over the guidewire through the endoscope working channel or in parallel, outside the endoscope. An average 7% perforation rate has been reported during the procedure and other minor complications can appear in the follow up. However, as a whole, this technique seems to compare favorably with surgery.

Key words: Self-expanding metal stent; Malignant colorectal obstruction; Emergency surgery; Interventional endoscopy

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INTRODUCTION

Patients with malignant colorectal obstruction (MCRO) usually present at the emergency room (ER) because of abdominal pain, vomiting and distension. After a physical examination, abdominal radiographs show typical signs of large bowel obstruction with air-fluid levels. First therapeutic measures include fluid resuscitation with electrolyte correction. Further diagnostic procedures have to be undertaken to confirm both the colonic obstruction and the exact anatomical location. According to individual hospital policies, the colon can be cleansed with enemas and a colonoscopy can be performed. Care has to be taken not to over insufflate in order to avoid perforation. Water instead of air should be employed to allow colonoscope advancement.

However, in patients with acute abdominal pain in whom perforation is suspected, a computed tomography (CT) scan is a preferable diagnostic modality after clinical and plain abdominal radiograph evaluation. If a tumoral obstruction in the left-side colon is diagnosed, insertion of a self-expanding metal stent (SEMS) as first treatment can be considered[1].

COLONIC OBTRUCTION RELIEF WITH SEMS

As in the esophagus, duodenum or biliary tree, MCRO can be also treated in the large bowel by means of SEMS.

Dohmoto *et al*[2] reported the treatment of a rectal tumoral obstruction by means of a SEMS for the first time in 1990. From that time, a large number of works dealing with this topic have been annually published. Initially, they were single or a few case reports[3]. Afterwards, large series were reported[4], in addition to review articles[5] and randomized studies comparing this new modality with the classical surgical approach[6].

Figure 1 shows the increase of publications on SEMS for MCRO when the words "colon AND stent" are searched for in PubMed.

The most valuable benefit provided by this relatively new interventional technique is to relieve obstruction by means of a minimally invasive procedure, avoiding an operation in an unstable patient. The colon can be cleansed properly and patients can undergo a scheduled surgical procedure. This kind of MCRO decompression is also called a bridge to surgery (BTS). The classical surgical approach involved a primary colostomy and a second or third operation for tumor removal and colostomy closure.

Right colon obstructions do not necessarily need bowel cleansing before surgery; therefore, the major impact of SEMS in MCRO are in the left colon[7]. In addition, non-operable patients (*i.e.*, multiple metastases) can have the stent as a palliative measure to avoid a colostomy.

Bowel perforation is the main contraindication for stenting. In addition, in cases of multiple strictures or short life expectancy (hours or few days), other options instead of stent insertion must be undertaken.

NONFLUOROSCOPIC INSERTION OF AN "OVER-THE-WIRE" STENT IN A RECTOSIGMOID MCRO

Once MCRO has been diagnosed and surgical consultation made, if the obstruction is below 25 cm from the anus (up to mid-sigmoid), a possibility is to bridge the stricture in the endoscopy office without fluoroscopy. The majority of such strictures can be traversed by means of ultrathin endoscopes (six or less millimeters in diameter). The endoscope is negotiated through the narrowed tumoral lumen until healthy colon is found. The endoscope is advanced as far as possible. A metallic Savary or a similar stiff guidewire is inserted through the working channel of the endoscope and placed beyond the malignant stenosis. The endoscope is withdrawn, leaving the guidewire in place. Important figures to record are tumoral length and the distance from the anus.

Afterwards, the endoscope is reinserted beside the guidewire and placed at the level of the stricture. A

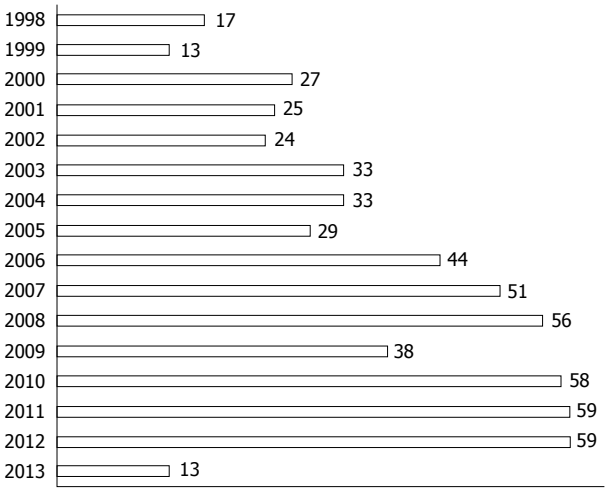

Figure 1 Number of scientific papers published in the last years about stents in tumoral colonic obstructions. Search was done with the terms "colon and stent" in PubMed. Year 2013 ends in the month of March.

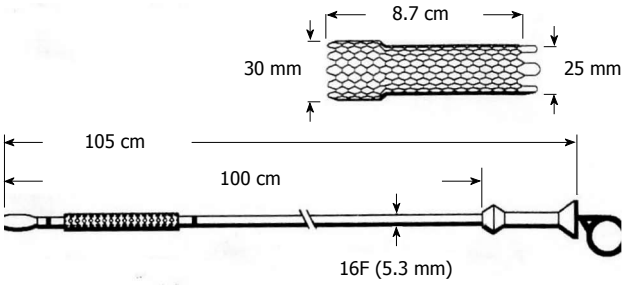

Figure 2 Ultraflex Precision stent from Boston Scientific. This self-expanding metal stent is called over the wire because it cannot be inserted through the working channel of a therapeutic endoscope. Many other stent manufacturers have similar stents.

folded stent that cannot be inserted through the working channel of the endoscope because it is greater than 3.7-4.2 mm, as shown in Figure 2, is slid over the guidewire. These SEMS are called over-the-wire (OTW) to differentiate from through-the-scope (TTS) stents that have a folded diameter that allows it to be inserted undeployed through the working channel of a therapeutic endoscope (Figure 3A).

The endoscope gives stiffness to the system stent guidewire and prevents it from bending. The advancement of the stent through the stricture is also monitored with the endoscope. The stent is released under endoscopic vision.

This insertion technique has been used for a long time[8,9] and it has been successful in the majority of occasions, allowing the MCRO to be resolved in the endoscopy suite. Nevertheless, several points have to be underlined.

First of all, the procedure tends to always be more difficult than anticipated. Despite bowel cleansing, there are always liquid or semisolid feces in the colon that impedes good vision. The placing of a hemostatic clip in the lowest stricture margin is helpful to clearly mark

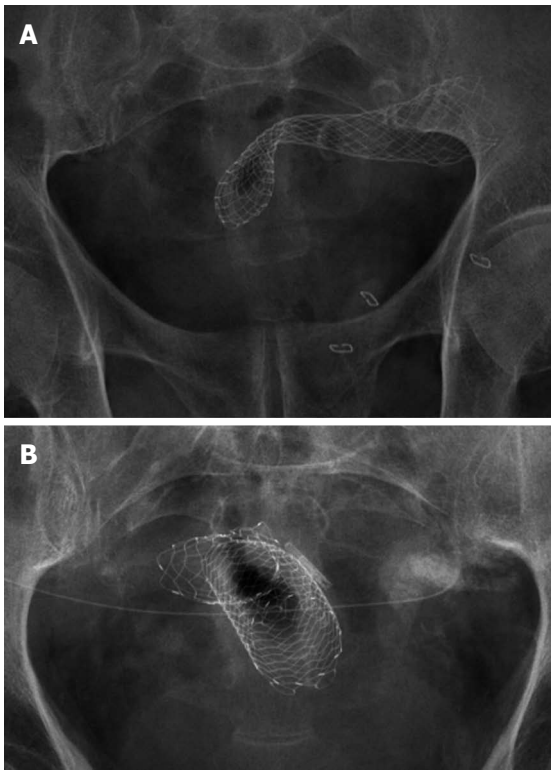

Figure 3 Wallflex (A) and Ultraflex (B) stents from Boston Scientific. A: This self-expanding metal stent (SEMS) is called a through the scope (TTS) stent because it can be inserted in the folded way through the working channel of a therapeutic endoscope. Many other stent manufacturers have similar stents; B: Ultraflex Precision inserted in a tumoral stricture in the sigmoid, a hemostatic clip was placed to mark the lower part of the stricture. Despite the strange configuration due to sigmoid bends, the stent was in correct position; the patient had an abdominal catheter for hydrocephaly decompression.

where the stent has to be placed in the endoscopic view.

The endoscopist has to have skills in interventional endoscopy. A recent paper[10] pointed out that at least 30 procedures of SEMS insertion in left MCRO are the initial learning curve for mastering the technique.

With the nonfluoroscopic technique, stent deployment events beyond the stricture are not seen so they have to be "supposed". In some OTW SEMS, like the Ultraflex Precision (Figure 2), deployment begins in the closest part to the endoscopic view, that is, in the distal tumoral end or downstream. Once the stent has been partially opened, it can be pushed if it is far from the stricture but it cannot be pulled because the open mesh can damage the colon.

After the procedure, pelvic or abdominal radiographs have to be taken to confirm proper stent deployment. When the stricture has been completely bridged, the SEMS takes an hourglass-like configuration with both ends open. Nevertheless, due to sigmoid bends, sometimes Rx images are not clear. As can be seen in Figure 3B, foreshortening occurs in the image but the SEMS was in correct position and the obstruction was resolved. In this figure, a hemostatic clip marking the lowest tumor margin is also seen. In addition, the patient had an abdominal catheter for hydrocephaly decompression.

NONFLUOROSCOPIC INSERTION OF A "TTS" STENT IN A LEFT COLON MCRO

Insertion of OTW stents far from the mid-sigmoid (around 25 cm from the anus) is difficult because the assembly stent guidewire tends to bend, despite the endoscope being placed side-to-side. If the MCRO has been traversed with the ultrathin endoscope, a 0.035 inch guidewire can be inserted through the working channel of the endoscope and placed as far as possible beyond the tumor (in upstream position). The ultrathin endoscope is removed, leaving the guidewire in place. This guidewire is back loaded in a therapeutic channel endoscope which is carefully advanced until the tumor. A TTS stent can be easily inserted. The endoscope gives enough stiffness to the system to advance the undeployed stent through the tumor.

Extreme care should be taken not to dislodge the guidewire placed beyond the stricture in the maneuvers of ultrathin endoscope withdrawal or therapeutic endoscope advancement.

MCRO must be never dilated before stenting because there is a great risk of tumor perforation.

ENDOSCOPIC INSERTION OF SEMS IN MCRO WITH FLUOROSCOPIC GUIDANCE

This method is considered as the ideal for many endoscopists[11]. Fluoroscopic facilities are necessary. C-arms fluoroscopic devices used sometimes for Endoscopic Retrograde Cholangiopancreatography (ERCP) are not good if they have no capacity to image the entire abdomen and if the patient table cannot be easily moved (Figure 4).

A therapeutic endoscope is advanced until the tumoral stricture is found. Using a gastroscope or short colonoscope with large working channel is very useful to facilitate devices exchange during the procedure.

With the endoscope in front of the stricture, an ERCP catheter loaded with a hydrophilic tip guidewire is passed through the working channel. The most important step is "cannulation" of the stricture with the guidewire. Almost all the strictures have an orifice, although sometimes it can be very difficult to find. As shown in Figure 5, gentle probing of the tumor with the guidewire leads to finally finding the path. The correct position of the guidewire beyond the stricture is given by the fluoroscopic view. If the patient is in the supine position (lying on his/her back), anatomical orientation is improved.

After traversing the tumor with the guidewire, the catheter is slid over it and contrast medium is injected to delineate the stricture. The catheter is removed, always leaving the guidewire tip as far as possible in the colon. A TTS stent is passed over the guidewire and deployed inside the tumor with fluoroscopic guidance of upstream maneuvers and endoscopic monitoring of downstream (in the endoscopic view) events.

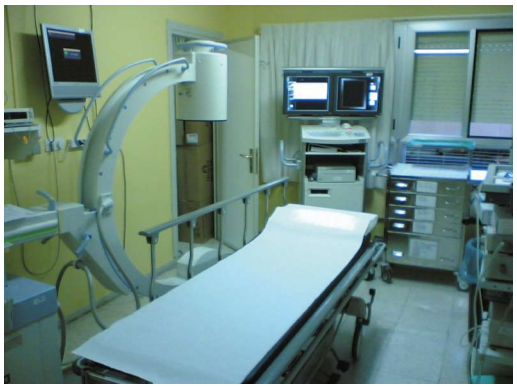

Figure 4 C-arms fluoroscopic devices used sometimes for endoscopic retrograde cholangiopancreatography are not good for colonic stenting unless they have capacity to image the entire abdomen and if the patient table cannot be easily moved.

SCIENTIFIC EVALUATION OF SEMS FOR MCRO

As previously said and as shown in Figure 1, a lot of papers have been published on this topic (Table 1). Nevertheless, few are randomized studies comparing the traditional surgical approach of MCRO with SEMS treatment.

In a recent review from a surgical standpoint[31], it appears that technical and clinical success rates for stenting are lower than expected. SEMS is sometimes associated with a high incidence of clinical and silent perforation. Stenting instead of loop colostomy can be recommended only if the appropriate expertise is available in the hospital. The goal of stenting, a decrease of the stoma rate, can be advocated only if the complication rates of stenting are lower than those of stoma creation in the emergency situation. Until now, this has been not demonstrated in a prospective randomized trial.

Furthermore, when pathology surgical specimens are compared, tumors resected after stenting differed significantly in terms of ulceration at or near the tumor, perineural invasion and lymph node invasion. These findings are found less in tumors operated on without previous stenting[32].

On the contrary, many studies in clinical practice favor stenting as first-line treatment for left MCRO. Randomized trials in this setting appear to be difficult and perhaps randomization is not the only answer for structured objective evaluation of endoscopic therapy[33].

In one of the largest retrospective endoscopic series published in 2010[20], there were reported outcomes on 168 patients who underwent SEMS placement for definitive palliation and 65 patients with SEMS inserted as a BTS. Technical and immediate clinical success rates were 96% and 99% in the palliative group and 95% and 98% in the preoperative group 41/168 (24%). Patients in the palliative group had complications, including perforation (9%), occlusion (9%), migration (5%) and erosion/ulcer (2%). Mean stent patency was 145 d. The majority of

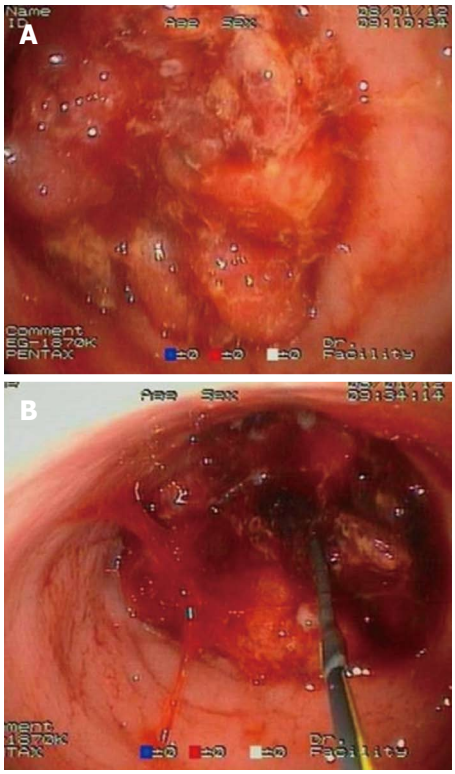

Figure 5 Endoscopic retrograde cholangiopancreatography catheter loaded with a hydrophilic tip guidewire. A: the obstructive tumor appears not to have any orifice that enabled stenting; B: gentle probing of the tumor with the guidewire leads to finally finding the path.

patients were free of obstruction from implantation until death. Therefore, this large group of patients had their normal intestinal transit restored without having undergone an operation and without a stoma. Unfortunately, patients on oncological bevacizumab treatment triple the perforation rate.

Preoperatively placed stents remained *in situ* for a mean of 25.4 d and remained patent until surgery in 73.8% of patients. Complications were present in 23.1% of patients and 94% of them underwent elective colectomy. Conclusions drawn from this large cohort of patient are that colorectal SEMS placement is relatively safe and effective but has a complication rate of nearly 25%. However, only perforation (less than 10%) is a life-threatening complication. Other complications such as stent occlusion can be managed endoscopically.

Some surgical groups found SEMS treatment for MCRO in operable patients (BTS) very useful to carry on a laparoscopic procedure. Law *et al*[34] evaluated surgical outcomes after stent insertion for obstructing colorectal malignancy and these patients were compared with a laparoscopic and open approach. Their experience showed that after successful SEMS insertion for MCRO, elective surgical resection could be performed safely. The combined endoscopic and laparoscopic procedure provided a less invasive alternative to the multistage open operations and it was found feasible for patients with obstructing colon cancer.

Table 1 Some series about self-expanding metal stents in malignant colorectal obstruction published in the last years *n* (%)

Ref.	Publication year	No. of patients	Technical success	Clinical success	Perforation rate
García-Cano *et al*[4]	2006	175	162 (92.6)	138 (78.8)	7 (4)
Ptok *et al*[12]	2006	48	44 (92)	44 (92)	0
Soto *et al*[13]	2006	62	58 (93.54)	56 (90.3)	3 (4.8)
Karoui *et al*[14]	2007	31	30 (97)	27 (87)	0
Lee *et al*[15]	2007	80	78 (97.5)	77 (96.2)	0
[1]Repici *et al*[16]	2007	44	42 (95.4)	41 (93.1)	0
Repici *et al*[17]	2008	42	40 (95.2)	40 (95.2)	1 (2.38)
Im *et al*[18]	2008	51	51 (100)	43 (84.3)	1 (1.9)
Fernández-Esparrach *et al*[19]	2010	47	44 (94)	44 (94)	3 (7)
Small *et al*[20]	2010	233	224 (96.1)	222 (95.2)	18 (7.7)
Park *et al*[21]	2010	151	149 (98.6)	140 (92.7)	0
Branger *et al*[22]	2010	93	86 (92.5)	80 (86)	3 (3.2)
Donnellan *et al*[23]	2010	43	40 (93)	40 (93)	2 (4.6)
Lee JH *et al*[24]	2010	46	46 (100)	39 (84.8)	2 (4.3)
Lee HJ *et al*[25]	2011	71	68 (95.8)	68 (94)	4 (5.6)
Luigiano *et al*[26]	2011	39	36 (92.3)	35 (89.7)	2 (5.1)
Jiménez-Pérez *et al*[27]	2011	182	177 (98)	141 (94)	5 (3)
Tominaga *et al*[28]	2012	24	24 (100)	20 (83)	0
Yoshida *et al*[29]	2013	33	33 (100)	32 (97)	0
Bonfante *et al*[30]	2013	48	46 (96)	46 (96)	1 (2)

[1]In 2007, there are two articles published by Repici *et al*. One about the Ultraflex Precision stent in the left colon and the other on right colon stenting.

SEMS in MCRO are also inserted by interventional radiologists. In one of the first reports comparing this new method with the surgical approach[35], Martinez-Santos *et al*[35] found that placement of a preoperative stent in patients with left-sided malignant colon and rectal obstruction prevented 94% of unnecessary operations and a large number of colostomies after elective surgery. These results were obtained with a lower rate of severe complications as well as a shorter hospital stay. This work cannot be considered a true randomized trial because patients with MCRO received a SEMS if they presented in the ER from Monday to Friday when an interventional radiologist was present in the hospital, whereas patients were operated on if they presented on week-ends. Besides, if patients with MCRO presented out of working hours (*i.e.*, during the night), they were stabilized with intravenous fluids, put on *nil per os* with a nasogastric tube and received a stent early the next morning.

Kim *et al*[36] found that when the colorectal obstruction had a tortuous, curved angulation of the colon or was located at or proximal to the descending colon, the endoscopic method of SEMS placement appears to be more useful than the radiological method. However, once SEMS placement was technically successful, the clinical success rate, complication rate and stent patency did not differ with the method of insertion.

In the midst of the debate between pros and cons of SEMS as the initial treatment for MCRO, a surgical group[37] reports on its experience stating that in case of colorectal obstruction, endoscopic colon stenting as a bridge to elective operation should be considered as the treatment of choice for resectable patients given the significant advantages for short and long-term outcomes. Palliative stenting is effective but associated with a high rate of long-term complications.

However, when surgery and stents are compared as a palliative measure[25], SEMS were found not only an effective and acceptable therapy for initial palliation of MCRO, but they also showed long-term efficacy comparable to that with surgery, reducing costs (*i.e.*, hospital stay).

Some plastic tubes (such as the Dennis colorectal tube) are less expensive alternatives to clean the obstructed colon before operation. But in a recent report[38], a 4.5% perforation rate with a 1.5% mortality was reported.

Finally, the distal part of the stent should be placed at least 6 cm from the anus on the contrary patients can suffer an unpleasant tenesmus.

CONCLUSION

Despite the still ongoing scientific debate[39-43], SEMS for MCRO appears to be the modern treatment for colonic obstruction[39,44,45]. Comparison between colonic SEMS manufactured by major stent companies show no important differences between them[40]. In addition, manufacturers are continuously working on stent improvement to allow a proper obstruction decompression[46]. It is better to use bare (uncovered) stents for MCRO rather than covered ones that are more prone to have complications[41].

Endoscopically, obstructions in the entire colon can be bridged with stents[42]; however, the major impact of SEMS for MCRO are left-sided tumoral strictures. In this setting, colonic stents represent the best option when skills are available[7].

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BRIEF ARTICLE

Post-Anaesthetic Discharge Scoring System to assess patient recovery and discharge after colonoscopy

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Abstract

AIM: To investigate whether discharge scoring criteria are as safe as clinical criteria for discharge decision and allow for earlier discharge.

METHODS: About 220 consecutive outpatients undergoing colonoscopy under sedation with Meperidine plus Midazolam were enrolled and assigned to 2 groups: in Control-group (110 subjects) discharge decision was based on the clinical assessment; in PADSS-group (110 subjects) discharge decision was based on the modified Post-Anaesthetic Discharge Scoring System (PADSS). Measurements of the PADDS score were taken every 20 min after colonoscopy, and patients were discharged after two consecutive PADSS scores $\geqslant$ 9. The investigator called each patient 24-48 h after discharge to administer a standardized questionnaire, to detect any delayed complications. Patients in which cecal intubation was not performed and those who were not found at follow-up phone call were excluded from the study.

RESULTS: Thirteen patients (7 in Control-group and 6 in PADSS-group) were excluded from the study. Recovery from sedation was faster in PADSS-group than in Control-group (58.75 ± 18.67 min *vs* 95.14 ± 10.85 min, respectively; $P < 0.001$). Recovery time resulted shorter than 60 min in 39 patients of PADSS-group (37.5%), and in no patient of Control-group ($P < 0.001$). At follow-up phone call, no patient declared any hospital re-admission because of problems related to colonoscopy and/or sedation. Mild delayed post-discharge symptoms occurred in 57 patients in Control-group (55.3%) and in 32 in PADSS-group (30.7%). The most common symptoms were drowsiness, weakness, abdominal distension, and headache. Only 3 subjects needed to take some drugs because of post-discharge symptoms.

CONCLUSION: The Post-Anaesthetic Discharge Scoring System is as safe as the clinical assessment and allows for an earlier patient discharge after colonoscopy performed under sedation.

Key words: Colonoscopy; Conscious sedation; Patient discharge; Recovery room; Complications

Core tip: About 220 consecutive outpatients undergoing colonoscopy under sedation were enrolled to investigate whether the Post-Anaesthetic Discharge Scoring System (PADSS) is a safe clinical assessment for earlier patient discharge after colonoscopy. The patients were assigned to two groups: in Control-group (110 subjects) discharge decision was based on the clinical assessment; in PADSS-group (110 subjects) discharge decision was based on the modified PADSS. Recovery from sedation was faster in PADSS-group than in Control-group (58.75 min *vs* 95.14 min, $P < 0.001$). Recovery time resulted shorter than 60 min in 39 patients in PADSS-group (37.5%), and in no patient in Control-group ($P < 0.001$).

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INTRODUCTION

Colonoscopy frequently causes considerable discomfort or pain to patients, and analgesia and sedation are often necessary for a successful colonoscopy. The decision to use premedication and the kind of premedication are influenced by national and cultural differences among countries[1], and by the rules regulating the drugs use. Propofol Deep Sedation is frequently used in some countries such as United States, whereas conscious sedation induced by means of a combination of a benzodiazepine and an opiate is more frequently used in other countries such as Italy[2-5], because of its excellent analgesic and sedative effects[6]. Moreover, Propofol can only be administered by anesthetists in Italy.

The annual number of colonoscopies performed on an outpatient basis is increasing, and the increase is expected to continue, because of the screening programs for the colon cancer prevention that are ongoing in many countries. Likewise, the number of examinations performed under sedation is also increasing, and this fact can cause some problems to digestive endoscopy centers, as they are often not provided with sufficiently spacious observation rooms. At the time of discharge from the digestive endoscopy center, patients should be home-ready: they should be clinically stable and able to rest at home. Although the discharge after ambulatory surgery and anesthesia can involve legal implications[7,8], there is very little information and documentation about the recovery pattern and home-readiness of the ambulatory gastrointestinal endoscopy. The Guidelines for Sedation in Digestive Endoscopy of the Italian Society of Digestive Endoscopy (SIED) do not recommend the use of discharge scoring systems to assess the home-readiness, and generically state that "the patient must be awake and well-oriented, and vital parameters must be acceptable and stable"[9,10].

Based on these observations and considering the aging population, it becomes even more important to have clear, evidence-based discharge criteria in clinical use, as patient safety must be our first priority. Several scoring systems have been devised to guide the process of discharge and home-readiness, to ensure patient safety[11]. This prospective study was planned to evaluate whether the discharge scoring criteria are as safe as clinical criteria for discharge decision and allow for earlier discharge.

MATERIALS AND METHODS

Study population

This prospective, non-randomized study was conducted on a population of 220 consecutive outpatients undergoing ambulatory elective colonoscopy in our Digestive Endoscopy Centre. Inclusion criteria were: age range 18 to 75 years, patients scheduled for elective sedated colonoscopy, and capability (evaluated by the endoscopist) of fully understanding the questionnaire. Exclusion criteria were: American Society of Anestesiology (ASA) risk class 3 or higher[12], previous colonic surgical procedure, willingness to undergo unsedated colonoscopy, inpatient status, planned endoscopic therapy, psychiatric diseases or long-term psychiatric drug addiction, concomitant neoplastic diseases, pregnancy or lactation. The first 110 subjects formed the control group (Co-group), in which discharge decision was based on clinical evaluation; the other 110 subjects formed the study group in which the discharge was based on the modified Post Anaesthetic Discharge Scoring System (PADSS-group)[13].

Oral 4-L polyethylene glycol solution was used in all patients as a preparation for colonoscopy. Conscious sedation was induced by means of an *iv* combination of Meperidine 40-60 mg plus Midazolam 2-5 mg according to our routine practice, in order to obtain a degree of sedation ranging from 2 to 4 of the Ramsay's scale[14].

The study protocol was approved by the Ethical Committee of our hospital, and all patients enrolled gave their written informed consent to participate in the study.

Outcome measurement

Pre-colonoscopy and during-colonoscopy assessment: For each patient, age, gender, blood pressure (BP), blood oxygen saturation (SaO2), and heart rate (HR) were recorded. Associated medical illnesses were graded according to the American Society of Anesthesiologists' Physical Status Classification (ASA grade)[12]. Before colonoscopy the anxiety level of the patient was evaluated on a four-point verbal scale, where 1 = no anxiety, 4 = very anxious. Pre-colonoscopy abdominal pain was assessed with the Numerical Analogue Scale (0 = no pain; 10 = unbearable pain)[15]. Heart rate, blood oxygen saturation, and blood pressure were monitored, and oxygen supplement (2 L/min) was provided throughout the duration of colonoscopy.

Post-colonoscopy assessment: Patients in which cecal intubation was not performed were excluded from the study. After colonoscopy, the patients were followed up in the recovery room, and 20 min after the end of colonoscopy they were scored using the Modified PADSS (Table 1)[13]. Afterwards, they were re-scored every 20 min, until two consecutive PADDS scores $\geq$ 9 were achieved.

Using a 9-item questionnaire, the investigator documented each patient's postoperative course in a follow-up phone call 24-48 h after discharge, to assess any delayed complication. Patients who were not found at follow-up phone call were excluded from the study.

Discharge criteria: (1) Co-group: After colonoscopy, the endoscopist settled the observation time on the basis

Table 1 Modified Post-Anaesthetic Discharge Scoring System

Categories	Points
Vital signs	
BP and HR ± 20% of pre-endoscopy value	2
BP and HR ± 20%-40% of pre-endoscopy value	1
BP and HR ± 40% of pre-endoscopy value	0
Activity	
Steady gait, no dizziness or meets pre-endoscopy level	2
Requires assistance	1
Unable to ambulate	0
Nausea and vomiting	
No or minimal/treated with p.o. medication	2
Moderate/treated with parenteral medication	1
Severe/continues despite treatment	0
Pain	
Minimal or no pain (Numerical Analogue Scale = 0-3)	2
Moderate (Numerical Analogue Scale = 4-6)	1
Severe (Numerical Analogue Scale = 7-10)	0
Surgical bleeding	
None or Minimal (not requiring intervention)	2
Moderate (1 episode of hematemesis or rectal bleeding)	1
Severe (⩾ 2 episodes of hematemesis or rectal bleeding)	0
Total score	...
(Patients' scoring ⩾ 9 for two consecutive measurements are considered fit for discharge home)	

BP: Blood pressure; HR: Heart rate.

Table 2 Patients characteristics and main results

	Co-group (n = 103)	PADSS-group (n = 104)
Age, mean ± SD, yr	58.45 ± 11.65	57.21 ± 11.6
Gender, M/F	46/57	46/58
ASA class Ⅰ / Ⅱ	40/63	41/63
Anxiety level, n		
1: none	16	9
2: mild	75	88
3: moderate	10	6
4: severe	2	1
Pain before colonoscopy, mean ± SD	1.9 ± 1.4	1.9 ± 0.6
Recovery time, mean ± SD, min[b]	95.14 ± 10.85	58.75 ± 18.67
Recovery time < 60 min, n (%)[b]	0 (0)	39 (37.5)
Early or late severe complications, n	0	0

[b]P < 0.001, Post-Anaesthetic Discharge Scoring System (PADSS)-group *vs* Co-group. ASA: American Society of Anestesiology.

of patient's age and clinical conditions, dosage of the administered drugs, and sedation degree. At the end of the observation time, the patient was discharged if BP, HR, and SaO2 were stable; and (2) PADSS-group: Recovery-room nurse discharged the patient after a PADSS score ⩾ 9 was achieved in two consecutive measurements. The time from the end of colonoscopy to the patient discharge was recorded.

Estimation of sample size: The test power was exclusively based on the presence of two groups (Co-group and PADSS-group) resulting to be higher than 95% and suitable to reveal differences between discharges times of at least 10 min preserving a P value < 0.05.

Table 3 Results of post-endoscopy evaluation phone call

	Co-group (n)	PADSS-group (n)
Go back to the hospital	0	0
Problems since discharge	57	32
Abdominal distension (with or without pain)	21	7
Fever	1	2
Pain at the injection site	4	4
Headache	15	4
Nausea and/or vomiting	3	2
Drowsiness or difficult to wake-up	31	22
Weakness	20	19
Did you take drugs for these problems?	2	1

PADSS: Post-Anaesthetic Discharge Scoring System.

Statistical analysis

Interval variables were analyzed using the non parametric Kruskal-Wallis test, and nominal variables were analyzed using the χ^2 test, or, if necessary, the Fisher's exact test. Results were considered statistically significant if P values were < 0.05.

RESULTS

Thirteen patients (7 in Co-group and 6 in PADSS-group) were excluded from the study, as cecal intubation was not performed or the patients were not found at follow-up phone call. Two hundred and seven patients (92 males and 115 females) could be evaluated. Their characteristics are summarized in Table 2. The two groups did not differ for age, gender, pre-colonoscopy anxiety level and ASA classification. No patient needed reversal agents.

Recovery from sedation was faster in PADSS-group than in Co-group (58.75 ± 18.67 min and 95.14 ± 10.85 min, respectively; P < 0.001) (Table 2 and Figure 1). Recovery time resulted shorter than 60 min in 39 patients of PADSS-group (37.5%), and in no patient of Co-group (P < 0.001).

No early complication occurred in both groups. At follow-up phone call, no patient declared any need of hospital re-admission because of problems related to colonoscopy and/or sedation. Fifty-seven patients in Co-group (55.3%) and 32 in PADSS-group (30.7%) complained of mild post-colonoscopy symptoms (Table 3), but only three of them (2 in Co-group e 1 in PADSS-group) needed to take some drugs for these symptoms. The most common symptoms were drowsiness, weakness, abdominal distension, and headache.

DISCUSSION

The increasing number of digestive endoscopic examinations performed under sedation has highlighted the problem of the space and personnel required to recover the patients, and the need to identify criteria that can be used to determine when they can safely go home under

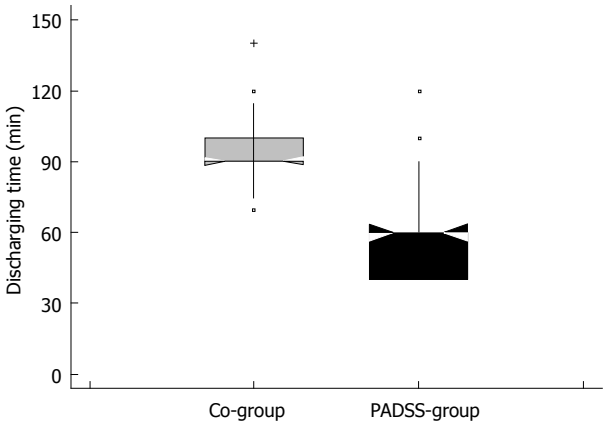

Figure 1 Comparison of recovery time for the two groups. PADSS: Post-Anaesthetic Discharge Scoring System.

the care of a friend or relative. Most centers still rely on clinical criteria for practical discharge decision after colonoscopy. Efforts to shorten recovery time by using sedative agents with shorter half life are gaining increasing popularity. The European Guidelines concerning Non-Anaesthesiologist Administered Propofol (NAAP) for Gastrointestinal Endoscopy was published in 2010[16], but 21 national societies of anaesthesiology in Europe signed a Consensus Statement to declare their disagreement with the NAAP guidelines[17]. Moreover, because of the well-known risks of Propofol administration, the manufacturers of the drug have added the following restriction: "For general anesthesia or monitored anesthesia care (MAC) sedation, DIPRIVAN Injectable Emulsion should be administered only by persons trained in the administration of general anesthesia and not involved in the conduct of the surgical/diagnostic procedure". For these reasons, drugs with a very short duration of action, such as Propofol and Remifentanil, are only administered by anesthetists in Italy, and their use under the direction of a gastroenterologist can have medico-legal implications[18]. Therefore, sedation is generally obtained by means of Meperidine and Midazolam. However, Meperidine is an opioid analgesic with long duration of action (2-4 h)[19], and the duration of the impairment after sedation and post-colonoscopy observation time are unavoidably long.

Several cognitive and psychomotor tests are available to assess the impairment after sedation, but most of them are toilsome and poorly suitable for clinical practice[20-22]. The clinical scoring systems are based on clear, concise and standardized discharge criteria that can be used to determine when patients can safely go home under the care of a relative. The Aldrete scoring system and the PADSS have received widespread acceptance in assessing postanesthetic recovery[23], and are currently used to assess home-readiness after ambulatory surgery. Conversely, to date there is very little information about their use in ambulatory gastrointestinal endoscopy.

In our study, the PADSS resulted as safe as clinical assessment and allowed for earlier patient discharge after colonoscopy performed under sedation. No patient had to be re-admitted because of complications, and just three patients (2 in Co-group and 1 in PADSS-group) taken some drugs for mild and transient symptoms (Table 3). Our data are comparable to those reported by a previous prospective study, in which the patients undergoing endoscopic procedures under sedation were assessed with the PADSS and were discharged within two hours[24]. Furthermore, in our study 37.5% of patients in PADSS-group could be discharged within 60 min from the end of colonoscopy. This observation is quite interesting, as the patients were only discharged after two consecutive measurements achieving a PADSS score $\geqslant 9$. Since the measurements were taken every 20 min, the theoretical shortest time for patient discharge would be 40 min. We prudentially planned to discharge the patients after two measurements of PADSS score, as there are very few studies dealing with its use in digestive endoscopy, and no specific information is provided in literature on potential discharge problems. However, the discharge time could probably be even shorter, as prior reports suggested that patients can be discharged without problems after just one PADSS score $\geqslant 9$[23].

The patient's readiness for discharge needs to be addressed in a simple, clear and reproducible manner, to replace subjective clinical impression by assigning numeric values to parameters. Our trial was conducted in a large busy hospital, and its results show that well-defined discharge scoring criteria offer measurable advantage in decreasing total procedure time by shortening recovery time, and can represent a useful tool for all digestive endoscopy centers in which Meperidine is routinely used for sedation. The use of a standardized discharge scoring system can increase the flow of patients through the recovery process and allows for safe discharge without increasing post-discharge complications and without using any additional resources. The shorter mean recovery time achieved in the PADDS-group in comparison with the Co-group (about 37 min) entails a shorter time spent by the nurse in the recovery room. However, it would be quite hard to quantify such a time saving in terms of cost saving, as several patients are contemporaneously followed up by the recovery-room nurse. Nonetheless, the use of a standardized discharge scoring system represents a more cost-efficient manner while still maintaining quality of care, and becomes essential if discharge decision is entrusted to the nursing staff, which needs to evaluate the post-endoscopy course of the patient in a systematic way, applying to physician for consultation only when necessary.

Our study has some limits. First, it is a single centre study. Second, it is not a randomized trial. Moreover, although the scoring criterion is a reliable tool, it can not replace the critical thinking or professional judgment, as it does not allow to identify all the possible problems

(for instance, a hypoglicemic crisis). Calculating scores of PADSS entails that post-endoscopy vital sign parameters should be compared with pre-endoscopy values, to ensure the patient's return to homeostasis. However, if some pre-endoscopy values were abnormally elevated because of anxiety or pain, expecting the post-endoscopy values to be within ± 20% range may not be appropriate.

In conclusion, having well-defined discharge scoring criteria is imperative in order to ensure a quick and safe discharge. Our study suggests that almost all patients undergoing sedation with Meperidine and Midazolam can be discharged within 2 h of colonoscopy, using the modified PADSS score. However, further and wider randomized trials are needed to confirm our observation.

COMMENTS

Background

The number of colonoscopies performed under sedation on an outpatient basis is increasing as the screening programs for the colon cancer prevention are ongoing in many countries. This fact can cause some problem to digestive endoscopy centres, as they are often not provided with sufficiently spacious recovery rooms.

Research frontiers

At the time of discharge after colonoscopy, patients should be home-ready, and this issue can involve legal implications. Nevertheless, there is very little information and documentation about the recovery patterns and home-readiness after colonoscopy, and many guidelines do not include the use of any standardized discharge scoring system.

Innovations and breakthroughs

In this prospective study, recovery from sedation resulted faster in Post-Anaesthetic Discharge Scoring System (PADSS)-group than in Control-group (58.75 min *vs* 95.14 min, $P < 0.001$), and no patient had to be re-admitted because of complications.

Applications

This study demonstrated that the use of PADSS is safe and allows for an earlier patient discharge after colonoscopy performed under sedation.

Terminology

PADSS is a clinical scoring system based on clear, concise and standardized discharge criteria, and is currently used to assess home-readiness after ambulatory surgery.

Peer review

This is an interesting study, which has important clinical applications.

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BRIEF ARTICLE

Usefulness of continuous suction mouthpiece during esophagogastroduodenoscopy: A single-center, prospective, randomized study

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Abstract

AIM: To develop a new continuous suction mouthpiece (CSM) and evaluate its usefulness for screening esophagogastroduodenoscopy (EGD).

METHODS: A total of 196 patients who were scheduled to undergo screening EGD were assigned to one of two groups: a group using the CSM and a group using a conventional mouthpiece. Extent of salivary flow, frequency of saliva suction, number of choking episodes during the examination, and incidence of aspiration pneumonia after the examination were evaluated and compared between the two groups. Adverse events during and after EGD were also examined. In addition, the oral cavity was meticulously examined after the EGD.

RESULTS: The same number of patients was randomly allocated to each group. There were no significant differences between the two groups in sex, age, biopsy procedure, duration of procedure and depth of sedation. Aspiration pneumonia and other significant adverse events were not observed in either group. The grade of extent of salivary flow was significantly lower in patients with the CSM than in patients with the conventional mouthpiece ($P < 0.001$). Although there was no significant difference, less frequent suctioning and fewer choking episodes were observed in patients with the CSM than in patients with the conventional mouthpiece ($P = 0.082$ and $P = 0.084$, respectively). In addition, there were no patients in the CSM group who required saliva suctioning during the procedure.

CONCLUSION: Use of the CSM during screening EGD can reduce the extent of salivary flow. The device is expected to reduce complications and contamination with saliva.

Key words: Mouthpiece; Esophagogastroduodenoscopy; Aspiration; Saliva; Suction

Core tip: Control of salivary flow during endoscopic examination is important. We focused on a mouthpiece designed for control of saliva in this study. First, we produced a new continuous suction mouthpiece (CSM). Then, we evaluated its usefulness for esophagogas-

troduodenoscopy (EGD). This study indicates that the CSM can reduce the extent of salivary flow during EGD. Moreover, it tended to reduce the frequencies of suction and choking episodes during EGD.

Maekita T, Kato J, Nakatani Y, Enomoto S, Takano E, Tsuji M, Nakaya T, Moribata K, Muraki Y, Shingaki N, Niwa T, Deguchi H, Ueda K, Inoue I, Iguchi M, Tamai H, Ichinose M. Usefulness of continuous suction mouthpiece during esophagogastroduodenoscopy: A single-center, prospective, randomized study. *World J Gastrointest Endosc* 2013; 5(10): 508-513 Available from: URL: http://www.wjgnet.com/1948-5190/full/v5/i10/508.htm DOI: http://dx.doi.org/10.4253/wjge.v5.i10.508

INTRODUCTION

Screening esophagogastroduodenoscopy (EGD) is a common examination that is useful in detecting upper gastrointestinal disease. Hence, it is increasingly performed for patients. However, performance of EGD is associated with the risk of certain adverse events, including aspiration, because EGD is often performed with sedation. A study reported that the rate of aspiration during EGD with sedation was as high as 3.94%[1] when subclinical cases were included. More attention should be paid to this risk.

One of the most important factors correlating with aspiration is the salivary flow induced by introduction/extraction of the endoscope into the oral cavity. Therefore, control of salivary flow during EGD is important for prevention of aspiration. However, few attempts have been made to control salivary flow, perhaps due to its difficulty. Currently, the endoscopist or an assistant must watch for the accumulation of saliva and suction it using a catheter, in case the patient undergoing EGD cannot discharge saliva from the mouth. In this context, control of salivary flow during EGD, if possible, might reduce the endoscopist's or nurse's suctioning efforts, resulting in prevention of complications associated with aspiration. Moreover, contamination of the patient's face or clothes with saliva could also be minimized.

During EGD, a hard plastic mouthpiece is used to protect the endoscope from being bitten and to enable its smooth insertion. A mouthpiece that can also suction saliva might be useful for preventing aspiration and contamination with saliva during EGD. Accordingly, we recently developed a new continuous suction mouthpiece (CSM), and reported its usefulness for prevention of complications associated with salivary flow during percutaneous endoscopic gastrostomy (PEG) procedures[2]. The background of the study patients in this study differed from that of the patients in the PEG study. PEG is performed with the patient in the supine position, is a lengthy process, and is indicated for elderly patients with dysphagia. In contrast, EGD is performed with the patient in the left lateral position, is a shorter process, and is indicated for patients without dysphagia and severe complications.

The aim of this study was to evaluate the usefulness and ability of the CSM for prevention of complications and contamination associated with saliva, including aspiration, during screening EGD.

MATERIALS AND METHODS

Equipment

The details of production of the CSM were reported previously[2]. In summary, after cutting the junction part of a non-toxic polyvinyl chloride (PVC) suction tube (Nipro Suction Catheter® 14-Fr, Nipro, Osaka, Japan), the tube was bent double and the two sides were connected with two movable short bands made of non-toxic PVC suction tubing (Nipro Suction Catheter® 16-Fr, Nipro). The three parts divided by the short bands were made into: a 2- to 5-cm-diameter, adjustable intraoral loop part with 6 smooth 2.7-mm-diameter holes for suction; a binding loop part to fit mouthpieces of various sizes; and an extraoral part having two ends, both of which were linked to the Y-shaped connector (ARAM, Osaka, Japan). Finally, the MB-142 mouthpiece (Olympus, Tokyo, Japan) was inserted into the binding loop part (Figure 1).

For screening EGD in the CSM group, patients were placed on their left side and asked to bite down on the mouthpiece, with the intraoral loop with holes placed inside the left cheek. During EGD, continuous low pressure (10 kPa) suctioning with a suction unit (Shin-Ei Industries, Tokyo, Japan) was performed through the unification tube attached to the Y-shaped connector (Figure 2). In control subjects, the MB-142 mouthpiece was used in the usual way.

Patients and study design

This was a single-center, prospective, randomized, controlled study. Patients who underwent screening EGD in Nakaya Hospital (Wakayama, Japan) from February 2011 to December 2011 were recruited. Patients were excluded if they had a history of respiratory problems that could increase the risk of complications associated with aspiration pneumonia and salivary flow. Eligible patients were randomly assigned to one of the following groups: the group using the CSM, or the group using the conventional mouthpiece for EGD. During the EGD, salivary flow and complications associated with aspiration were evaluated and compared between the two groups. However, due to its nature, this study could not be blinded.

This study was approved by the ethics committee of Nakaya Hospital. Written, informed consent was obtained from each patient. This study was registered with the University Hospital Medical Information Network (UMIN) (registration number UMIN000009294). The CSM was developed solely by our institute without any financial or equipment support from companies.

EGD

A conventional gastrointestinal videoscope (GIF-XP260N;

Table 1 Patients' characteristics

	CSM	MB-142	*P* value
Sex, male/female	56/42	59/39	0.125
Age, yr, median (range)	66 (33-99)	56 (35-96)	0.269
Biopsy (yes/no)	30:68	24:74	0.344
Duration of procedure, min, median (range)	8 (4-21)	7 (3-21)	0.194
Sedation, none/mild/moderate/deep	11/7/17/63	17/3/8/70	0.090

CSM: Continuous suction mouthpiece.

Olympus) was orally inserted into the stomach to observe the upper gastrointestinal tract. During the examination, patients were placed on their left side. EGD for all patients was performed by one endoscopist and one assistant nurse.

Premedication with anticholinergic agents or glucagon was not used. Lidocaine (8%) was sprayed into the posterior pharynx of all patients before insertion of the endoscope to reduce the gag reflex. Then, midazolam (1-5 mg) was administered intravenously for sedation. Adequate monitoring of vital signs and oxygen saturation was performed throughout the examination.

Outcome assessment and evaluations

The primary outcome was occurrence of aspiration pneumonia. Secondary outcomes were extent of salivary flow, frequency of saliva suction, and the number of choking episodes during the procedure. Adverse events during and after EGD were also examined. In addition, the oral cavity was meticulously examined after the EGD to determine whether blood blisters or any suction tube fragments were present.

The duration of EGD using the CSM included the time required to bite down on the mouthpiece with the intraoral loop placed inside the left cheek. The level of sedation was defined as follows: mild, conscious sedation; moderate, between conscious and deep sedation; and deep, deep sedation. None means no use of sedatives. The extent of salivary flow was defined as follows: grade 1, no flow of saliva from mouth; grade 2, flow to the cheek; grade 3, flow to the ear; and grade 4, flow to hair or clothing. When a gurgling sound was heard in the oropharyngeal region, the assistant nurse promptly suctioned the saliva using the suction catheter (Nipro Suction Catheter® 14-Fr, Nipro). Choking episodes were counted each time they occurred during the examination, while consecutive coughs or chokes were counted as one choking episode.

Statistical analysis

The data are expressed as medians with ranges. Data were analyzed using the unpaired Mann-Whitney *U* test and Fisher's exact test. The level of statistical significance was $P < 0.05$. All analyses were performed using the SPSS 21.0 software package (SPSS Inc., Chicago, IL, United States).

RESULTS

A total of 196 subjects (115 men and 81 women, median age 62 years (range, 33-99 years) were recruited during the study period; all were considered eligible. Patients were divided equally into the CSM group and conventional mouthpiece groups (both $n = 98$). The patients' characteristics are summarized in Table 1. There were no significant differences between the two groups in sex, age, biopsy procedure, duration of the examination and depth of sedation.

Obvious aspiration pneumonia was not observed in any of the participating patients. The extent of salivary flow was significantly less in patients with the CSM than in patients with the conventional mouthpiece ($P < 0.001$) (Figure 3A). Although there was no statistical significance, less frequent suctioning and choking episodes were observed in patients with the CSM than in patients with the conventional mouthpiece ($P = 0.082$, and $P = 0.084$, respectively) (Figure 3B, C). In addition, no patients in the CSM group required saliva suctioning during the procedure. Complete failure of suctioning function did not occur in any patients with the CSM. In addition, neither blood blisters nor fragments of the PVC suction tubes were observed in the mouths of patients who used the CSM. No other significant adverse events were observed in any of the patients.

DISCUSSION

This is the first attempt to control salivary flow by continuous suctioning during screening EGD examination. Previously, little attention has been paid to the troubles and complications associated with endoscopy-related salivary flow. This study showed that, during EGD, salivary flow did not extend as far out of the mouth in patients with the CSM as in patients with the conventional mouthpiece. Moreover, fewer suctioning and choking episodes were observed in patients with the CSM, although the difference was not statistically significant.

The most relevant finding of this study is that the CSM could reduce the extent of salivary flow during screening EGD. As shown in the results, the grade of extent of salivary flow was higher in patients with the conventional mouthpiece, despite relatively short examination times. In contrast, patients with the CSM discharged less saliva during the procedure. This advantage implies that use of the CSM during EGD could prevent exposure of the patient's body or clothing and operating bed to saliva, resulting in relief for the patient from the discomfort associated with drooling of saliva. Moreover, reduced contamination of the operating bed with saliva could decrease the effort, time and cost required for cleanup.

In the present study, use of the CSM tended to reduce the frequencies of saliva suction and choking episodes during screening EGD, although statistical differences were not observed. The fact that there were no episodes

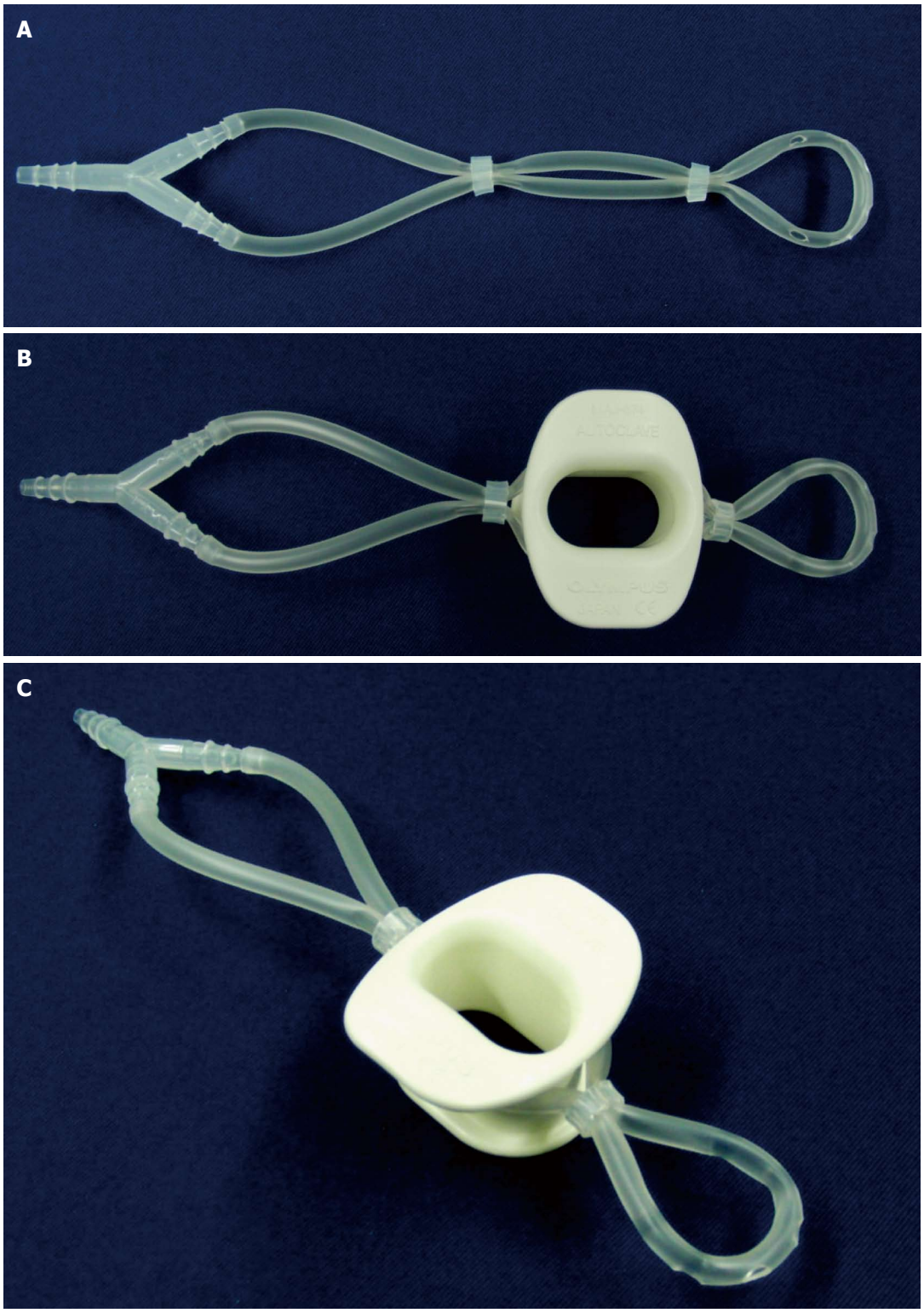

Figure 1 The continuous suction mouthpiece. A: The continuous suction mouthpiece (CSM) without the mouthpiece; B, C: The CSM with the mouthpiece.

of suctioning in the CSM group could imply that the assistant nurse's time and effort can be directed towards other, more important tasks during EGD. Reduced choking episodes from use of the CSM may decrease the complication of aspiration during EGD, although no aspiration pneumonia was observed in patients in both groups, perhaps due to the small number of patients in this study. Thus, use of this equipment, which can be easily prepared with no special materials and at a low cost, is recommended during screening EGD.

Moreover, the CSM's continuous suction creates airflow in the oral cavity, which may reduce the discomfort in the oral cavity caused by endoscopy. In the questionnaire administered after EGD, 3 of 11 patients in the CSM group who did not use sedation answered that continuous suction during the procedure was comfortable. In this study, most

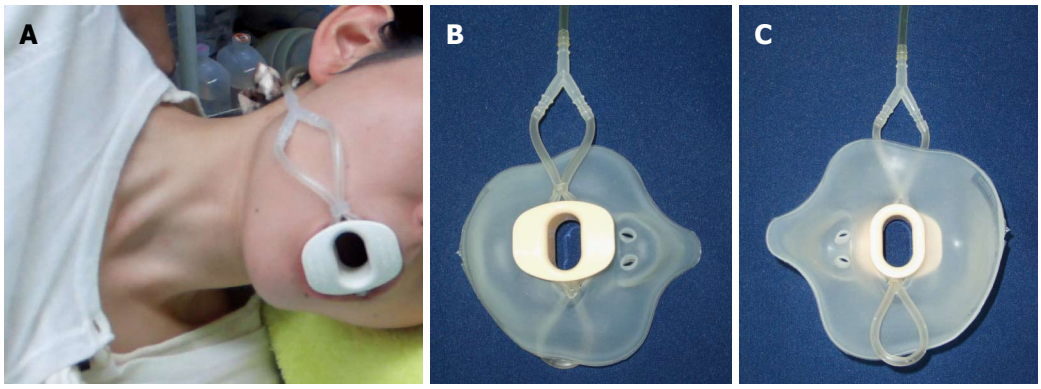

Figure 2 Use of the continuous suction mouthpiece. A: Image showing actual use of the continuous suction mouthpiece (CSM); B: Endoscopist's view of the CSM during its use; C: Patient's view of the CSM during its use.

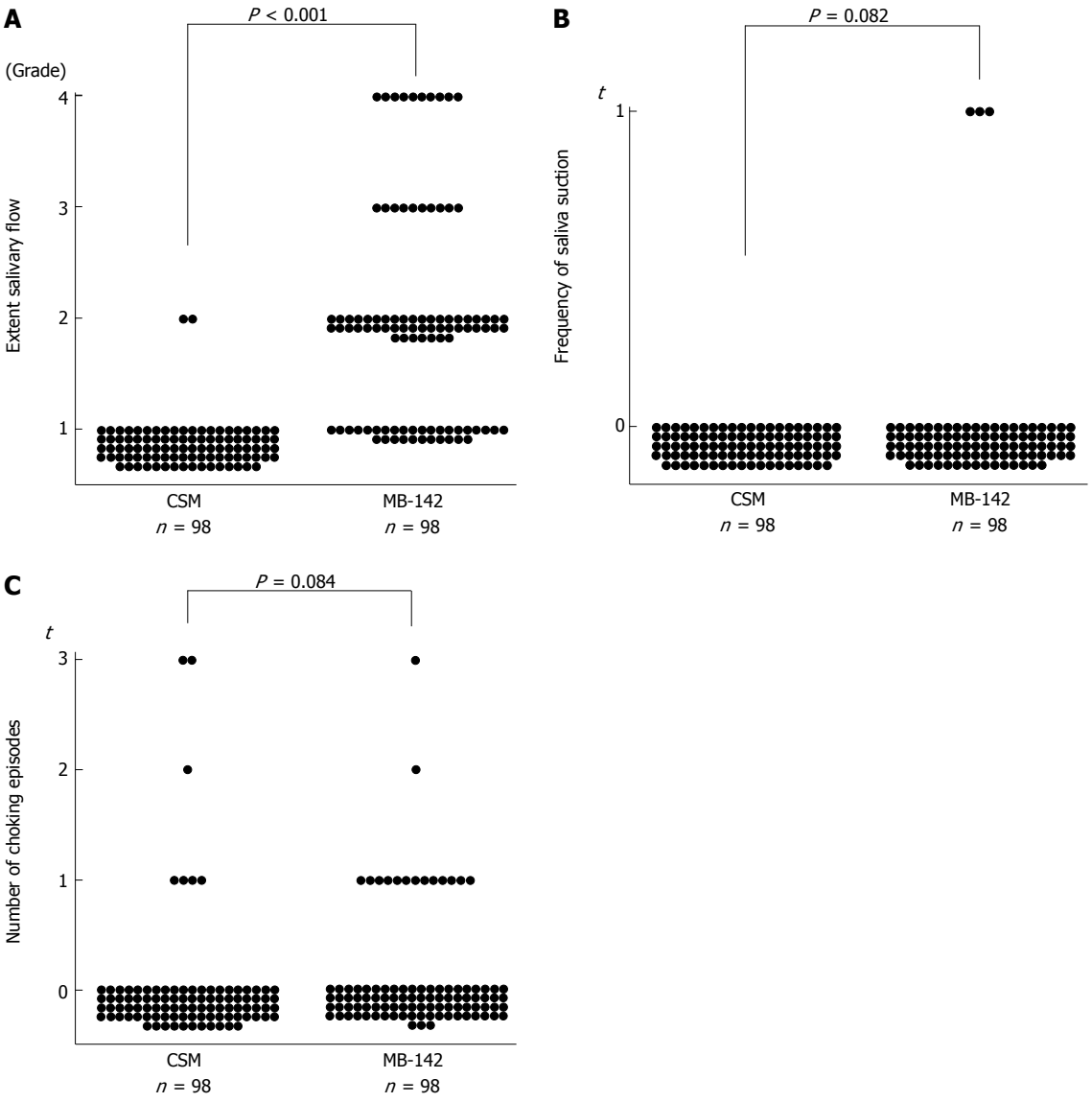

Figure 3 Obvious aspiration pneumonia was not observed in any of the participating patients. A: Extent of salivary flow. The grade of extent of salivary flow was significantly lower in patients with the continuous suction mouthpiece (CSM) than in patients with the conventional mouthpiece ($P < 0.001$); B: Frequency of saliva suction. No suction events were observed in patients with the CSM, while 3/98 (3.1%) of the patients with the conventional mouthpiece required suctioning during esophagogastroduodenoscopy (EGD) ($P = 0.082$); C: Number of choking episodes. Although not statistically significant, less frequent choking episodes were observed in patients with the CSM than in patients with the conventional mouthpiece ($P = 0.084$).

of the patients were sedated with midazolam and could not comment about the CSM after the procedure. Future stud-

ies should confirm the level of comfort associated with use of the CSM during EGD performed without sedation.

Administration of anticholinergic agents is an alternative strategy to reduce salivary secretion and peristaltic activity of the gut during EGD. However, these agents cannot be used in patients with heart disease, glaucoma or prostate enlargement. In contrast, the CSM can be used in all patients because its use is not associated with any serious adverse effects. Thus, the improved mouthpiece would be superior to anticholinergics in terms of controlling salivary secretion during EGD.

The CSM may also be effective in endoscopic procedures other than EGD. Recently, we reported that the CSM is effective during PEG[2]. Besides EGD and PEG, many other kinds of time-consuming upper endoscopic procedures have become commonplace, such as endoscopic submucosal dissection and peroral double-balloon enteroscopy. Since these procedures are also associated with an increased risk of aspiration[3,4], use of the CSM may be recommended in all patients who undergo these procedures. Hence, the usefulness of this item in various procedures should be evaluated in the future.

This study had several limitations. First, neither the endoscopist nor the assistant nurse was blind as to which mouthpiece was used. Since the shape of the mouthpiece was different from conventional mouthpieces, blinding was not possible. Second, the number of patients was too small to evaluate some endoscopy-related complications, such as the frequency of aspiration pneumonia, the primary outcome of this study. This could be partly attributed to the study design, since the diagnosis of aspiration pneumonia was based on patients' symptoms alone. The reported rate of aspiration pneumonia with conventional EGD methods is 3.94%, as assessed by ^{18}F-FDG PET scan[1]. Therefore, the advantage of the CSM in terms of aspiration needs to be confirmed in studies that are designed for evaluating subclinical aspiration pneumonia and in older patients who have difficulty swallowing. Third, several factors may have influenced the outcome of this study. In particular, the amount of midazolam administered (1-5 mg) for sedation varied widely. The sedative agent might have influenced the extent of salivary flow. To overcome this limitation, it would have been preferable if we had defined the amount of sedative agent to be administered in mg/kg. Finally, use of the CSM involves a certain amount of time and cost. However, construction of a single CSM costs no more than $1 (1 US dollar), in addition to the cost of the MB-142 mouthpiece.

The CSM reduced the extent of salivary flow during EGD. Moreover, it tended to reduce the frequencies of suction and choking episodes during EGD. This type of simple and inexpensive device is expected to reduce not only patient discomfort, but also the burden on medical staff during EGD. Therefore, use of the device in routine clinical practice is highly recommended.

COMMENTS

Background

Screening esophagogastroduodenoscopy (EGD) is a common examination that is useful in detecting upper gastrointestinal disease. Hence, it is increasingly performed for patients. However, more attention should be paid to the risk of aspiration during the procedure. One of the most important factors correlating with aspiration is salivary flow. No mouthpiece has previously been designed to control salivary flow during endoscopic examination.

Research frontiers

A new continuous suction mouthpiece (CSM) was developed and its usefulness during percutaneous endoscopic gastrostomy (PEG) was recently reported.

Innovations and breakthroughs

This is the first attempt to control salivary flow by continuous suctioning during screening EGD examination. Previously, little attention had been paid to the troubles and complications associated with endoscopy-related salivary flow. This study showed that, during EGD, salivary flow did not extend as far out of the mouth in patients with the CSM as in patients with the conventional mouthpiece. Moreover, fewer suctioning and choking episodes were observed in patients with the CSM, although the difference was not statistically significant.

Applications

The CSM may also be effective in endoscopic procedures other than EGD and PEG.

Terminology

A mouthpiece is used to protect the endoscope from being bitten and for smooth insertion of the endoscope, without hindrance from the tongue, during EGD.

Peer review

This is an interesting original article introducing a new continuous suction mouthpiece during EGD. The idea is very good. There was no statistical difference between choking episodes and the incidence of aspiration pneumonia in this article. However, it could reduce the extent of salivary flow during EGD. This is advantageous from a hygienic point of view. Use of this device is a good option during screening EGD and other endoscopic procedures. This device has the potential to make a significant contribution to the practice procedures of readers in the field.

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CASE REPORT

Duodenal subepithelial hyperechoic lesions of the third layer: Not always a lipoma

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Abstract

Endoscopic ultrasonography is the most accurate procedure for the evaluation of subepithelial lesions. The finding of a homogeneous, hyperechoic, well-delimited lesion, originating from the third layer of the gastrointestinal tract (submucosa) suggests a benign tumor, generally lipoma. As other differential diagnoses have not been reported, echoendoscopists might not pursue a definitive pathological diagnosis or follow-up the patient. This case series aims to broaden the spectrum of differential diagnosis for duodenal hyperechoic third layer subepithelial lesions by providing four different and relevant pathologies with this echoendoscopic pattern.

Key words: Endoscopic ultrasonography; Endoscopic ultrasound-guided fine needle aspiration; Duodenum; Subepithelial tumor; Lipoma

Core tip: This case series reports four different and relevant pathologies with an echoendoscopic pattern usually suggestive of lipoma.

Figueiredo PC, Pinto-Marques P, Mendonça E, Oliveira P, Brito M, Serra D. Duodenal subepithelial hyperechoic lesions of the third layer: Not always a lipoma. *World J Gastrointest Endosc* 2013; 5(10): 514-518 Available from: URL: http://www.wjgnet.com/1948-5190/full/v5/i10/514.htm DOI: http://dx.doi.org/10.4253/wjge.v5.i10.514

INTRODUCTION

Endoscopic ultrasonography (EUS) has long been considered the most accurate procedure for the evaluation of subepithelial lesions[1-3]. It provides important information, namely the layer of origin, size, borders and echogenic structure. Using Doppler findings it may also differentiate vascular structures from cysts or assess the tumor blood supply. These findings allow for a presumptive diagnosis in most cases, although histopathology remains the gold standard[2].

Gastrointestinal (GI) lipomas are benign tumors that occur anywhere along the gut, most commonly in the colon[4]. The typical EUS finding is a homogeneous, hyperechoic, well-delimited lesion, originating from the third layer of the GI tract (submucosa)[3,5]. The only differential diagnosis for this EUS pattern reported in the literature is Brunner's gland hamartoma[5,6].

This case series aims to broaden the spectrum of

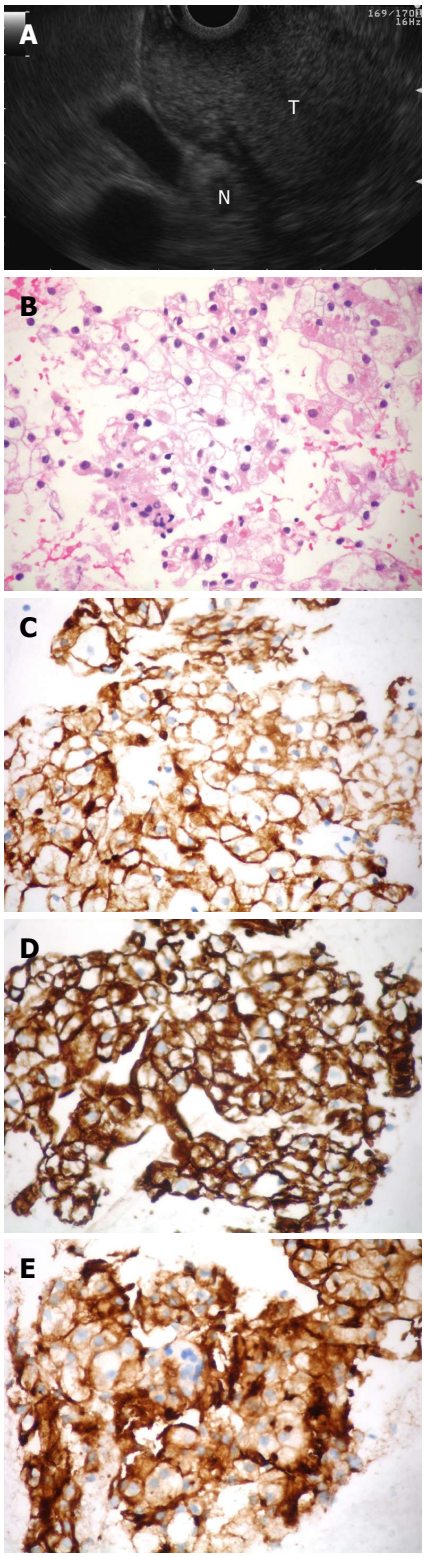

Figure 1 Endoscopic ultrasonography and cytology findings of a renal cell carcinoma metastasis. A: Hyperechoic mass in the duodenal bulb, apparently originating from the third layer. Adjacent, a small lymph node is noted; B-E: Fine-needle aspiration cell blocks, × 400 magnification; Hematoxylin and eosin staining showing clear cell aggregates (B). Positive immunostaining for cytokeratin AE1/AE3 (C), vimentin (D) and CD10 (E): consistent with an epithelial carcinoma of renal origin.

EUS differential diagnosis for duodenal hyperechoic third layer subepithelial lesions.

CASE REPORT

Case 1: Renal cell carcinoma metastasis

A 58-year-old woman was admitted for melena and upper GI endoscopy revealed an ulcerated mass in the duodenal bulb. Biopsies using "bite-on-bite" technique were inconclusive. EUS with a linear echoendoscope (Olympus Medical Systems Corp., Tokyo, Japan) showed a well-delimited hyperechoic mass, apparently originating from the third layer at the bulb (Figure 1A). Fine-needle aspiration (FNA) was performed with a 22-gauge EZ Shot needle (Olympus Medical Systems Corp., Tokyo, Japan). FNA smear and cellblock sections showed clear cell aggregates with positive immunostaining for cytokeratin AE1/AE3, vimentin and CD10, which were consistent with an epithelial carcinoma of renal origin (Figure 1B-E). Three years before the patient had a left kidney nephrectomy for a Grawitz tumor and was referred for cephalic pancreatoduodenectomy to treat the disease recurrence.

Case 2: Ampullary carcinoma

A 64-year-old man presented with jaundice at the emergency department. An abdominal US and CT scan showed dilated bile ducts down to the level of the ampullary region, where a polypoid mass was found. Using a linear echoendoscope a mildly hyperechoic homogeneous lesion was found on the duodenal submucosa, adjacent to the ampulla, compressing the bile duct (Figure 2A). FNA with a 25-gauge EZ Shot needle (Olympus Medical Systems Corp., Tokyo, Japan) retrieved a cytology sample consistent with adenocarcinoma (Figure 2B, C). The patient was submitted to cephalic pancreatoduodenectomy which confirmed the diagnosis of ampullary carcinoma (Figure 2D-F).

Case 3: Hamartomatous duodenal polyp

A 62-year-old man was admitted for melena and upper GI endoscopy revealed an ulcerated semipedunculated polyp in the second portion of the duodenum (Figure 3A). EUS, performed using a radial echoendoscope, showed a homogeneous hyperechoic polypoid lesion originating from the submucosa (Figure 3B, C). Following polypectomy, histopathological examination unveiled fibroadipose tissue covered by intestinal mucosa, which was consistent with a hamartomatous polyp (Figure 3D).

Case 4: Gangliocytic paraganglioma

A 51-year-old woman was submitted to an upper GI endoscopy for dyspepsia. A 20 mm subepithelial lesion was found on the posterior wall of the second part of the duodenum. On linear EUS, this was shown to be a well-delimited slightly hyperechoic lesion apparently originating from the submucosa (Figure 4A). A tissue sample was obtained using a 22-gauge ProCore needle (Cook Endoscopy Inc, Limerick, Ireland) (Figure 4B-E). Cytopathological examination suggested a possible gastrointestinal stromal tumor (GIST) which led to the decision to perform endoscopic resection (Figure 4F). Further

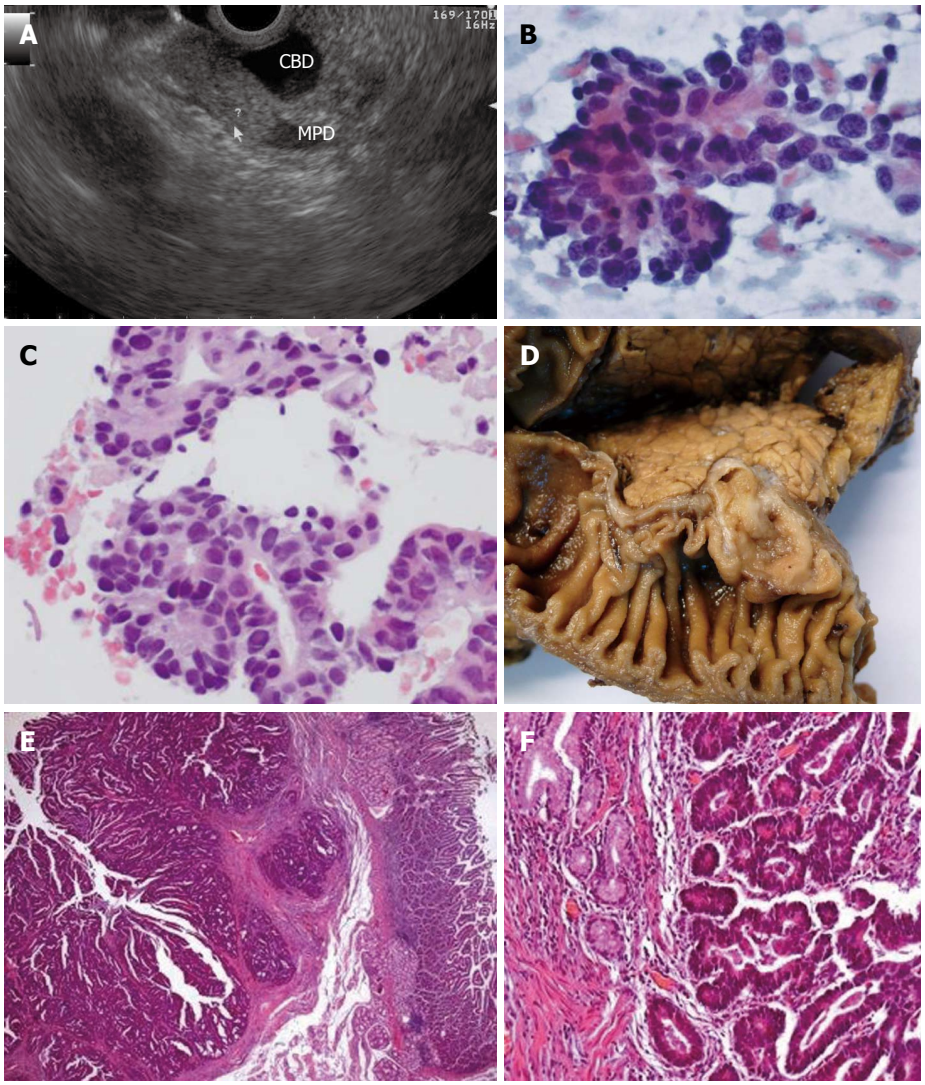

Figure 2 Endoscopic ultrasonography and pathological findings of an ampullary carcinoma. A: Mildly hyperechoic third-layer lesion adjacent to the ampulla, compressing the bile duct; B, C: Fine-needle aspiration, × 400 magnification; B: Smears with acinar groups, irregularly distributed nuclei, coarse chromatin, conspicuous nucleoli (Papanicolaou); C: Cell-block preparation of aspirated sample [hematoxylin and eosin (HE)]; D: Surgical pathology specimen confirming the full excision of an ampullary carcinoma; E: Ampullary area well-differentiated adenocarcinoma, HE × 25; F: HE × 100.

histopathological analysis of the resected tumor brought about another diagnosis-gangliocytic paraganglioma (Figure 4G-I).

DISCUSSION

Although EUS does not provide gastroenterologists with a definitive diagnosis for subepithelial lesions, the ultrasonographic findings and knowledge of the epidemiology allow for an educated guess in many situations. This, along with the likelihood of malignancy, guides management decisions regarding biopsy and resection.

Both lipomas and Brunner's gland hamartomas are regarded as benign tumours, which are usually asymptomatic[7,8]. Given their benign nature, treatment is only recommended if they become symptomatic[9]. Moreover, in the absence of other differential diagnosis for hyperechoic lesions of the third layer of the GI tract, the ecoendoscopist might be tempted not to obtain a tissue sample or even not follow-up the patient.

In our case series, two subepithelial lesions presented with bleeding and a third one with jaundice. EUS favored the diagnosis of lipoma in all of these lesions and resection was required. In the first two cases, surgery was the preferred approach due to the tumors characteristics-size, ulceration and location. The surgical team required a histopathological evaluation to confirm the diagnosis and establish the therapeutic strategy, therefore EUS with FNA was performed. In the third case, the tumor was pedunculated and endoscopic resection was feasible, thus FNA was not required.

The fourth case was an incidental lesion. EUS features were felt suspicious for lipoma although the pattern was not typical. Based on these findings and our prior experience with the first three cases, a FNA was performed. The diagnosis was GIST, which is a fairly uncommon diagnosis in the third layer[3]. Management options were discussed with the patient and the decision for resection was based on the tumor's size (2 cm), location (small bowel confers worse prognosis) as well as the

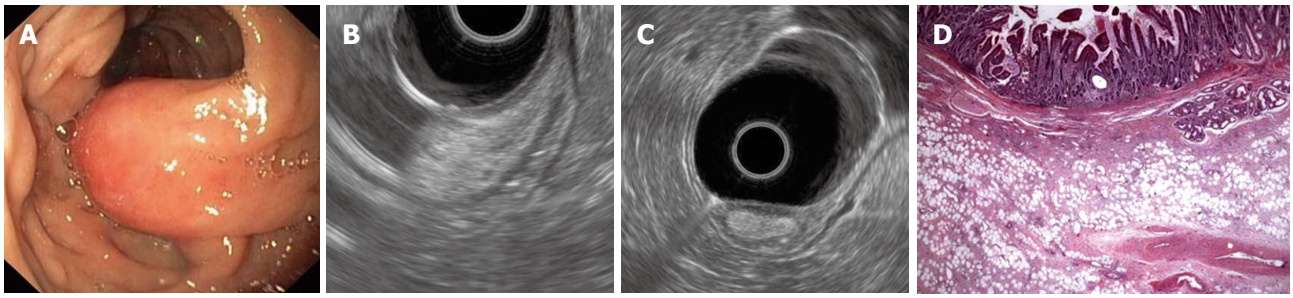

Figure 3 Endoscopic, endoscopic ultrasonography and pathological findings of hamartomatous polyp. A: Semipedunculated polyp in the second portion of the duodenum; B: Longitudinal view of the polyp's stalk-originating from the duodenal wall; C: Top of the polypoid lesion-cross-sectional view; D: Hamartomatous polyp, HE × 25.

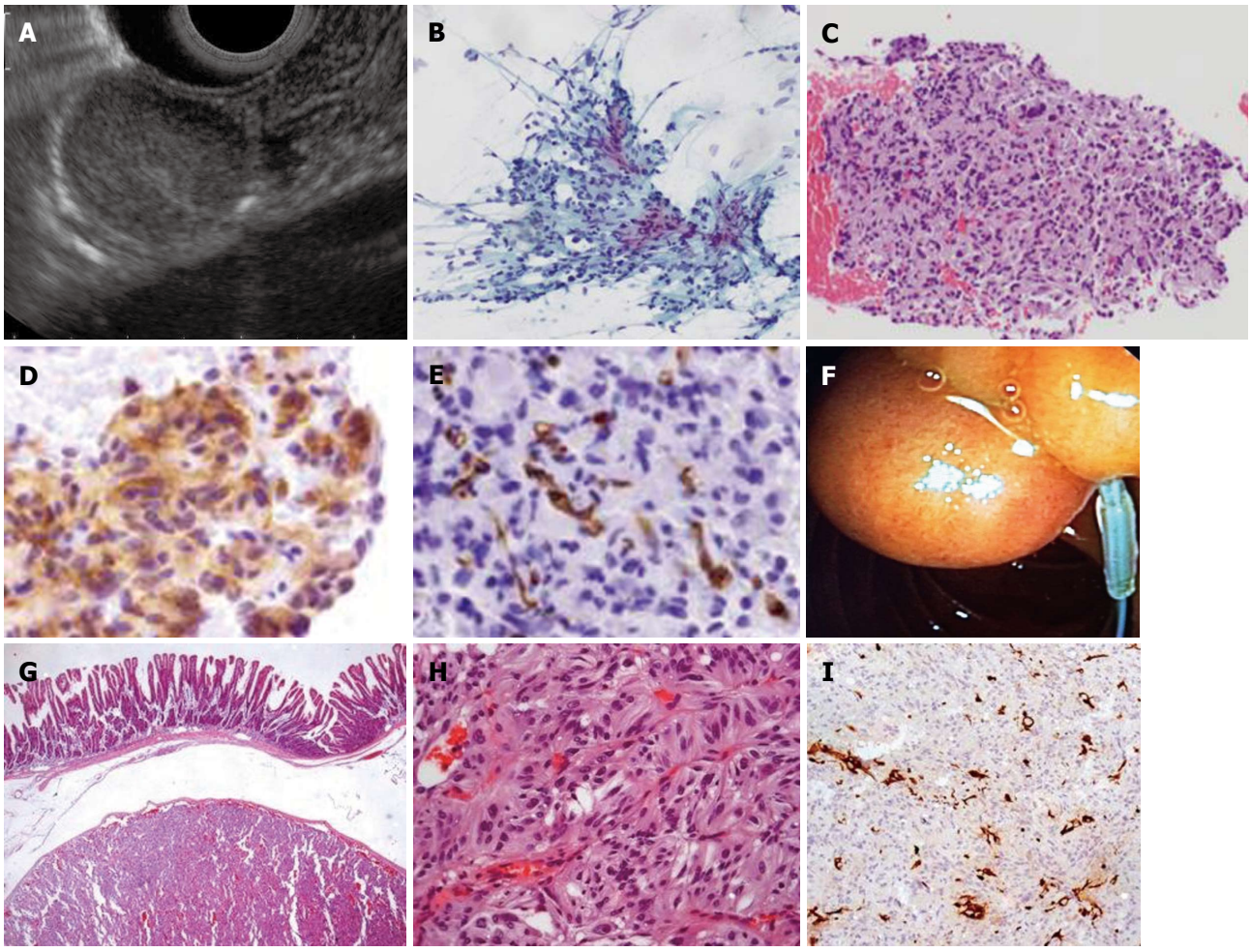

Figure 4 Endoscopic, endoscopic ultrasonography and pathological findings of gangliocytic paraganglioma. A: Slightly hyperechoic lesion of the third layer of the duodenal wall; B-E: Endoscopic ultrasonography-fine needle aspiration with cytological features suggestive of GIST; B: Few fragments of loose mesenchymal spindle cell tissue fragments (Papanicolaou staining × 100); C: Cell block preparation of aspirated material, discrete nuclear atypia [Hematoxylin and eosin (HE) × 100]; D: Most cells stain positive for CD117 (× 400); E: Rare cells stained with CD34 (× 400); F: Resection of the subepithelial lesion using endoloop; G-I: Histopathological analysis of the resected tumor; G: Duodenal gangliocytic paraganglioma (HE × 25); H: Duodenal gangliocytic paraganglioma (HE × 200); I: Sustentacular S-100 positive cells documented (S100 ×100). GIST: Gastrointestinal stromal tumor.

patient's wish[10]. The surgical specimen pathology report showed the lesion to be a gangliocytic paraganglioma-an exceedingly rare entity[11]. Previous EUS reports described it as a hypoechoic or isoechoic homogeneous lesion, in the proximity of the duodenal papilla[12,13]. Its characteristic triphasic microscopic appearance (epithelioid cells, spindle cells, and ganglion cells) histological appearance might account for our inability to differentiate it from a GIST on FNA[14].

In conclusion, this case series presents relevant and previously unreported differential diagnosis for duodenal hyperechoic subepithelial lesions in the third layer.

The EUS operator should always take time to assess the transition zone to assess the layer of origin and, in our opinion, have a low threshold to perform FNA, namely, if the EUS features are felt not typical.

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CASE REPORT

Contribution of endosonography in an uncommon case of pancreatic cysts

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Abstract

Here we present the case of a 35-year-old female patient with long standing dyspepsia and imaging studies showing the presence of multiple cysts in the head and tail of the pancreas. The patient underwent endosonography that confirmed the presence of multiple simple cysts throughout the entirety of the pancreas without dilation of the pancreatic duct. The majority of the cysts were less than one centimeter in size, and the largest cyst showed a honeycomb appearance. Cytology of aspirates from the two largest cysts was compatible with benign pancreatic cysts. Endosonography also revealed cysts within the left kidney and spleen. Genetic testing confirmed Von Hippel-Lindau disease. We highlight this case because it is unusual for Von Hippel-Lindau disease, a rare clinical entity, to present solely with cysts in the absence of more common manifestations, such as hemangioblastomas in the central nervous system and malignancy.

Key words: Von Hippel-Lindau disease; Endosonography; Pancreatic cysts; Hereditary disease; Cysts

Core tip: This is a case of a rare clinical entity, Von Hippel-Lindau disease, with an unusual presentation. The patient had only pancreatic cysts without more common manifestations, particularly hemangioblastomas and malignancy. The imaging methods used in this case were important for the diagnosis, particularly endosonography, which showed the honeycomb appearance of the pancreatic serous cystadenomas. This case should alert endoscopists to the possible occurrence of this hereditary disease in the presence of multiple pancreatic cysts without other manifestations or family history.

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INTRODUCTION

Von Hippel-Lindau (VHL) disease is an autosomal dominant disorder caused by germline mutations in the VHL tumor suppressor gene. VHL mutations predispose patients to the development of a variety of tumors, which are most commonly retinal and central nervous system hemangioblastomas, clear cell renal carcinoma and pheochromocytomas[1,2]. Hemangioblastomas are the most common tumors associated with VHL disease and affect 60% to 84% of patients[3]. There are few studies assessing pancreatic lesions in VHL disease[4-7]. Hammel *et al*[4] found pancreatic involvement in 77.2% of patients with

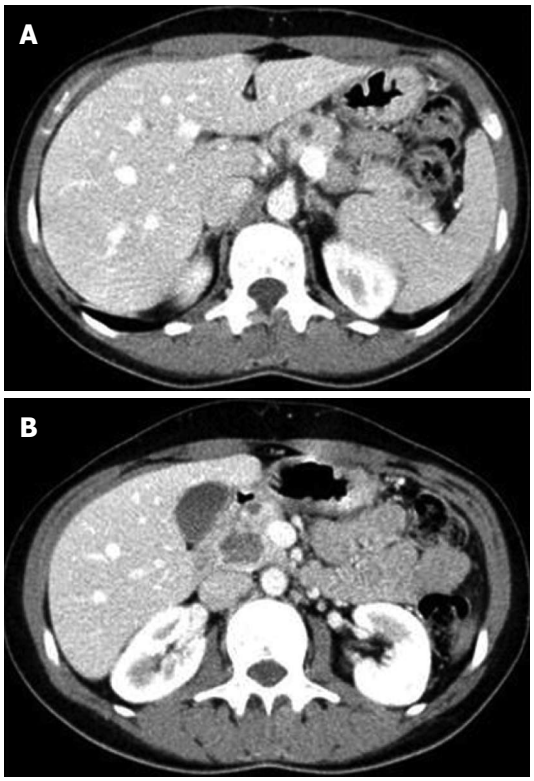

Figure 1 Computed tomography abdominal scan. A: Small cystic lesions dispersed throughout the pancreas; B: The largest lesion.

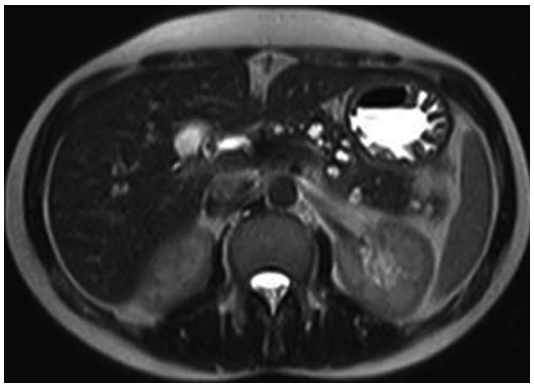

Figure 2 Magnetic resonance imaging. Cyst lesions are bright on T2-weighted images.

VHL, and these pancreatic lesions can manifest as cysts (91.1%), serous cystadenomas (12.3%), neuroendocrine tumors (12.3%) or combined lesions (11.5%). However, the frequency of the pancreas as the only organ affected is low (7.6%), and the majority do not require treatment[4].

CASE REPORT

This case concerns a 35-year-old woman referred to our Gastroenterology Department with long-standing dyspepsia and pancreatic cysts detected by ultrasound examination. There were no other symptoms, such as abdominal pain, weight loss, visual or hearing changes, headache or urinary complaints. The past medical and family histories were not of significance. There were no abnormal findings on examination.

The patient underwent an abdominal computed tomography (CT) scan (Figure 1), which showed an enlargement of the pancreas, especially in the cephalic region, with heterogeneous density due to the presence of multiple hypodense nodules dispersed throughout the parenchyma. The majority of these lesions were small, but one larger contrast-enhancing lesion of 22 mm was present in the uncinate process.

Given the findings of the CT scan, we performed an abdominal magnetic resonance imaging (MRI) (Figure 2), which revealed several cysts that had a high signal intensity on T2 weighted images.

The patient underwent endosonography that confirmed the presence of multiple simple cysts throughout the entirety of the pancreas. The majority of the cysts were less than 1 cm in diameter, but two cysts were larger than 1 cm. One of the larger cysts was 16 mm in diameter and was located at the isthmus-body transition. This cyst and did not communicate with the main pancreatic duct and was aspirated. The content had a serous appearance, and cytological analysis revealed amorphous material, few erythrocytes and inflammatory cells (Figure 3).

The largest cyst was 23 mm in diameter and was located in the head of the pancreas. The cyst had a honeycomb appearance characteristic of serous cystadenomas (Figure 4A). The cytology did not show evidence of cellular atypia (Figure 4B). The carninoembryonic antigen was < 0.6 ng/dL, and the amylase in the cystic content was 135 U/L.

The endosonography also showed cysts in the left kidney and in the spleen (Figure 5). The findings described were compatible with simple cysts and pancreatic serous cystadenomas and provided an indication for genetic testing for VHL. The sequencing of the VHL gene revealed one pathogenic heterozygous mutation in exon 1 (c.269A > T), confirming the diagnosis of VHL disease.

The patient underwent a MRI of the brain and entire spine and no hemangioblastomas were detected. The abdominal MRI scan excluded renal carcinoma. The plasma and urinary catecholamines and the urinary vanilmandelic acid were normal, excluding pheocromocytoma. The patient was also referred for examination of the retina and ear, nose and throat, including audiometry. There were no abnormal findings, which excluded angiomas of the retina and endolymphatic sac tumors, respectively.

Her family was genetically tested, and the same mutation was found in her 7 year-old daughter.

DISCUSSION

This case is important not only due of the rarity of VHL disease but also because the only manifestation in this patient was cysts diagnosed by imaging tests. This

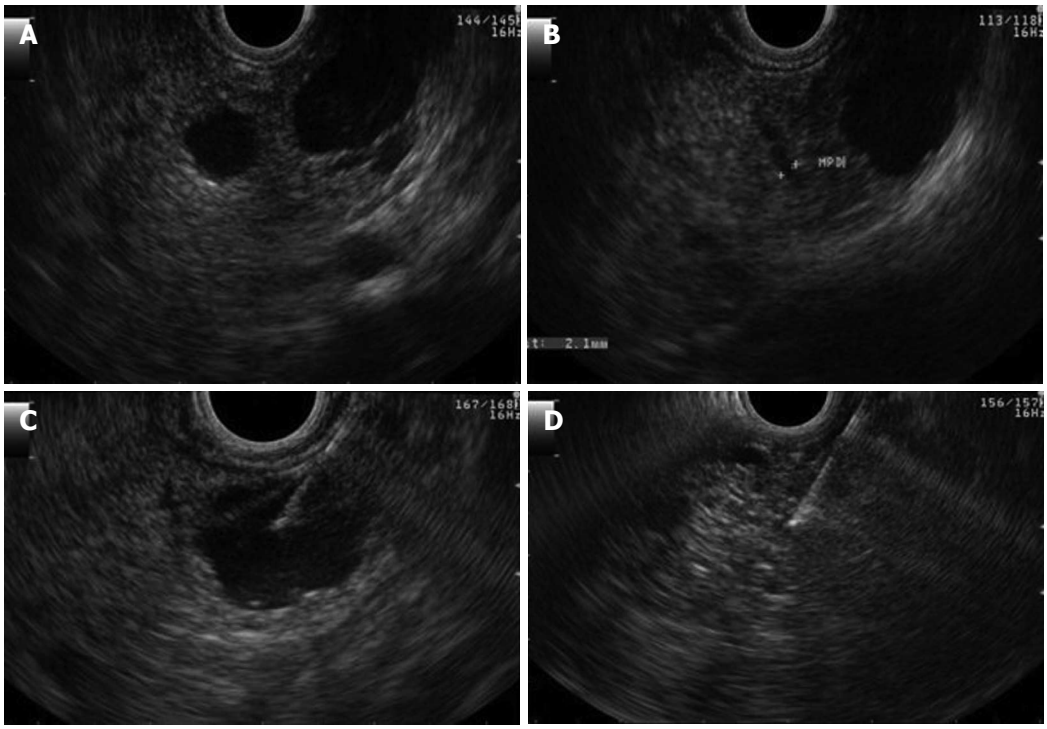

Figure 3 Endosonography. A, B show a large cyst of 16 mm in diameter without communication or dilatation of the pancreatic duct; C: Demonstrates aspiration of the cyst; D: Demonstrates its appearance after total aspiration.

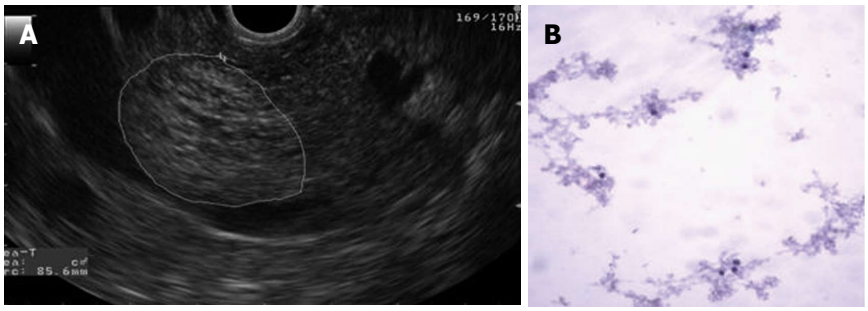

Figure 4 The largest cyst was 23 mm in diameter and was located in the head of the pancreas. A: Endosonography. Cyst with a honeycomb appearance; B: Cytology (papanicolaou stain, × 100). Benign pancreatic cysts.

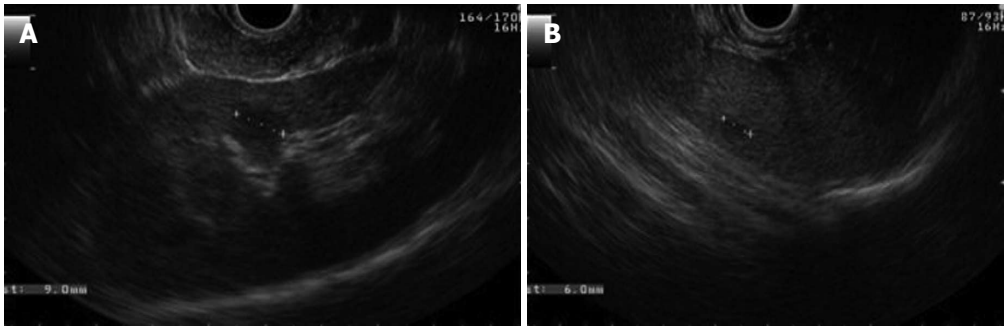

Figure 5 Endosonography. A: A cyst in the renal cortex; B: A cyst in the spleen.

finding emphasizes the importance of endosonography for better characterization of lesions, particularly in the absence of family history or more common manifestations.

According to criteria from Massachusetts General Hospital, if patients are found to have more than one pancreatic serous cystadenoma or have multiple pancreatic cysts and any VHL associated lesion (including

pancreatic serous cystadenoma), they should be referred to a VHL specialist clinic[8]. Serous cystadenomas are rare pancreatic exocrine tumors that occur at an unusually high frequency in patients with VHL disease. They account for nearly 10% of pancreatic lesions[4]. This percentage may actually be higher due to the difficulty in distinguishing this tumor from a cluster of multiple small true cysts, although the differentiation between the two does not modify the approach to management. Hammel *et al*[4] found that VHL disease was discovered by chance in 6% of patients during abdominal imaging performed for unrelated reasons. Therefore, the possibility of VHL disease must be considered when pancreatic lesions are observed. Isolated pancreatic involvement can be a key factor in establishing the diagnosis of VHL when there is no family history or the concomitant existence of more conventional lesions, such as hemangioblastomas. Most of the pancreatic cysts in VHL are clinically indolent and generally do not require treatment[4,5,7]. In our case, imaging studies, such as endosonography, revealed the characteristic appearance of pancreatic serous cystadenoma and was crucial for the diagnosis of VHL disease. This diagnosis has multiple implications, including requiring an adequate annual surveillance and the possibility of transmission of this disease to descendants. Pancreatic lesions can be the first manifestation in some VHL patients. The mean age of initial detection is 37 years and precedes hemangioblastomas in the central nervous system by 5-7 years. This result emphasizes the importance of surveillance with an annual MRI of the brain and spine[7]. However, the series by Mukhopadhyay *et al*[5] retrospectively evaluated the pancreatic lesions in 17 VHL disease patients and found the lesions were not the presenting feature in any patient. *De novo* mutations of VHL are estimated to occur in approximately 20% of probands[2], which most likely occurred in our case. Unfortunately, her daughter was born with the same mutation. With a diagnosis of VHL more than 7 years earlier, our patient could have been offered prenatal screening.

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CASE REPORT

Migration of a biliary stent causing duodenal perforation and biliary peritonitis

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Abstract

Migration of endoscopically placed biliary stents is a well-recognized complication of endoscopic retrograde cholangiopancreatography. Less than 1% of migrated stents however cause intestinal perforation. We present a case of a migrated biliary stent that resulted in duodenal perforation and biliary peritonitis.

Key words: Biliary stents; Migration; Duodenal perforation; Biliary peritonitis

Core tip: Biliary stent migration complicated by duodenal perforation is rare and should be included in the differential diagnosis of those presenting with abdominal pain after endoscopic retrograde cholangiopancreatography with stent placement and physicians caring for these patients should be aware of such complication. To reduce the chance of stent migration, endoscopists should assess for the size and shape of the stent in each patient.

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INTRODUCTION

The use of biliary stents was introduced in the late 1970s, and since then endoscopic and percutaneous insertion of biliary stents is the treatment of choice as a palliative measure for patients suffering from obstructive jaundice secondary to unresectable malignant hepatobiliary tract tumors and to relieve obstruction of the bile ducts secondary to benign stricture or choledocholitheiasis[1,2].

Biliary stents however are not without complications. The complication rate ranges between 8% and 10%, with a mortality rate below 1%[3-5]. Complications specific to the stents include migration, occlusion, and intestinal perforation. Migration of endoscopically placed biliary stents is a well-recognized complication of endoscopic retrograde cholangiopancreatography (ERCP). Serious complications can result from stent migration but fortunately less than 1% of migrated stents cause intestinal perforation. Of those that do perforate the bowel, the vast majority occur in the duodenum[5-7]. There have been several case reports of intestinal perforation distal to the duodenum including the small intestines, cecum, right side of colon and sigmoid colon[8-15]. Although the majority of migrated stents pass spontaneously or can be retrieved using endoscopy and fluoroscopy, few of them can cause biliary peritonitis necessitating an emergency laparotomy. This report describes an unusual case of biliary stent migration where part of the stent remained in the common bile duct and the rest perforated the

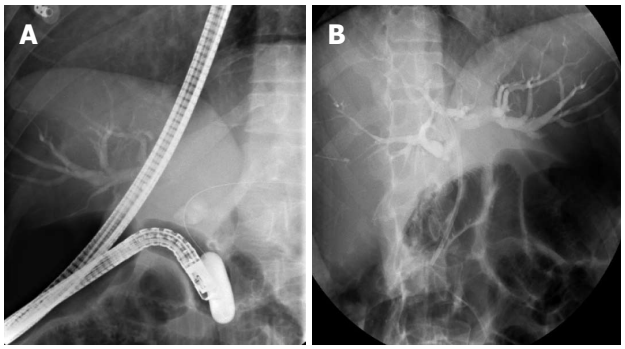

Figure 1 Endoscopic retrograde cholangiopancreatography which showed dilated common bile duct (A) and intra hepatic biliary radicles dilation (B) followed by insertion of 10 Fr × 10 cm endobiliary plastic stent.

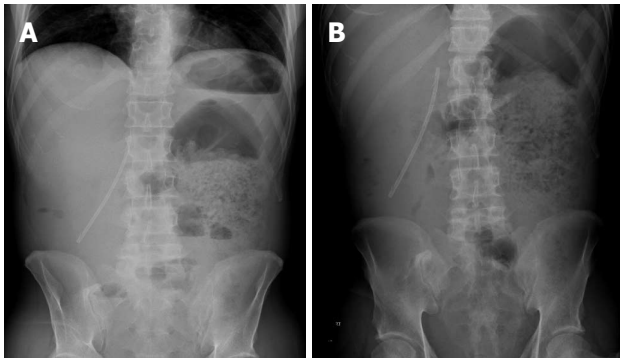

Figure 2 Abdominal X-rays showing an abnormal position of the biliary stent highly suspicious of distal migration with free air (A) and markedly dilated left side of colon and retained fecal material (B).

duodenum causing biliary peritonitis.

CASE REPORT

A 51-year-old male presented to the emergency department complaining of severe abdominal pain, constipation, vomiting and progressive jaundice over a period of 3 d. He underwent an abdominal ultrasound and computed tomography (CT) scan which showed distended gallbladder with no stones, dilated common bile duct up to 17.5 mm with a 9 mm stone in the distal common bile duct (CBD) and intra hepatic biliary radicles dilation. He underwent an ERCP in his primary hospital which failed due to an abnormal anatomy as reported. A second ERCP two weeks prior to his presentation was technically difficult, prolonged with a lot of manipulation and maneuvers to gain a biliary access. Sphinecterotomy was done and there was a suspicious distal biliary stricture for which controlled radial expansion balloon dilation up to 15 mm was done followed by insertion of 10 French, 10 cm long endobiliary plastic stent (Figure 1). At the time of presentation to our hospital, he was ill looking, in pain, deeply jaundiced. His temperature was 37.3 ℃, blood pressure 122/60 mmHg, and pulse 120 per minute. Abdominal examination showing distended abdomen with diffuse tenderness and rigidity, and sluggish bowel sounds. Cellular blood count showed leucocytosis 21.56 × 10^9 /L, Hb 14 g/dL, Platelets 368 × 10^9 /L. Liver panel showed total bilirubin 74.65 μmol/L, direct bilirubin 35 μmol/L, alkaline phosphatase 269 U/L, γ-glutamyl transpeptidase 417 U/L, alanine aminotransaminase 50 U/L, aspartate aminotransferase 73 U/L. Abdominal X-ray showed an abnormal position of the biliary stent highly suspicious of distal migration with markedly dilated left colon segment (Figure 2). Urgent abdominal CT-scan was done which confirmed the inferior migration of the biliary stent causing perforation of the second part of duodenum, with protrusion of the stent into the peritoneal cavity causing biliary peritonitis (Figure 3). He was covered with antibiotics and underwent an urgent laparotomy which showed the stent penetrating the second part of duodenum and draining bile into the peritoneal cavity causing biliary peritonitis (Figure 4). The perforation was closed and the closure was reinforced using an omental patch. Postoperatively, he did well and was discharged on the 12th postoperative day.

DISCUSSION

In 1980 Soehendra *et al*[16] introduced transpapillary biliary drainage using plastic biliary stent. Since then biliary stents are often used for the treatment of benign obstructive biliary disease. Biliary stents nevertheless causes serious complications and one of these is stent migration which occurs in up to 10% of patients[2-4]. This is more so in those with benign pathology without severe stenosis of the bile duct or papilla. Malignant strictures, larger diameter stents, and short stents are known to be associated with proximal biliary stent migration. Stent related factors such as the type of stent, length and caliber of the stent offer potential avenues to minimize the risk of migration. The presence of previous abdominal surgeries is an important factor for endoscopists to ascertain the location of a migrated stent. Fortunately, most of these stents can be retrieved using endoscopy and if the stent migrates to the intestines, then 43% pass spontaneously[4,5]. Arhan *et al*[5] in a review of 204 plastic biliary stents for benign biliary disease reported a migration rate of 13.4% with an equal proportion of stents found in the proximal and distal gastrointestinal tract. All of the migrated stents were retrieved without complication. This however is not the case always and occasionally biliary stents impact and perforate the intestines, usually in the fixed parts namely the duodenum and right side of the colon or in other fixed areas of the intestines because of adhesions due to a previous operation. There are also reports of biliary stents causing bowel perforation through bowel loops incarcerated in a hernial sac, in duodenal diverticula, in a colon diverticulum and also in healthy sigmoid colon[8-10,14,15].

Biliary stent migration is not unusual and may result in intramural or transmural intestinal perforation. The perforation can be retroperitoneal in duodenal perforation causing bilioma or the perforation can be intra-

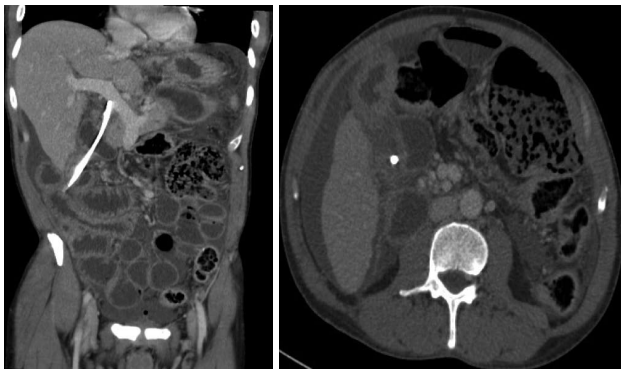

Figure 3 Computed tomography-scan of the abdomen which confirmed the inferior migration of the biliary stent causing perforation of the second part of duodenum, with protrution of the stent into the peritoneal cavity causing biliary peritonitis.

peritoneal leading to biliary peritonitis[13,17]. Our case is unique as the stent was found partly in the biliary duct and the rest perforated the duodenum causing bile leak with total bile diversion into the peritoneal cavity and biliary peritonitis. In these patients there are signs of peritonitis and radiological images will show the stent outside the intestinal wall. Ang *et al*[18] described a case of duodenocolic fistula caused by a stent and Rosés *et al*[17] described the case of a plastic stent perforating the duodenal wall causing a retroperitoneal duodenal perforation and bilioma. Figueiras *et al*[19] reported a colocutaneous fistula secondary to the migration of a biliary stent.

The majority of migrating biliary stents pass spontaneously but whenever a perforation is suspected, operative extraction is the treatment of choice. There is a report stressing the successful endoscopic extraction of the migrating stent and clip placement in the duodenal perforation[17]. This was however in a patient with a biliary stent causing a localized retroperitoneal duodenal perforation and bilioma. Others have reported the successful percutaneous extraction of migrating biliary stents[20]. In our case, the perforation was in the peritoneal cavity and part of the stent was still in the biliary ducts causing biliary diversion into the peritoneal cavity and although percutaneous retrieval of the stent was possible, the fact that the patient was already having biliary peritonitis made operative extraction and closure of duodenal perforation the appropriate choice.

In conclusion, biliary stent migration complicated by duodenal perforation is rare and should be included in the differential diagnosis of those presenting with abdominal pain after ERCP with stent placement and physicians caring for these patients should be aware of such complication. Radiologically, it is possible to locate the site of stent migration and perforation and in the presence of peritonitis, surgery is the treatment of choice. To reduce the chance of stent migration, endoscopists should assess for the size and shape of the stent in each patient. A straight biliary stent may migrate since there is nothing to hold it in place, even though there are side flaps. Inappropriately long stent may exert pressure on the duodenal wall causing tissue necrosis and perforation. Curved (Amesterdam) stent or a double pigtail biliary stent may be associated with less migration and perforation.

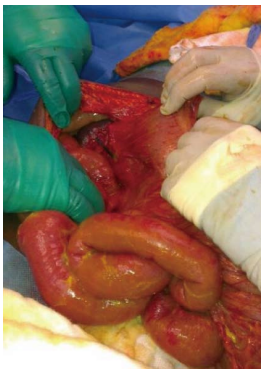

Figure 4 Intraoperative photograph showing the stent perforating the duodenum and protruding into the peritoneal cavity.

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

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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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