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REVIEW

Update on endoscopic management of gastric outlet obstruction in children

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Abstract

Endoscopic balloon dilatation (EBD) and surgical intervention are two most common and effective treatments for gastric outlet obstruction. Correction of gastric outlet obstruction without the need for surgery is an issue that has been tried to be resolved in these decades; this management has developed with EBD, advanced treatments like local steroid injection, electrocauterization, and stent have been added recently. The most common causes of pediatric gastric outlet obstruction are idiopathic hypertrophic pyloric stenosis, peptic ulcer disease followed by the ingestion of caustic substances, stenosis secondary to surgical anastomosis; antral web, duplication cyst, ectopic pancreas, and other rare conditions. A complete clinical, radiological and endoscopic evaluation of the patient is required to make the diagnosis, with complimentary histopathologic studies. EBD are used in exceptional cases, some with advantages over surgical intervention depending on each patient in particular and on the characteristics and etiology of the gastric outlet obstruction. Local steroid injection and electrocauterization can augment the effect of EBD. The future of endoscopic treatment seems to be aimed at the use of endoscopic electrocauterization and balloon dilatations.

Key words: Gastric outlet obstruction; Endoscopic balloon dilatation; Electrocauterization; Steroid injection; Children

Core tip: Correction of gastric outlet obstruction without the need for surgery is an issue that has been tried to be resolved in these decades; this management has evolved with the development of pneumatic dilators and, more recently, local steroid injection and electrocauterization have been added. Endoscopic balloon dilatation (EBD) are used in exceptional cases, some with advantages over surgical intervention depending on each patient in particular and on the characteristics and etiology of the gastric outlet obstruction. Local steroid injection and electrocauterization can augment the effect of EBD.

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INTRODUCTION

In the last few decades, upper gastrointestinal endoscopy is a technique widely employed for diagnostic and therapeutic purposes for evaluation of esophageal, gastric or duodenal diseases. Upper gastrointestinal endoscopy has become the common complementary test for investigation of gastric diseases due to its accessibility and safety assures extensive clinical utilization in patients with gastric or duodenal diseases. Recent technological advances in endoscopic imaging and tissue analysis obtained from the stomach aid to identify the characterization of diseases such as inflammation, infection and neoplasia. Recent technological advances have increased the capability of endoscopy in treating gastrointestinal diseases, including those affecting the stomach.

Diseases affecting the stomach have been described and eventually treated by endoscopy in routine clinical practice. Using endoscopy to elucidate gastric outlet obstruction (GOO) in children has been still a field of intensive and challenging research. This review provides an update on the role of endoscopy in the management of GOO, highlights the latest advances in the endoscopic management of GOO, and focuses on the efficacy of endoscopic balloon dilatation (EBD) in the pediatric population. We also point out recent evidence regarding the utility of magnifying endoscopy in the management of GOO.

Data search

The searches were limited to articles published in English as well as clinical articles or case studies to identify objective articles related to GOO from January 1975 to June 2016. All articles considered eligible were evaluated, and finally selected on the basis of research and case series. The articles of gastric volvulus were searched, but this entity is excluded from this review, due to gastric volvulus is specific complex disease entity with varied causes (congenital, idiopathic, or acquired), and the gold standard treatment of pediatric gastric volvulus remains surgical intervention.

ETIOLOGY

GOO is an obstruction in the antrum, pylorus or bulbar duodenum. Unlike adult patients, most of the pediatric patients with GOO have benign disease. Peptic ulcer disease and corrosive ingestion are the leading causes of benign outlet obstruction in adults[1]; while idiopathic hypertrophic pyloric stenosis (IHPS) and peptic ulcer disease (PUD) remains the two most common cause of GOO in children[2-4]. Table 1 shows the etiology of GOO in children. IHPS are the most common cause of GOO in children. The typical presentation is increasing vomiting that becomes projectile between 2 and 8 wk in age. Gastric retention after prolonged obstruction contributes to gastric atony, while most cases are caused by antral, pyloric or duodenal ulceration. Scarring and tissue remodeling may cause GOO in chronic PUD. A significant decline of the incidence of PUD due to the discovery of *Helicobacter pylori* (*H. pylori*) and proton pump inhibitors (PPI)[5,6]. *H. pylori* infection participated a less significant role in children with GOO, compared to adults[3].

Table 1 Etiology of gastric outlet obstruction in children

Idiopathic hypertrophic pyloric stenosis
Peptic ulcer disease
Caustic injury
Congenital causes
Gastric autral web
Duplication cyst
Ectopic pancreas
Aunular panaeas
Gastric volvulus
Inflammatory causes
Cholecystitis
Pancreatitis
Eosinophilic gastritis
Crohn's disease
Tuberculosis
NSAID induced stricture
Iatrogenic (secondary to surgery)
Post-anastomosis stricture
Post-pylorotomy
Post-esophagectomy
Post-vagotomy
Polyps/tumors
Hyperplastic polyp
Inflammatory polyp
Adenomyoma
Inflammatory myofibroblastoma
Lymphoma
Other causes
Bezoars (lactobezoar, trichobezoar)
Cytomegalovirus infection
Late onset primary gastric outlet obstruction
Idiopathic gastric outlet obstruction
Idiopathic or acquired gastric volvulus
Foveolar cell hyperplasia

NSAID: Nonsteroidal Anti-inflammatory Drug.

Caustic ingestion remains a major social and medical issue in children, especially for infants and young children. Case series of corrosive injury related gastric outlet obstruction have still been reported in these two decades[7-9]. GOO is a significant complication of corrosive ingestion[8]. Caustic ingestion (alkali or acid) can cause GOO as a result of antral/pyloric scarring. Other rare causes are gastric antral web[10], gastric duplication[11], ectopic pancreas[12], gastric volvulus[3], gastric polyps[3], idiopathic gastric outlet obstruction[13], foveolar cell hyperplasia[14], and bezoars[15,16]. Antral web, known as antral mucosal diaphragm or prepyloric web,

is a rare etiology in pediatric GOO. Histologically the web is composed of normal, non-inflammed mucosal and submucosal gastric mural layers. Gastric duplication cyst are the least common of the alimentary duplications, they usually presented before 1 year of age with symptoms of obstruction, pain, bleeding or ulceration[11]. Heterotopic pancreas is generally an asymptomatic lesion and is a rare cause of GOO. Gastric volvulus is characterized by a rotation of the stomach of more than 180° along its short or long axis causing variable extents of GOO. Acute gastric volvulus may create a closed-loop obstruction leading to incarceration and strangulation. In general, emergency surgery remains the standard treatment for acute gastric volvulus. Foveolar cell hyperplasia is a rare disease entity, described as a possible cause of for long-lasting GOO in patients with IHPS, it requires the excision to resolve the obstruction. Gastric polyps are often hyperplastic and asymptomatic. Gastric polyps are usually diagnosed at endoscopy incidentally. Lactobezoar is a condensed mass of undigested milk concretions to be found within the gastrointestinal tract[14]. Lactobezoar is often found in infants, it can precipitate GOO, resulting in medical or surgical conditions. The trichobezoar is another rare cause of obstruction of the gastrointestinal tract, and it is usually presented as GOO[15].

Inflammatory causes like Crohn's disease and tuberculosis have been reported in adult patients with pyoric obstruction[17,18], these two disease entities are relatively rarely reported in pediatric patients. Isolated gastroduodenal Crohn's disease is rare, occurring in fewer than 5% of patients. A continuity that involves the antrum, pylorus, and proximal duodenum have been reported in about 60% of patients[17]. In tuberculosis, involvement of stomach or duodenum occurs in 0.3% to 2.3% of patients, and 61% of patients with gastroduodenal tuberculosis present as GOO[18]. Gastric polyps or neoplasms are rare in children but should always be considered as an etiology of GOO in children, especially in older patients[19].

EVALUATION

Clinical manifestations

The usual presentations were nausea, vomiting, epigastric pain, early satiety, abdominal distention, abdominal mass, visible peristalsis, weight loss and electrolyte imbalances. Epigastric pain, nausea and vomiting, abdominal distention, early satiety and weight loss are the most common presenting symptoms of GOO[20]. The onset of symptoms varies based on the etiology, symptoms usually occur rapidly with gastric volvulus, corrosive injury, food impaction (bezoar), prolapse of a large gastric polyp[3,8,15]. Other causes are inclined to follow a more slothful course. Malignant cause usually has a shorter duration of symptoms compared with benign causes. Patients with benign causes commonly presented with early satiety (53%) and bloating (50%) whereas in the patients with malignant causes presented more commonly with vomiting, pain, and weight loss[20].

Persistent succussion splash (a "splash" reflective of retained gastric material) detected by auscultation of for more than four after meals, suggesting GOO with a sensitivity of 50%[21].

Investigations

GOO patients with repeated vomiting may have electrolyte imbalances with hypokalemia or a hypochloremic metabolic alkalosis. Anemia, elevated inflammatory markers (C-reactive protein, erythrocyte sedimentation rate), and abnormal biochemical tests in hepatobiliary function, pancreatic function, or renal function may reflect the underlying disease. Elevation of serum gastrin concentration as a result of distention-induced gastrin release may occur in GOO patients and this condition can be confused with Zollinger-Ellison syndrome.

Plain radiographs may demonstrate an enlarged stomach. Small bowel may not be visualized because of air paucity. Calcified gall stone and/or pancreatic calcification may be revealed. Diagnosis was easy clinically and confirmed by barium studies and/or upper gastrointestinal endoscopy. Contrast studies with barium or water soluble contrast aid in providing diagnostic clues to the underlying diseases. Failure of contrast passing into the small bowel is highly suggestive of complete GOO. Barium studies are helpful in delineating the site of obstruction as well its extent. Adequate gastric decompression should be initiated before performing barium or water soluble contrast to reduce the risk of aspiration. Computed tomography (CT) scan may disclose additional anatomical details, specially the wall thickness in the stomach, pylorus and duodenum, biliary lesions, pancreatic abnormalities or lesions, and enlarged lymph nodes not visualized on regular imaging studies[21].

Endoscopy is often required to ascertain the diagnosis of GOO and identify a specific etiology in company with a therapeutic assistance. Patients should fast for at least four hours before the endoscopic procedure. Nasogastric tube suction is recommended before endoscopic procedure to reduce the risk of aspiration. Endoscopic biopsy provides histological diagnosis in specific diseases and aid in confirming or excluding malignancy.

MANAGEMENT

All patients with symptoms of persistent GOO need hospitalization. Intravenous volume resuscitation with normal saline; replacement of electrolytes; and measurements of electrolytes and arterial pH are the principles of fluid and electrolyte resuscitation for GOO[21]. Hypokalemia and metabolic alkalosis should be looked for and treated.

Gastric decompression by nasogastric tube should be done at admission, this procedure is useful in relieving pain and discomfort of distention in patients who have edema and spasm due to active ulceration. Nasogastric

decompensation also helps to clear the stomach for endoscopic procedures and reduce gastric capacity which is essential for endoscopic examination and further surgery or endoscopic treatment. Administration of antacid (H2-receptor antagonists or proton pump inhibitors) is usually required.

ENDOSCOPIC INTERVENTION

A definite treatment is required if the GOO is persistent, secondary to fibrotic scarring, or an irreversible condition. In place of traditional surgical intervention or rigid esophagoscopy, therapeutic fibreoptic endoscopy is concluded to be an effective and safe treatment modality in pediatric patients[22]. Endoscopic treatment offered depended on the cause of GOO. Unless the etiology of GOO is evident from the antecedent history, such as PUD, caustic ingestion, or prior surgery, one must exclude rare diseases like Crohn disease, tuberculosis or malignancy by endoscopy and biopsy.

EBD

The through-the-scope (TTS) balloon catheter with variable diameter balloons are available from 6 mm to 20 mm which are inflated with a hydrostatic device attached to a pressure gauge. A radio-opaque wire can guide the stricture segment and augment the efficacy of the EBD in difficult strictures. A single and short stricture provides the best result with EBD; hence patients should be evaluated with proper imaging studies (barium studies/CT scan) before EBD procedure.

Although the devices and techniques used in the EBD procedure for pediatric patients are basically identical to those procedures in adult patients, several anatomic limitations must be addressed. Endoscopic procedure is difficult in newborns due to remarkable anatomic limitations. The length and diameter of esophagus is 8-10 cm, and around 5 mm in neonates, causing compression of trachea during endoscopic intervention. TTS balloon dilations are possibly performed in toddlers and children, but this technique is limited in neonates or small infants as there are no balloon catheters that fit through a 2-mm channel. Balloon dilatation can be performed in neonates or infants who cannot tolerate a standard-size endoscopy by using biliary dilation balloons in size of 4-10 mm and length of 2-8 cm. These balloons can be applied endoscopically with 0.035-inch guidewires. Balloon sizes are usually increased by 2 mm for subsequent EBD sessions. The balloon catheter upon removal may reveal blood clots or bloods if an effective dilatation had been reached.

Experiences of EBD in recent decades

Most reports regarding EBD management of GOO were found in adult population, the technique of EBD in GOO is less performed in pediatric population. A series of case studies observed that surgical treatment can give definitive therapy in PUD related GOO without *H. pylori* infection[2]. Until the advent of EBD, surgery was the only treatment for these patients. Vagotomy with antrectomy or pyloroplasty was performed in PUD patients with GOO who were refractory to medical therapy[4].

Many evidences prove that EBD is an effective alternative in the management of GOO[17,23-39]. The EBD management combined endoscopic placement of guidewire with fluoroscopically-guided balloon dilation to treat GOO. A study of EBD of upper digestive tract stricture in 23 adult patients had gastric or pyloric strictures were evaluated. Percent of 92 were successfully dilated, with a complication rate of 3%[23]. EBD has become the first-line therapy in most of the patients with benign causes of GOO[24]. Subsequently, a number of reports appeared highlighting the safety and efficacy of the procedure[24,25,27-36].

Compared to adult patients, endoscopic management in pediatric patients is limited by their anatomical limitation with difficulty in passing endoscopy through pharyngeal inlet and difficulty to perform EBD because of smaller size of pylorus and duodenal bulb, especially in neonates or infants. Besides, a relatively higher risk of complications was noted in pediatric population. In pediatric patients, the technique of EBD treatment in esophageal stricture is relatively more mature than EBD treatment in pyloric stricture. We reviewed the endoscopic management both in adult and pediatric patients with GOO, and further point to recent evidence regarding the utility of magnifying endoscopic treatment in the management of pediatric diseases related GOO.

PUD

Fibrotic scarring in PUD may cause irreversible GOO which requires intervention. Traditionally, surgery has been the standard mode of treatment for PUD-related GOO. In adult series of patients with PUD-related GOO, 80%-90% underwent surgery[40], about 60% received surgery in the first hospitalization and 20% in the subsequent hospitalizations[41]. Recently, many case series studies indicate that balloon dilatation is an effective alternative to surgery in adult patients with PUD-related GOO[28-35]. A major surgery and associated morbidity can be obviated with the development of TTS EBD. EBD has emerged as an effective alternative to surgery in selected groups of patients. EBD has been shown to be effective in ulcer related GOO. The performance of EBD is preferred with balloon catheters of incremental diameter gradually to achieve the end-point of 15 mm. Fluoroscopic study is not routinely used by most endoscopists although fluoroscopic evaluation it is recommended for EBD. Previous experiences indicated that the requirement of EBD varied from once a week to once in three weeks in PUD-related GOO. EBD procedure related complications are uncommon, massive bleeding is rare, perforation occurs more frequent with balloon sizes larger than 15 mm. A Review of cumulative experience in 30 patients who underwent

EBD for peptic ulcer-induced GOO and had follow-up of a mean of 15 mo (range 4-28 mo), 6-18-mm (median 15-mm) balloons were inflated a median of 2 times (range 1-4 times) for a median of 60 s (range 30-180), 20 (67%) patients had one treatment and 10 (33%) had multiple treatments, 24 (80%) patients achieved sustained symptom relief. The authors concluded that EBD is safe and effective for most patients with ulcer-induced GOO[16].

In view of the confounding factors of *H. pylori* eradication, chronic usage of NSAID, use of PPI in patients with PUD-related GOO, immediate response is prominent, but with variable long-term results. EBD must be combined with eradication of *H. pylori*. Studies specify that the eradication of *H. pylori* contributed to a good long-term response in 70%-80% of patients during a follow-up period of 9-98 mo[29,32,34,37]. In an adult series, 25 patients with proven GOO secondary to PUD were managed with EBD using TTS balloons, 80 % of patients remained asymptomatic (follow-up: median 9 mo, range 2-24 mo)[39].

Literatures regarding to the use of EBD in pediatric GOO patients are limited in recent decades. Chan *et al*[42] reported 3 children (ages 2, 4, and 8 years) suffering from peptic pyloric stenosis with EBD followed by H2-receptor antagonist therapy. There were no complications due to the procedures, and no recurrences of symptoms over a follow-up of 5-30 mo (mean, 17 mo). The authors suggest that EBD is an option for the initial nonoperative treatment of pediatric peptic pyloric stenosis.

IHPS

IHPS is typically treated with surgical pyloromyotomy. If the child is well-hydrated with normal electrolytes, and if surgeons with expertise in the procedure are available, surgery usually takes place on the day of diagnosis. EBD had been used to treat IHPS in recent decades. EBD was considered as a safe procedure for treating IHPS infants and was recommend to be as an initial approach before pyloroplasty in such presentations[43-45]. Recurrent pyloric stenosis is rare in IHPS patients after balloon dilatation[43]. However, because balloon dilatation does not consistently destroy the muscular ring[46], EBD is preferably reserved for patients in whom with a significant risk for general anesthesia or in whom with difficulty for surgical intervention.

Caustic injury

GOO is one of the most common gastric complications of caustic agent ingestion that may require surgical treatment[7-9]. Sodium hydroxide and potassium hydroxide, and hydrochloric acid were the common ingested caustic agents for GOO[7].

The severity of mucosal injury at the antrum and pylorus decided the variety of surgical treatment. Moderate mucosal injury (superficial ulcerations with intact mucosa) may induce partial pyloric obstruction; severe mucosal injury (deep ulcerations, hemorrhagic erosions, eschar formation) may cause complete pyloric obstruction. For adult patients with caustic-induced GOO, surgery had been the only option available as well[47]. The standard treatment of pediatric caustic-induced GOO is surgery, gastrojejunostomy provides good long-term results with minimal morbidity particularly in patients without severe gastric injury[9]. An early surgical intervention has decreased the morbidity and mortality[7].

Adult experiences specify more difficulty of using EBD to dilate caustic-induced GOO than PUD-related GOO, besides; those patients with caustic-induced GOO have more recurrences and requiring more sessions of EBD. The mean number of sessions (range, 2-13) for caustic GOO is significantly more than the number of sessions for peptic GOO which required only 1-3 sessions[32].

Successful results of a caustic stricture by EBD management offers guidelines for the use of this procedure[37,48]. Kochhar *et al*[37] reviewed 41 patients with EBD management, 39 (95.1%) underwent successful responses after repeated dilations with a mean (SD) of 5.8 (2.6) sessions (range, 2-13) to reach the end point of 15 mm. The mean (SD) size of the initial dilatation was 8.2 (0.6) mm (range, 8-10). Finally, 2 patients received surgery including one with perforation and the other with intractable pain every time he received EBD. Other complications included minor self-limiting pain (n = 8) or bleeding (n = 7). The authors concluded that EBD is a safe, effective, and long-term alternative to surgery for caustic GOO[37]. Another adult report (n = 31) of caustic GOO found all patients successfully respond to repeated dilations to reach the end point of 15 mm with a range of 3-18 (median, 9) sessions of dilations during a mean period of 7 wk (range, 1.5-16) of follow-up[49].

There are only few reports of EBD management in pediatric cases with caustic injury related GOO. A pediatric study enrolled 8 cases caustic ingestion indicated that caustic injury related GOO could be successfully treated through EBD in suitable patients, surgery can be avoided[50].

A pediatric case series of 6 children (mean age was 2.9 years, range 1.5-3 years) with caustic injury related GOO (2 ingested acid corrosives, 4 ingested alkali corrosives). Balloon dilatation of the pylorus was performed in 1 patient successfully, the others received pyloroplasty (3 patients), and Billroth I procedures (2 patients). The authors recommended early definitive surgical intervention in cases with severe pyolric stricture[51].

Gastric antral web

Treatment of antral web usually consisted of incision of the web and construction of a patulous gastric outlet by surgery, and most patients remained asymptomatic after operation[10]. Endoscopic treatment had been

used to treat antral web, endoscopic diathermy and EBD successfully resolved the pyloric web[10,21,51]. Lu *et al*[52] successfully treated antral web with EBD in an young infant, the EBD was attempted sequentially using different sized water-inflated balloons (8, 10 and 12 mm). The stenosis was dilated with balloons incrementally to 12 mm diameter.

Post-operative GOO

EBD resolved the in nearly 70% of GOO patients with postvagotomy gastric outlet stenosis[30]. Lanuti *et al*[53] evaluated the role of pyloromyotomy and management with endoscopic pyloric dilatation in the patients with Post-esophagectomy GOO, the results showed that post-operative GOO could be effectively managed with endoscopic pyloric dilatation, the authors concluded that routine pyloromyotomy for the prevention of post-esophagectomy GOO may be unwarranted. Swanson *et al*[54] affirmed that EBD could obviate the requirement of pyloroplasty at esophagectomy.

The application of EBD as treatment of post-operative GOO was described in an 11-year-old boy with surgical injury to the vagus and two infants after insufficient pyloromyotomy, EBD achieved successful results and was considered a good alternative to surgery in these conditions[55].

EBD has successfully dilated the anastomotic strictures following gastric bypass surgery or vertical band gastroplasty in the patients with morbid obesity[56].

Late-onset primary GOO

Late-onset primary GOO in childhood is a rare condition. A series of 8 pediatric cases received succeeded in treating late-onset primary GOO by using EBD, there is no recurrence for one year[57]. Another experience successfully used EBD to treat 5 pediatric cases with late-onset pyloric stenosis, 3 cases need repeated EBD[58].

Nonsteroidal Anti-inflammatory Drug related GOO

NSAIDs are among the most frequently prescribed medications. Although NSAID related GOO is a rare condition, chronic NSAID consumption could cause GOO[58-60]. Duodenal web-like strictures associated with long-term NSAID use has been described[61].

The literature about the role of EBD management in NSAID-induced GOO is still scarce. A case series (n = 10) with endoscopic management for NSAID-induced pyloroduodenal obstruction found that duodenum was the most common site of involvement (50%), followed by both pylorus and duodenum (40%) and pylorus (10%). The strictures in a majority of patients were web-like, 90% of cases were successfully treated with repeated EBD. Among these successful cases, a 15-mm balloon diameter was achieved after a mean (SD) of 2 (1.6) sessions, and a mean (SD) of 5.3 (2.7) sessions was required to during a mean period of 4.5 mo (range, 2-15). There were no complications or mortality. The literature in relation to EBD management of pediatric NSAID related GOO is scant, EBD was used to treat NSAID related GOO successfully in a child[62].

Inflammatory conditions

A definite treatment for the antecedent disease is crucial and may avert the need for EBD or surgery in inflammatory diseases (eosinophilic gastritis, Crohn's disease, *etc.*) or infectious disease like tuberculosis related GOO, Crohn's disease or tuberculosis related GOO may respond to balloon dilatation, however, multiple recurrences usually occurs if the underlying disease is not effectively treated. Gastroduodenal Crohn's disease and tuberculosis had been successfully treated with EBD procedure[31,63].

Complications of EBD

In general, EBD is relatively a safe procedure with infrequent complications. Perforation and bleeding are rarely reported for balloon dilatation smaller than 15 mm. Two of 30 patients (6.7%) dilated to 18 mm suffered perforation[6]. Both recovered uneventfully after surgery. A large case series of 23 patients with PUD related stenosis encountered only one perforation with EBD management[35]. Another large series of 54 cases by Lau *et al*[28] reported 4 perforations with EBD management, 2 of 16 patients who underwent EBD with a 16-mm diameter balloon encountered perforation while 2 of 3 patient with 20-mm diameter balloon had perforation. It therefore appears that EBD management with balloon diameter greater than 15 mm is more prone to be complicated with perforation.

Pain during EBD is not uncommon, but is often self-limited. A recent study observed that 19.5% of patients with caustic GOO had self-limiting pain during EBD[37]. The complications with EBD procedure observed in a case series (n = 31) with caustic GOO included self-limiting pain (n = 10), bleeding at the time of the procedure (n = 9), and one perforation (3.2%) who required surgery[41]. Kochhar *et al*[37] reviewed 41 corrosive injury patients with GOO could be successfully taken for EBD, and self-limiting pain (n = 8) or bleeding (n = 7), perforation (n =1) were noted among these patients.

Outcome of EBD intervention

A good result can be anticipated in the majority of patients with PUD- and corrosive-related GOO after EBD intervention[32]. EBD for benign GOO in adults is a generally accepted method of treatment. Previous literatures advocate that more than 75% of patients with PUD-related GOO respond to EBD and the long-term use of proton pump inhibitor is needed to obviate recurrences after *H. pylori* eradication. The results of EBD for PUD-related GOO is variable because not all studies consider the confounding factors, such as *H. pylori* infection, use of NSAIDs, practice and compliance of proton pump inhibitor. Immediate relief of obstruction with EBD has been commonly found in the majority of patients, but achieved varied long-term response from

16%[36] to 100%[32]. The eradication of *H. pylori* have reported a good long-term response in 70%-80% of patients over a period of 9-98 mo[6,29,30,35,39].

Lam *et al*[38] compared the response rates of EBD between 14 patients with positive *H. pylori* infection and 11 *H. pylori*-negative, EBD management was responsive in 78.6% of *H. pylori*-positive, while only 45.4% in *H. pylori* negative patients. Eradication of *H. pylori* combined with EBD had a lower rate of ulcer complications such as bleeding or obstruction compared to *H. pylori* negative group (21% *vs* 55%) over a follow-up of 24 mo. A case series (n = 11) indicated that eradication of *H. pylori* with 1-3 sessions of EBD successfully resolved obstruction in all of the patients[32]. A study by Cherian *et al*[34] indicated comparable results in long-term follow-up of their Peptic-GOO patients with EBD and drug therapy.

Patients with young age, continuous use of NSAIDs, or long-lasting symptoms requiring repeated EBD had unfavorable outcomes with the need for multiple dilations or surgery for GOO[40]. DiSario *et al*[6] observed that a long-length stricture was associated with poor outcome for GOO. The majority of studies did not describe the duration of proton pump inhibitors making comparisons incomparable between studies.

Need of more than 2 sessions of dilations is a risk factor for EBD failure and requirement for surgery. Rapid recurrence of symptoms is found in patients with malignant GOO. As many benign GOO patients had underlying PUD, eradication of *H. pylori* at the time of balloon dilation will guarantee higher long-term successful rates[25].

An adult study of 45 patients with pyloric stenos did a follow-up of mean 32 mo (range, 4-126) indicated that immediate response rate of the EBD treatment was observed in 43 cases (95.6%), and clinical remission was observed in 38 cases (84.4%)[64]. Over a period of 30 mo, no recurrence was noted in 55.8% of patients with clinical remission, relapse was observed in 39.5% of patients over a mean period of 22.9 mo. Three patients (6.7%) had complications (one bleeding and 2 perforations). Thirteen patients (29%) underwent surgery. *H. pylori* was positive in 97.7% of the patients, and 78.4% of them had successful eradication of *H. pylori*. This study further found that unsuccessful eradication of *H. pylori* and smoking were two risk factors for the recurrence of pyloric stenosis[64].

EBD can make surgery unnecessary for postoperative GOO and later for peptic, corrosive and postvagotomy gastric outlet stenosis in nearly 70% of patients with benign GOO[30]. Kochhar *et al*[37] performed EBD in 31 patients with caustic-induced gastric injury, 30 (96.8%) did not have recurrence of stenosis over a mean follow-up of 21 mo (range, 3-72).

There is less experience of evaluating outcome of EBD for GOO in children. A pediatric case series (n = 14) evaluated the effect of endoscopic balloon dilatation and surgical treatment in children's pyloric stricture, surgical correction is still the most common treatment in the majority of cases of pyloric stenosis[50]. In this series, the authors stated that benign GOO can be effectively and successfully treated through EBD in suitable patients, surgery can be avoided in patients with successful pyloric balloon dilatation[50]. There are two long-term studies on EBD management for children with benign pyloric stenosis, response rates were varied between 16% and 80%[6,36].

Advanced techniques augmenting EBD

A number of practitioners have used supplementary techniques to augment the efficacy of EBD. EBD could be augmented with local (intralesional) steroid injections and endoscopic incision with electrocauterization.

Intralesional steroid injections

Intralesional steroid injections augmented the effect of balloon dilation had been reported in patients with caustic GOO[65,66], the GOO responded with 1-2 sessions of steroid injections. Intralesional steroid injections have been illustrated to inhibit stricture formation by impeding the synthesis of collagen, chronic scarring, and fibrosis[66]. Ketchum *et al*[67] specify that steroid (Triamcinolone) offers cross linking of collagen leading to scar contracture; the contracture will not occur if stretch of scar occurs with steroid injection. Steroids may diminish scar formation by reduction of fibrotic healing that appears after balloon dilation[68]. Efficacy of steroids augmenting EBD in GOO has been also demonstrated in the other two studies by Kochhar *et al*[69] and Lee *et al*[70] Successfully cases treated with steroids and balloon dilations included three patients with caustic GOO, one peptic, and another post-pyloroplasty.

Endoscopic incision

EBD with additional endoscopic incision achieved successful results in caustic-induced GOO. Boron *et al*[71] successfully used electrocauterization endoscopically to incise the stenotic segment with standard sphincterotomy in a patient with refractory pyloric stenosis. Hagiwara *et al*[72] also successfully resolved the stenosis by using combined EBD with electrosurgical incisions in the patients with refractory post-operative pyloric stenosis. I have also successfully used this technique in a young infant with refractory pyloric stenosis secondary to surgical excision of gastric antral web, a satisfactory result after 2 sessions of combined endoscopic electrocauterization and balloon dilatation was achieved[73].

END POINT OF EBD

No consensus has been reached on the issue of end point of EBD for GOO, especially in pediatric cases. Most experts[27,29,32-73] have used 15 mm balloons as the end point for GOO while some of them have only dilated to 10-12 mm[30,35]. Balloons of 16, 18 and 20 mm are uncommonly used[28,30,35]. The size of balloon catheters for adult GOO was recommended to be used with step-

wise manner, from 10-12mm to 12-15 mm[31,72] The EBD should be more cautiously performed on pediatric patients than on adult ones if with peptic, caustic or post-operative causes induced GOO. I usually dilate with step-wise manner of catheter balloons inflated with the use of a pressure gauge system for 60-120 s in pediatric patients. Balloon catheter sizes were increased by 2 mm for subsequent EBD sessions, from 6-8 mm to 10-12 mm in infants and toddlers, from 8-10 mm to 10-12 mm in younger children, and from 10-12 mm to 12-15 mm subsequently in older children.

OTHER INTERVENTIONS

Gastric peroral endoscopic pyloromyotomy

Gastric peroral endoscopic pyloromyotomy (G-POEM) is performed with similar techniques to esophageal per-oral endoscopic myotomy. Replacing traditional laparotomy and laparoscopic approaches, G-POEM provides a natural orifice procedure to incise and divide the pyloric sphincter.

Surgical pyloromyotomy has shown to be effective in reducing pyloric stenosis or gastroparesis symptoms, but it requires advanced skills for laparoscopic suturing and carries a risk of leakage and potential further narrowing of gastric outlet. Therefore, G-POEM as a less invasive treatment, is used to deal with gastroparesis recently.

Although laparoscopic pyloromyotomy is still considered as a simple, and safe treatment for pediatric IHPS, G-POEM technique is similarly simple, safe, but less invasiveness, and this procedure can be performed at outpatient department[74]. A case series of 10 IHPS infants (7 boys, 3 girls; aged 3-7 wk) underwent endoscopic pyloromyotomy with an electrosurgical needle knife to incise the pylorus from antral to duodenal side, most (90%) of the patients were done at outpatient department. All patients did not encounter any complications and tolerated regular feedings as they recovered from sedation. All of them were discharged on the same day of endoscopic procedure and doing well during follow-up (range, 6 mo-2 years)[74].

A growing body of evidence suggests that G-POEM may be a salvage therapy improves gastric emptying in patients with different types of refractory gastroparesis. Those patients with refractory gastroparesis may respond to endoscopic pyloromyotomy. An adult case series of G-POEM using selective circular myotomy for patients with refractory gastroparesis symptoms due to varied cause (post-infectious, post-surgical, or idiopathic) were successfully performed without any complications. All cases experienced obvious success after G-POEM[75,76].

Endoscopic stent

Endoscopic stent was usually used to manage malignant GOO. As gastric or duodenal malignancy is very rare in children, there is no pediatric literature about the use of endoscopic stent for malignant GOO. Palliation of the obstructive symptoms is the primary aim of treatment in the cancer related GOO. Self-expandable metal stents have emerged as a promising treatment option[77]. Topazian *et al*[78] firstly reported endoscopic treatment of GOO with endoluminal self-expanding metallic stents in 1992. In recent two decades, experiences of the use of endoscopic stents have gradually increased. Several studies have reported that patients who are having high risk for long-term GOO should undergo endoscopic stents, given its safety, minimal invasiveness, and cost-effectiveness[79,80].

Endoscopic mucosal resection for gastric polyps

Although most pediatric gastric polyps are considered benign lesions, removal of symptomatic polyps are necessary for symptom relief, histological diagnosis, and avoidance of malignant potential. A standard-size polypectomy snare can be accessed through a 2.8-mm channel endoscopically to do polypectomy in the majority of children. Pontone *et al*[81] did the endoscopic mucosal resection in the patients with multiple large antral hyperplastic polyps causing GOO with the use of a submucosal cushion under the lesion allowing a steady positioning of the polyp in the gastric lumen without further infiltration. The authors concluded that endoscopic mucosal resection provides tissue for histopathology to diagnose the nature of the polyp and achieves symptomatic resolution.

Endoscopic fragmentation for bezoars

Surgery is the treatment of choice for tricobezoar. However, endoscopic treatments have been described, such as endoscopic fragmentation, extracorporeal lithotripsy and laparoscopic extraction[16].

SURGERY

Benign GOO may, however, still require operative intervention when non-operative treatment fails[82]. Peptic ulcer-induced gastric outlet obstruction can be treated safely with EBD. About 65% of patients have sustained symptom relief, but many require more than one dilation session. Outcomes may be improved with effective ulcer therapy with acid reduction and eradication of *H. pylori*[82]. Compared to endoscopic access, surgical approach is more associated with morbidity and mortality, surgery is considered to be reserved for failure of endoscopic treatment[83]. Surgeries for peptic GOO include antrectomy with vagotomy, pyloroplasty with vagotomy, gastrojejunostomy with truncal vagotomy, and pyloroplasty. In peptic GOO gastrojejunostomy can be combined with truncal vagotomy and antrectomy, gastrojejunostomy (Billroth II reconstruction) was considered in peptic GOO with altered anatomy. Laparoscopic gastrojejunostomy become a favorable modality of surgery in peptic GOO for its shorter hospitalization due to quick postoperative recovery compared with

conventional laparotomy surgery[84].

FUTURE DIRECTIONS

With further development of technologies in therapeutic endoscopy, EBD could become the worldwide treatment of choice for pediatric GOO. The future of endoscopic treatment seems to be aimed at the combined use of endoscopic electrocauterization with balloon dilatations in intractable pyloric stricture, and G-POEM appears to be technically feasible and effective in IHPS or gastroparesis patients.

CONCLUSION

Correction of GOO without the need for surgery is an issue that has been tried to be resolved in these decades. With the development of therapeutic endoscopy in pediatric patients, the therapeutic endoscopy becomes an integral part of the management of pediatric patients with GOO.

In recent decades, the endoscopic management of GOO has developed with EBD and additional advanced devices and techniques like local steroid injection, electrocauterization, G-POEM, and stent have been added to augment the efficacy of EBD.

With improvements in techniques and devices, therapeutic results of EBD have been achieved in pediatric patients with peptic pyloric stricture, IHPS, caustic injury related pyloric stricture, congenital antral web, postoperative GOO, and NSAID related GOO despite the inherent technical difficulties of this procedure in children. Local steroid injection and electrocauterization can augment the effect of EBD. Gastric peroral endoscopic pyloromyotomy (G-POEM) appears to be technically feasible in IHPS patients. Clinical applications of G-POEM in pediatric patients with gastroparesis can be considered after confirmation of its efficacy and safety in additional pediatric studies.

REFERENCES

1 **Kochhar R**, Kochhar S. Endoscopic balloon dilation for benign gastric outlet obstruction in adults. *World J Gastrointest Endosc* 2010; **2**: 29-35 [PMID: 21160676 DOI: 10.4253/wjge.v2.i1.29]

2 **Patel RA**, Baker SS, Sayej WN, Baker RD. Two Cases of Helicobacter pylori-Negative Gastric Outlet Obstruction in Children. *Case Rep Gastrointest Med* 2011; **2011**: 749850 [PMID: 22606426 DOI: 10.1155/2011/749850]

3 **Yen JB**, Kong MS. Gastric outlet obstruction in pediatric patients. *Chang Gung Med J* 2006; **29**: 401-405 [PMID: 17051838]

4 **Edwards MJ**, Kollenberg SJ, Brandt ML, Wesson DE, Nuchtern JG, Minifee PK, Cass DL. Surgery for peptic ulcer disease in children in the post-histamine2-blocker era. *J Pediatr Surg* 2005; **40**: 850-854 [PMID: 15937829 DOI: 10.1016/j.jpedsurg.2005.01.056]

5 **Graham DY**. Ulcer complications and their nonoperative treatment. In: Sleisenger M, Fordtran J (eds). *Gastrointestinal Disease* 1993: 698

6 **DiSario JA**, Fennerty MB, Tietze CC, Hutson WR, Burt RW. Endoscopic balloon dilation for ulcer-induced gastric outlet obstruction. *Am J Gastroenterol* 1994; **89**: 868-871 [PMID: 8198096]

7 **Ciftci AO**, Senocak ME, Büyükpamukçu N, Hiçsönmez A. Gastric outlet obstruction due to corrosive ingestion: incidence and outcome. *Pediatr Surg Int* 1999; **15**: 88-91 [PMID: 10079337 DOI: 10.1007/s003830050523]

8 **Ozokutan BH**, Ceylan H, Ertaşkin I, Yapici S. Pediatric gastric outlet obstruction following corrosive ingestion. *Pediatr Surg Int* 2010; **26**: 615-618 [PMID: 20443118 DOI: 10.1007/s00383-010-2613-6]

9 **Ozcan C**, Ergün O, Sen T, Mutaf O. Gastric outlet obstruction secondary to acid ingestion in children. *J Pediatr Surg* 2004; **39**: 1651-1653 [PMID: 15547828 DOI: 10.1016/j.jpedsurg.2004.07.008]

10 **Bell MJ**, Ternberg JL, McAlister W, Keating JP, Tedesco FJ. Antral diaphragm--a cause of gastric outlet obstruction in infants and children. *J Pediatr* 1977; **90**: 196-202 [PMID: 830910 DOI: 10.1016/s0022-3476(77)80629-x]

11 **Macpherson RI**. Gastrointestinal tract duplications: clinical, pathologic, etiologic, and radiologic considerations. *Radiographics* 1993; **13**: 1063-1080 [PMID: 8210590 DOI: 10.1148/radiographics.13.5.8210590]

12 **Ozcan C**, Celik A, Güçlü C, Balik E. A rare cause of gastric outlet obstruction in the newborn: Pyloric ectopic pancreas. *J Pediatr Surg* 2002; **37**: 119-120 [PMID: 11782002 DOI: 10.1053/jpsu.2002.29443]

13 **Sharma KK**, Ranka P, Goyal P, Dabi DR. Gastric outlet obstruction in children: an overview with report of Jodhpur disease and Sharma's classification. *J Pediatr Surg* 2008; **43**: 1891-1897 [PMID: 18926227 DOI: 10.1016/j.jpedsurg.2008.07.001]

14 **Morinville V**, Bernard C, Forget S. Foveolar hyperplasia secondary to cow's milk protein hypersensitivity presenting with clinical features of pyloric stenosis. *J Pediatr Surg* 2004; **39**: E29-E31 [PMID: 14694404 DOI: 10.1016/j.jpedsurg.2003.09.040]

15 **DuBose TM**, Southgate WM, Hill JG. Lactobezoars: a patient series and literature review. *Clin Pediatr* (Phila) 2001; **40**: 603-606 [PMID: 11758960 DOI: 10.1177/000992280104001104]

16 **Ruiz HD**, Palermo M, Ritondale O, Pest E, Pest P, Villafañe V, Bruno M, Tarsitano FJ. Gastro-duodenal trichobezoars: a rare cause of obstruction of the gastrointestinal tract. *Acta Gastroenterol Latinoam* 2005; **35**: 24-27 [PMID: 15954733]

17 **Nugent FW**, Roy MA. Duodenal Crohn's disease: an analysis of 89 cases. *Am J Gastroenterol* 1989; **84**: 249-254 [PMID: 2919581]

18 **Padussis J**, Loffredo B, McAneny D. Minimally invasive management of obstructive gastroduodenal tuberculosis. *Am Surg* 2005; **71**: 698-700 [PMID: 16217956]

19 **Miner PB**, Harri JE, McPhee MS. Intermittent gastric outlet obstruction from a pedunculated gastric polyp. *Gastrointest Endosc* 1982; **28**: 219-220 [PMID: 7129059 DOI: 10.1016/S0016-5107(82)73075-5]

20 **Jaka H**, Mchembe MD, Rambau PF, Chalya PL. Gastric outlet obstruction at Bugando Medical Centre in Northwestern Tanzania: a prospective review of 184 cases. *BMC Surg* 2013; **13**: 41 [PMID: 24067148 DOI: 10.1186/1471-2482-13-41]

21 **Ferzoco SJ**, Soybel DI. Gastric outlet obstruction, perforation and other complications of gastroduodenal ulcer. In: Wolfe HM, editor. Therapy of digestive disorders. 2007: 357-375

22 **Goenka AS**, Dasilva MS, Cleghorn GJ, Patrick MK, Shepherd RW. Therapeutic upper gastrointestinal endoscopy in children: an audit of 443 procedures and literature review. *J Gastroenterol Hepatol* 1993; **8**: 44-51 [PMID: 8439662 DOI: 10.1111/j.1440-1746.1993.tb01174.x]

23 **Lindor KD**, Ott BJ, Hughes RW. Balloon dilatation of upper digestive tract strictures. *Gastroenterology* 1985; **89**: 545-548 [PMID: 4018500 DOI: 10.1016/0016-5085(85)90449-4]

24 **Rana SS**, Bhasin DK, Chandail VS, Gupta R, Nada R, Kang M, Nagi B, Singh R, Singh K. Endoscopic balloon dilatation without fluoroscopy for treating gastric outlet obstruction because of benign etiologies. *Surg Endosc* 2011; **25**: 1579-1584 [PMID: 21052720 DOI: 10.1007/s00464-010-1442-y]

25 **Yusuf TE**, Brugge WR. Endoscopic therapy of benign pyloric stenosis and gastric outlet obstruction. *Curr Opin Gastroenterol* 2006; **22**: 570-573 [PMID: 16891891 DOI: 10.1097/01.mog.0000239874.13867.41]

26 **Benjamin SB**, Cattau EL, Glass RL. Balloon dilation of the pylorus: therapy for gastric outlet obstruction. *Gastrointest Endosc* 1982; **28**: 253-254 [PMID: 7173580 DOI: 10.1016/S0016-5107(82)73105-0]

27 **Benjamin SB**, Glass RL, Cattau EL, Miller WB. Preliminary

experience with balloon dilation of the pylorus. *Gastrointest Endosc* 1984; **30**: 93-95 [PMID: 6714610 DOI: 10.1016/S0016-5107(84)72329-7]
28 **Lau JY**, Chung SC, Sung JJ, Chan AC, Ng EK, Suen RC, Li AK. Through-the-scope balloon dilation for pyloric stenosis: long-term results. *Gastrointest Endosc* 1996; **43**: 98-101 [PMID: 8635729 DOI: 10.1016/S0016-5107(06)80107-0]
29 **Boylan JJ**, Gradzka MI. Long-term results of endoscopic balloon dilatation for gastric outlet obstruction. *Dig Dis Sci* 1999; **44**: 1883-1886 [PMID: 10505729]
30 **Solt J**, Bajor J, Szabó M, Horváth OP. Long-term results of balloon catheter dilation for benign gastric outlet stenosis. *Endoscopy* 2003; **35**: 490-495 [PMID: 12783346 DOI: 10.1055/s-2003-39664]
31 **Misra SP**, Dwivedi M. Long-term follow-up of patients undergoing ballon dilation for benign pyloric stenoses. *Endoscopy* 1996; **28**: 552-554 [PMID: 8911802 DOI: 10.1055/s-2007-1005553]
32 **Kochhar R**, Sethy PK, Nagi B, Wig JD. Endoscopic balloon dilatation of benign gastric outlet obstruction. *J Gastroenterol Hepatol* 2004; **19**: 418-422 [PMID: 15012779 DOI: 10.1111/j.1440-1746.2003.03283.x]
33 **Perng CL**, Lin HJ, Lo WC, Lai CR, Guo WS, Lee SD. Characteristics of patients with benign gastric outlet obstruction requiring surgery after endoscopic balloon dilation. *Am J Gastroenterol* 1996; **91**: 987-990 [PMID: 8633593]
34 **Cherian PT**, Cherian S, Singh P. Long-term follow-up of patients with gastric outlet obstruction related to peptic ulcer disease treated with endoscopic balloon dilatation and drug therapy. *Gastrointest Endosc* 2007; **66**: 491-497 [PMID: 17640640 DOI: 10.1016/j.gie.2006.11.016]
35 **Kozarek RA**, Botoman VA, Patterson DJ. Long-term follow-up in patients who have undergone balloon dilation for gastric outlet obstruction. *Gastrointest Endosc* 1990; **36**: 558-561 [PMID: 2279642 DOI: 10.1016/S0016-5107(90)71163-7]
36 **Kuwada SK**, Alexander GL. Long-term outcome of endoscopic dilation of nonmalignant pyloric stenosis. *Gastrointest Endosc* 1995; **41**: 15-17 [PMID: 7698619 DOI: 10.1016/S0016-5107(95)70270-9]
37 **Kochhar R**, Dutta U, Sethy PK, Singh G, Sinha SK, Nagi B, Wig JD, Singh K. Endoscopic balloon dilation in caustic-induced chronic gastric outlet obstruction. *Gastrointest Endosc* 2009; **69**: 800-805 [PMID: 19136104 DOI: 10.1016/j.gie.2008.05.056]
38 **Lam YH**, Lau JY, Fung TM, Ng EK, Wong SK, Sung JJ, Chung SS. Endoscopic balloon dilation for benign gastric outlet obstruction with or without Helicobacter pylori infection. *Gastrointest Endosc* 2004; **60**: 229-233 [DOI: 10.1016/S0016-5107(04)01569-X]
39 **Griffin SM**, Chung SC, Leung JW, Li AK. Peptic pyloric stenosis treated by endoscopic balloon dilatation. *Br J Surg* 1989; **76**: 1147-1148 [PMID: 2597970 DOI: 10.1002/bjs.1800761112]
40 **Weiland D**, Dunn DH, Humphrey EW, Schwartz ML. Gastric outlet obstruction in peptic ulcer disease: an indication for surgery. *Am J Surg* 1982; **143**: 90-93 [PMID: 7053661 DOI: 10.1016/0002-9610(82)90135-0]
41 **Jaffin BW**, Kaye MD. The prognosis of gastric outlet obstruction. *Ann Surg*1985;**201**: 176-179 [PMID: 3970597 DOI: 10.1097/00000658-198502000-00007]
42 **Chan KL**, Saing H. Balloon catheter dilatation of peptic pyloric stenosis in children. *J Pediatr Gastroenterol Nutr* 1994; **18**: 465-468 [PMID: 7915308 DOI: 10.1097/00005176-199405000-00011]
43 **Nasr A**, Ein SH, Connolly B. Recurrent pyloric stenosis: to dilate or operate? A preliminary report.*J Pediatr Surg*2008;**43**: e17-e20 [PMID: 18280264 DOI: 10.1016/j.jpedsurg.2007.10.039]
44 **Karnsakul W**, Cannon ML, Gillespie S, Vaughan R. Idiopathic non-hypertrophic pyloric stenosis in an infant successfully treated via endoscopic approach. *World J Gastrointest Endosc* 2010; **2**: 413-416 [PMID: 21191516 DOI: 10.4253/wjge.v2.i12.413]
45 **Ogawa Y**, Higashimoto Y, Nishijima E, Muraji T, Yamazato M, Tsugawa C, Matsumoto Y. Successful endoscopic balloon dilatation for hypertrophic pyloric stenosis. *J Pediatr Surg* 1996; **31**: 1712-1714 [PMID: 8986998 DOI: 10.1016/S0022-3468(96)90059-7]
46 **Hayashi AH**, Giacomantonio JM, Lau HY, Gillis DA. Balloon catheter dilatation for hypertrophic pyloric stenosis.*J Pediatr Surg*1990;**25**: 1119-1121 [PMID: 2273424 DOI: 10.1016/0022-3468(90)90744-T]
47 **Chaudhary A**, Puri AS, Dhar P, Reddy P, Sachdev A, Lahoti D, Kumar N, Broor SL. Elective surgery for corrosive-induced gastric injury. *World J Surg* 1996; **20**: 703-706; discussion 706 [PMID: 8662156 DOI: 10.1007/s002689900107]
48 **Treem WR**, Long WR, Friedman D, Watkins JB. Successful management of an acquired gastric outlet obstruction with endoscopy guided balloon dilatation. *J Pediatr Gastroenterol Nutr* 1987; **6**: 992-996 [PMID: 3681588 DOI: 10.1097/00005176-198711000-00031]
49 **Kochhar R**, Poornachandra KS, Dutta U, Agrawal A, Singh K. Early endoscopic balloon dilation in caustic-induced gastric injury. *Gastrointest Endosc* 2010; **71**: 737-744 [PMID: 20363415 DOI: 10.1016/j.gie.2009.11.038]
50 **Temiz A**, Oguzkurt P, Ezer SS, Ince E, Gezer HO, Hicsonmez A. Management of pyloric stricture in children: endoscopic balloon dilatation and surgery. *Surg Endosc* 2012; **26**: 1903-1908 [PMID: 22234589 DOI: 10.1007/s00464-011-2124-0]
51 **Tekant G**, Eroğlu E, Erdoğan E, Yeşildağ E, Emir H, Büyükünal C, Yeker D. Corrosive injury-induced gastric outlet obstruction: a changing spectrum of agents and treatment. *J Pediatr Surg* 2001; **36**: 1004-1007 [PMID: 11431765 DOI: 10.1053/jpsu.2001.24725]
52 **Lu JP**, Huang Y, Wu J, Chen SY. Uncommon congenital antral web misdiagnosed twice as a pyloric ulcer: successful treatment with endoscopic balloon dilatation. *Turk J Pediatr* 2014; **56**: 100-102 [PMID: 24827957]
53 **Lanuti M**, de Delva PE, Wright CD, Gaissert HA, Wain JC, Donahue DM, Allan JS, Mathisen DJ. Post-esophagectomy gastric outlet obstruction: role of pyloromyotomy and management with endoscopic pyloric dilatation. *Eur J Cardiothorac Surg* 2007; **31**: 149-153 [PMID: 17166733 DOI: 10.1016/j.ejcts.2006.11.010]
54 **Swanson EW**, Swanson SJ, Swanson RS. Endoscopic pyloric balloon dilatation obviates the need for pyloroplasty at esophagectomy. *Surg Endosc* 2012; **26**: 2023-2028 [PMID: 22398960 DOI: 10.1007/s00464-012-2151-5]
55 **Heymans HS**, Bartelsman JW, Herweijer TJ. Endoscopic balloon dilatation as treatment of gastric outlet obstruction in infancy and childhood. *J Pediatr Surg* 1988; **23**: 139-140 [PMID: 3343648 DOI: 10.1016/S0022-3468(88)80142-8]
56 **Sataloff DM**, Lieber CP, Seinige UL. Strictures following gastric stapling for morbid obesity. Results of endoscopic dilatation. *Am Surg* 1990; **56**: 167-174 [PMID: 2316938]
57 **Boybeyi O**, Karnak I, Ekinci S, Ciftci AO, Akçören Z, Tanyel FC, Senocak ME. Late-onset hypertrophic pyloric stenosis: definition of diagnostic criteria and algorithm for the management. *J Pediatr Surg* 2010; **45**: 1777-1783 [PMID: 20850620 DOI: 10.1016/j.jpedsurg.2010.04.014]
58 **Geraghty RJ**, Black D, Bruce SA. The successful medical management of gastric outflow obstruction associated with the use of non-steroidal anti-inflammatory drugs in the elderly. *Postgrad Med J* 1991; **67**: 1004-1007 [PMID: 1775405 DOI: 10.1136/pgmj.67.793.1004]
59 **Weaver GA**, Harper RL, Storey JA, Jenkins PL, Merrell NB. Nonsteroidal antiinflammatory drugs are associated with gastric outlet obstruction. *J Clin Gastroenterol* 1995; **20**: 196-198 [PMID: 7797825 DOI: 10.1097/00004836-199504000-00006]
60 **Kannan S**, McGreevy PS, Fullerton TE. Nonsteroidal anti-inflammatory drug induced duodenal web. *S D J Med* 1997; **50**: 393-394 [PMID: 9401436]
61 **Puri AS**, Monga R, Garg S, Sharma BC, Satapathy S, Sarin SK. Diaphragm disease of duodenum following long-term NSAIDs use: endoscopic management. *Indian J Gastroenterol* 2004; **23**: 189-190 [PMID: 15599008]
62 **Gobbi D**, Billi P, Fascetti Leon F, Alvisi P, Lambertini A, Lima M. Pneumatic pyloric dilatation for the treatment of gastric outlet obstruction in a child. *Pediatr Int* 2013; **55**: 382-385 [PMID: 23782371 DOI: 10.1111/ped.12022]
63 **Kim JH**, Shin JH, Di ZH, Ko GY, Yoon HK, Sung KB, Song HY. Benign duodenal strictures: treatment by means of fluoroscopically guided balloon dilation. *J Vasc Interv Radiol* 2005; **16**: 543-548 [PMID: 15802456 DOI: 10.1097/01.RVI.0000150033.13928.D4]

64 **Hamzaoui L**, Bouassida M, Ben Mansour I, Medhioub M, Ezzine H, Touinsi H, Azouz MM. Balloon dilatation in patients with gastric outlet obstruction related to peptic ulcer disease. *Arab J Gastroenterol* 2015; **16**: 121-124 [PMID: 26440958 DOI: 10.1016/j.ajg.2015.07.004]

65 **Kochhar R**, Sriram PV, Ray JD, Kumar S, Nagi B, Singh K. Intralesional steroid injections for corrosive induced pyloric stenosis. *Endoscopy* 1998; **30**: 734-736 [PMID: 9865568 DOI: 10.1055/s-2007-1001400]

66 **Ashcraft KW**, Holder TM. The expeimental treatment of esophageal strictures by intralesional steroid injections. *J Thorac Cardiovasc Surg* 1969; **58**: 685-691 passim [PMID: 5348158]

67 **Ketchum LD**, Smith J, Robinson DW, Masters FW. The treatment of hypertrophic scar, keloid and scar contracture by triamcinolone acetonide. *Plast Reconstr Surg* 1966; **38**: 209-218 [PMID: 5919604 DOI: 10.1097/00006534-196609000-00005]

68 **Gandhi RP**, Cooper A, Barlow BA. Successful management of esophageal strictures without resection or replacement. *J Pediatr Surg* 1989; **24**: 745-749; discussion 749-750 [DOI: 10.1016/S0022-3468(89)80529-9]

69 **Kochhar R**, Ray JD, Sriram PV, Kumar S, Singh K. Intralesional steroids augment the effects of endoscopic dilation in corrosive esophageal strictures. *Gastrointest Endosc* 1999; **49**: 509-513 [PMID: 10202068 DOI: 10.1016/S0016-5107(99)70052-0]

70 **Lee M**, Kubik CM, Polhamus CD, Brady CE, Kadakia SC. Preliminary experience with endoscopic intralesional steroid injection therapy for refractory upper gastrointestinal strictures. *Gastrointest Endosc* 1995; **41**: 598-601 [PMID: 7672557 DOI: 10.1016/S0016-5107(95)70199-0]

71 **Boron B**, Gross KR. Successful dilatation of pyloric stricture resistant to balloon dilatation with electrocautery using a sphinctertome. *J Clin Gastroenterol* 1996; **23**: 239-241 [PMID: 8899513 DOI: 10.1097/00004836-199610000-00020]

72 **Hagiwara A**, Sonoyama Y, Togawa T, Yamasaki J, Sakakura C, Yamagishi H. Combined use of electrosurgical incisions and balloon dilatation for the treatment of refractory postoperative pyloric stenosis. *Gastrointest Endosc* 2001; **53**: 504-508 [PMID: 11275897 DOI: 10.1067/mge.2001.113281]

73 **Chao HC**, Luo CC, Wang CJ. Elimination of postoperative pyloric stricture by endoscopic electrocauterization and balloon dilatation in an infant with congenital antral web. *Pediatr Neonatol* 2011; **52**: 106-109 [PMID: 21524632 DOI: 10.1016/j.pedneo.2011.02.005]

74 **Ibarguen-Secchia E**. Endoscopic pyloromyotomy for congenital pyloric stenosis. *Gastrointest Endosc* 2005; **61**: 598-600 [PMID: 15812419 DOI: 10.1016/S0016-5107(05)00075-1]

75 **Khashab MA**, Stein E, Clarke JO, Saxena P, Kumbhari V, Chander Roland B, Kalloo AN, Stavropoulos S, Pasricha P, Inoue H. Gastric peroral endoscopic myotomy for refractory gastroparesis: first human endoscopic pyloromyotomy (with video). *Gastrointest Endosc* 2013; **78**: 764-768 [PMID: 24120337 DOI: 10.1016/j.gie.2013.07.019]

76 **Mekaroonkamol P**, Li LY, Dacha S, Xu Y, Keilin SD, Willingham FF, Cai Q. Gastric peroral endoscopic pyloromyotomy (G-POEM) as a salvage therapy for refractory gastroparesis: a case series of different subtypes. *Neurogastroenterol Motil* 2016; **28**: 1272-1277 [PMID: 27197717 DOI: 10.1111/nmo.12854]

77 **van Hooft J**, Mutignani M, Repici A, Messmann H, Neuhaus H, Fockens P. First data on the palliative treatment of patients with malignant gastric outlet obstruction using the WallFlex enteral stent: a retrospective multicenter study. *Endoscopy* 2007; **39**: 434-439 [PMID: 17516350 DOI: 10.1055/s-2007-966338]

78 **Topazian M**, Ring E, Grendell J. Palliation of obstructing gastric cancer with steel mesh, self-expanding endoprostheses. *Gastrointest Endosc* 1992; **38**: 58-60 [PMID: 1377147 DOI: 10.1016/S0016-5107(92)70334-4]

79 **Adler DG**. Enteral stents for malignant gastric outlet obstruction: testing our mettle. *Gastrointest Endosc* 2007; **66**: 361-363 [PMID: 17643713 DOI: 10.1016/j.gie.2006.12.053]

80 **Tringali A**, Didden P, Repici A, Spaander M, Bourke MJ, Williams SJ, Spicak J, Drastich P, Mutignani M, Perri V, Roy A, Johnston K, Costamagna G. Endoscopic treatment of malignant gastric and duodenal strictures: a prospective, multicenter study. *Gastrointest Endosc* 2014; **79**: 66-75 [PMID: 23932009 DOI: 10.1016/j.gie.2013.06.032]

81 **Pontone S**, Pironi D, Eberspacher C, Pontone P, Filippini A. Endoscopic management of multiple large antral hyperplastic polyps causing gastric outlet obstruction. *Ann Ital Chir* 2011; **82**: 297-300 [PMID: 21834480]

82 **Søreide K**, Sarr MG, Søreide JA. Pyloroplasty for benign gastric outlet obstruction--indications and techniques. *Scand J Surg* 2006; **95**: 11-16 [PMID: 16579249]

83 **Khullar SK**, DiSario JA. Gastric outlet obstruction. *Gastrointest Endosc Clin N Am* 1996; **6**: 585-603 [PMID: 8803569]

84 **Al-Rashedy M**, Dadibhai M, Shareif A, Khandelwal MI, Ballester P, Abid G, McCloy RF, Ammori BJ. Laparoscopic gastric bypass for gastric outlet obstruction is associated with smoother, faster recovery and shorter hospital stay compared with open surgery. *J Hepatobiliary Pancreat Surg* 2005; **12**: 474-478 [PMID: 16365822 DOI: 10.1007/s00534-005-1013-0]

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ORIGINAL ARTICLE

Retrospective Study

Efficacy and safety of endoscopic papillary balloon dilation for the removal of bile duct stones: Data from a "real-life" multicenter study on Dilation-Assisted Stone Extraction

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Author contributions: Di Mitri R and Mocciaro F designed and performed the research and wrote the paper; Mocciaro F and Pecoraro GM contributed to the analysis; Pallio S, Tortora A, Zulli C, Attardo S and Maurano A supervised the report.

Institutional review board statement: This study was approved by the Ethics Committee of the ARNAS Civico-Di Cristina-Benfratelli Hospital, Palermo, Italy.

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Abstract

AIM

To report data on Dilation-Assisted Stone Extraction (DASE) use in clinical practice and its efficacy and safety trough three Italian referral centers for biliopancreatic diseases treatment.

METHODS

From January 2011 to December 2015 we collected data on 120 patients treated with DASE. Technical success was obtained when the endoscopist was able to place the balloon trough the papilla inflating the balloon until the final diameter for an adequate time (at least 30 s). Clinical success was obtained after complete stone removal (no remaining stones were visible at the cholangiogram).

RESULTS

Forty-nine male (40.8%) and 71 female (59%) were enrolled. The mean age was 67.8 years ± 15.7. The mean common bile duct (CBD) dilation was 19.2 mm

± 3.9 and the mean size of stones 15.8 ± 2.9. DASE was applied as first approach in 38% (62% after initial failure of stones extraction). Technical and clinical success was of 91% and 87% respectively. In those in which DASE failed alternative treatment were adopted. After DASE 18% of patients experienced a complication (bleeding 9%, pancreatitis 8%, perforation 0.8%). At univariable analysis, elective endoscopic retrograde cholangiopancreatography (P = 0.031), DASE as first approach (P = 0.032), and cannulation of major papilla followed by guidewire insertion (P = 0.004) were related to low risk of complications. Pre-cut was related to an increased risk of complications (P = 0.01).

CONCLUSION

DASE allowed a higher first-session success rate and can be consider a valid alternative to endoscopic sphincterotomy not only for bigger CBD stones.

Key words: Endoscopic retrograde cholangiopancreatography; Dilation-Assisted Stone Extraction; Common bile duct stone; Endoscopic sphincterotomy; Endoscopic papillary balloon dilation

Core tip: Endoscopic papillary large-balloon dilation after endoscopic sphincterotomy resulted effective for "difficult" common bile duct (CBD) stones treatment. This endoscopic technique has gradually spread to the current Dilation-Assisted Stone Extraction (DASE), in which balloon dilation was associated to a full or partial incision of the transverse fold, enhancing stones removal and reducing the risk of complications. Technical and clinical success was of 91% and 87% respectively; 18% of patients experienced a complication (bleeding 9%, pancreatitis 8%, perforation 0.8%). DASE allowed a higher first-session success rate and can be consider a valid alternative to endoscopic sphincterotomy not only for bigger stones of the CBD.

Di Mitri R, Mocciaro F, Pallio S, Pecoraro GM, Tortora A, Zulli C, Attardo S, Maurano A. Efficacy and safety of endoscopic papillary balloon dilation for the removal of bile duct stones: Data from a "real-life" multicenter study on Dilation-Assisted Stone Extraction. *World J Gastrointest Endosc* 2016; 8(18): 646-652 Available from: URL: http://www.wjgnet.com/1948-5190/full/v8/i18/646.htm DOI: http://dx.doi.org/10.4253/wjge.v8.i18.646

INTRODUCTION

Endoscopic sphincterotomy (EST) during endoscopic retrograde cholangiopancreatography (ERCP) represents the standard endoscopic treatment for common bile duct (CBD) stones, present in up to 10% of patients who underwent cholecistectomy[1]. EST was introduced in 1974[2], and up to now is widely used in the current clinical practice despite 5%-15% of all CBD stones are unable to be managed with EST alone (*e.g.*, large CBD stones) increasing the number of complications as cholangitis and pancreatitis[3]. In patients with large CBD stones, endoscopic mechanical lithotripsy (EML) using a mechanical lithotripter[4], extra-corporeal shock wave lithotripsy or laser lithotripsy have proven useful to enhance stones removal[5]. In 2003 some authors showed as endoscopic papillary large-balloon dilation (EPLBD) after EST resulted effective for "difficult" CBD stones (≥ 15 mm)[6]. This "combined" endoscopic technique has gradually spread to the current Dilation-Assisted Stone Extraction (DASE) in which balloon dilation was associated to a full or partial incision of the transverse fold[7,8], enhancing stones removal and reducing the risk of post-ERCP pancreatitis compared to EPLBD alone[9,10]. This endoscopic approach can be applied safely for the treatment of CBD stones of all size as showed in a large randomized trial published in 2014 by Li *et al*[8].

In the current study we reported "real-life" data on DASE use in clinical practice and its efficacy and safety trough three Italian referral centers for biliopancreatic diseases treatment.

MATERIALS AND METHODS

Patients and study design

This retrospective study collected data from three referral centers for biliopancreatic diseases diagnosis and treatment [Gastroenterology and Endoscopy Unit, ARNAS Civico-Di Cristina-Benfratelli Hospital, Palermo; Endoscopy Unit, Policlinico G. Martino, Messina University, Messina; Endoscopy Unit, Amico Gaetano Fucito Hospital, Mercato San Severino (SA)].

All the included patients had either a single or more CBD stones documented trough one or more abdominal imaging technique (ultrasound, computer tomography scan or magnetic resonance imaging). DASE was performed due to failure of the standard approach or as first approach due to the large size of the stones (≥ 12 mm).

Endoscopic technique

ERCP were performed by experienced endoscopists, and with patients under conscious or deep sedation according to the hospital guidelines of each center (short-acting benzodiazepine either alone or in combination with an opioid analgesic for conscious sedation, while propofol for deep sedation). Full blood count, biochemistry and coagulation parameters were obtained before the ERCP. Prior to the ERCP antimicrobial agent was administered in all patients to prevent post-procedural infection. ERCP was performed using a side-viewing endoscope (JF or TJF series scopes, Olympus Medical Systems, Co. Ltd, Tokyo, Japan). After selective cannulation, the CBD was imaged using diluted contrast medium injection and the endoscopist was able to evaluate the number and

the size of stones, and the diameter of the distal bile duct. In "naive" patients, EST was performed before attempting to remove the CBD stones. The breadth of the sphincterotomy incision was performed according to endoscopist evaluation, the limit of the transverse fold or the presence of ampullary/periampullary diverticulum. After EST, stones were removed with retrieval balloon catheter or Dormia basket according to the decision of each endoscopist. In those with stones removal failure, DASE was applied in order to reach or complete stones removal. DASE was performed using a balloon catheter (CRE Wireguided, Boston Scientific, Massachusetts, United States) passed over the guidewire and positioned across the main duodenal papilla. X-ray markers confirmed the correct placement of the balloon. The final diameter of the balloon was selected to correspond to the diameter of the distal bile duct. The balloon was gradually pressurized using diluted contrast medium injection trough each diameter according to the corresponding atmosphere, reported by the manufacturer's instructions, and until waist disappearance. Final balloon dilation was maintained until 60 s thereafter. After that the balloon was gradually deflated and removed. Finally the stones were extracted using a retrieval balloon catheter or a Dormia basket. In patients with difficult-to-extract stones, the stones were removed after being crushed using EML. If the stones could not be removed a plastic stent insertion was performed and alternative approaches were planned (extra-corporeal shock wave lithotripsy, laser lithotripsy or surgical treatment).

Evaluation of efficacy and complications

To confirm the complete cleaning of the CBD each patient underwent contrast-enhanced imaging after occlusion with the retrieval balloon catheter. Technical success was obtained when the endoscopist was able to place the balloon trough the papilla inflating the balloon until the final diameter for an adequate time (at least 30 s). Clinical success was obtained after complete stone removal (no remaining stones were visible at the cholangiogram).

All post-ERCP complications were recorded according to definitions standardized in the 1991 consensus conference. Post-ERCP pancreatitis were defined as clinical evidence of pancreatitis and elevation of pancreatic enzymes to three times the upper limit of normal 24 h after the procedure (mild if 2-3 d duration, moderate if 4-9 d, severe if longer than 10 d). Hemorrhage was considered only if there was clinical evidence of bleeding (melena or hematemesis), with an associated decrease in the hemoglobin concentration of at least 2 g/dL, the need for a blood transfusion or significant bleeding requiring endoscopic hemostasis. Cholangitis was recorded if there were symptoms as right upper quadrant abdominal tenderness, a temperature of 38 ℃, and elevated liver enzyme levels. Perforation was recorded if evident during the ERCP or according to postoperative patient's symptoms combined with abdominal radiography and/or abdominal computed tomography.

Statistical analysis

All data were collected by the three centers trough an excel database. Each center filled out the own database according a unique encoding of the variables so that to have uniform data for the final analysis. Data were analysed using the SPSS 15 (SPSS Inc., Chicago, IL, United States) software package. Continuous variables were summarized as mean (± SD) or median (range) according to their distribution. Categorical variables were summarized as frequency and percentage. Significant differences were calculated using a χ^2 test for categorical variables, and logistic regression for continuous variables. Differences were considered significant at a "*P* value" of less than 0.05. The variables that were significant on univariate analysis were evaluated in a subsequent multivariate model.

RESULTS

From January 2011 to December 2015, 1908 ERCP for CBD stones were performed in the three included referral centers. Finally we collected data on 120 patients treated with DASE (20% of all ERCP): 49 male (40.8%) and 71 female (59%), mean age of 67.8 years ± 15.7. Patient characteristics are summarized in Table 1. There were no significant differences between the three enrolled centers and the baseline characteristics were well balanced. Indication for DASE was large stones in 69.2% (83/120 patients) and periampullary diverticulum in 30.8% (37/120 patients) as showed in Table 2. Almost all ERCP were performed electively and only 2.5% of those treated with DASE underwent rescue ERCP due to acute severe cholangitis. The majority of the treated patients underwent ERCP for the first time and only ¼ of the patients presented an ampullary/periampullary diverticulum. The mean CBD dilation was 19.2 mm ± 3.9 and the mean size of stones 15.8 ± 2.9. In 87.5% of patients, CBD cannulation was made trough cannulation of major papilla followed by guidewire insertion and contrast medium injection. After cholangiogram the endoscopists decided to perform DASE as first approach in 45 out of 120 patients (38%) while 62% of patients were treated after initial failure of stones extraction. The EST before DASE was "full length" in nearly half of patients, but as expected was much less common in those with ampullary/periampullary diverticulum (9/52 *vs* 43/52). After DASE technical success was of 91% with a significant rate of clinical success and stones extraction (87%). The mean size of the balloon dilation was 16.7 mm ± 3.6. There were no differences between in retrieval balloon or Dormia basket using to achieve CBD clearance. In those in which DASE failed (16 patients), alternative treatment were adopted (mechanical lithotripsy in 12 patients, extra-corporeal shock wave lithotripsy in 3 patients, laser lithotripsy in one patient). Eighty-two

Table 1 Patients' characteristics

Gender (male/female), *n* (%)	49 (40.8)/71 (59)
Age (years), mean ± SD	67.8 yr ± 15.7
Patients at 1st ERCP, *n* (%)	91 (75.8)
Patients previously treated with endoscopic sphincterotomy, *n* (%)	29 (24.2)
Ampullary/periampullary diverticulum, *n* (%)	37 (30.8)
Bile duct stones size (mm), mean ± SD	15.8 ± 2.9
Bile duct size (mm), mean ± SD	19.2 ± 3.9
Billroth I reconstruction, *n* (%)	3 (2.5)

Table 2 Final results

Elective ERCP *vs* rescue ERCP, *n* (%)	117 (97.5) *vs* 3 (2.5)
Common bile duct cannulation technique, *n* (%)	
Cannulation of major papilla followed by contrast medium injection	5 (4.2)
Cannulation of major papilla followed by guidewire insertion	105 (87.5)
Pre-cut	10 (8.3)
Involuntary insertion of the guidewire into Wirsung, *n* (%)	25 (20.8)
Indication for DASE, *n* (%)	
Large stones	83 (69.2)
Periampullary diverticulum	37 (30.8)
DASE, *n* (%)	
As first approach	45 (38)
After stone extraction	75 (62)
Balloon size (mm), mean ± SD	16.7 ± 3.6
Dilation time (s), mean ± SD	51 ± 13.8
Sphincterotomy incision, *n* (%)	
Limited to one-third of the transverse fold	68 (56.7)
Full length of the transverse fold	52 (43.3)
Procedural success, *n* (%)	
Technical success	109 (90.8)
Clinical success	104 (86.7)
Stones extraction, *n* (%)	
Retrieval balloon	61 (51.8)
Dormia basket	59 (49.2)
Post-ERCP pancreatitis prophylaxis, *n* (%)	
None	38 (31.4)
Pancreatic plastic stent	14 (11.8)
Indometacin suppositories	68 (56.8)

ERCP: Endoscopic retrograde cholangiopancreatography; DASE: Dilation-Assisted Stone Extraction.

patients were treated with pancreatic stent placement (12%) or with 100 mg indomethacin suppositories (57%) to reduce the risk of post-ERCP pancreatitis.

After DASE in less than ¼ of patients (18%) a complication was recorded. Bleeding and post-ERCP pancreatitis were the most common (9% and 8% respectively), while only in 1 patient a perforation was observed (he underwent DASE after CBD access made trough cannulation of major papilla followed by guide-wire insertion). The majority of complications occurred during the ERCP or within 24 h, and they were resolved conservatively (59%) or endoscopically (36%); only 1 patient underwent surgery due to post-procedural perforation. No adverse events related to the anesthetic technique were recorded (Table 3).

At univariable analysis, elective ERCP (P = 0.031, OR = 0.10; 95%CI: 0.009-1.21), DASE as first approach (P = 0.032, OR = 0.35; 95%CI: 0.136-1.11) and cannulation of major papilla followed by guidewire insertion (P = 0.004, OR = 0.21; 95%CI: 0.065-6.64), were related to low risk of complications. Pre-cut before DASE was related to an increased risk of complications (P = 0.01, OR = 5.11; 95%CI: 1.340-19.492). Indomethacin suppositories reduced the number of post-ERCP pancreatitis despite statistical significance was not reached (P = 0.07). Size of sphincterotomy incision, ampullary/periampullary diverticulum, balloon size, dilation time or devices for stones extraction resulted not related to complications. None of the significant variables resulted significant after multivariable analysis.

DISCUSSION

Our retrospective study showed as, in clinical practice of three referral centers for biliopancreatic diseases treatment, DASE was used in 20% of all ERCP for CBD stones removal. The efficacy and safety of this approach for difficult CBD stones were significant trough the three participating centers.

Kawai *et al*[2] have revolutionized the endoscopic approach of the CBD stones treatment with EST decreasing the need of surgery. Nevertheless 10%-15% of patients had "difficult" CBD stones and EST alone cannot be sufficient to remove the stones from the biliary tract. Difficulties can be related to the bile duct access (acute distal CBD angulation, sigmoid shaped CBD, periampullary diverticulum, CBD strictures Billroth type Ⅰ gastrectomy, Roux-en-Y-gastrojejunostomy), the size or number of stones, unusually shaped stones (barrel-shaped), impaction of stones, the location of the stones (intra hepatic, cystic duct), the Mirizzi syndrome[3]. Staritz *et al*[11] introduced endoscopic papillary balloon dilation as an alternative approach to EST but, despite the efficacy in CBD clearance, subsequent reports showed as this technique was related to the increased risk of severe pancreatitis (up to 15%) compared to sphincterotomy alone. In 2003 Ersoz *et al*[6] introduced the combinations of EST and endoscopic papillary balloon dilation revolutioning the treatment of CBD stones with successful clearance in up to 95% of patients with difficult stones. In the last years the use of EPLBD has evolved to the modern concept of DASE in which the use of this approach it is consolidated with the advantage to dilate both the papillary sphincter and distal bile duct, allowing for easy removal of the stones[8]. In our retrospective series the technical success of DASE was more than 90% with a final successful clearance of the CBD near to 90%. These data are quite comparable to those from several studies compared EST alone with EST plus EPLBD (size of dilation was between 10 and 20 mm)[7,12-15]. A systematic review and a recent meta-analysis[16,17] showed, also, that the combined approach resulted effective and safe as EST alone but with a less needing in EML. Efficacy of DASE improved with increasing in stones size and resulted in low EML

Table 3 Complications after Dilation-Assisted Stone Extraction

Complications, *n* (%)	
No	98 (81.7)
Yes	22 (18.3)
Type of complications, *n* (%)	
Bleeding	11 (9.2)
Post-ERCP pancreatitis	10 (8.3)
Perforation	1 (0.8)
Timing of complications, *n* (%)	
Immediate	8 (6.7)
Within 24 h from the ERCP	11 (9.2)
After 24 h from the ERCP	3 (2.5)
Treatment of complications, *n* (%)	
Medical	13 (10.8)
Endoscopic	8 (6.7)
Surgical	1 (0.8)
Outcome of complications, *n* (%)	
Resolved	21 (17.5)
Unresolved (patient's exitus)	1 (0.8)

ERCP: Endoscopic retrograde cholangiopancreatography; DASE: Dilation-Assisted Stone Extraction.

needing, less procedure and fluoroscopy time compared to EST. In the current study only 10% of patients underwent EML due to DASE failure.

As showed in the results section DASE was used as first approach less frequently than as "second line" after stone extraction (38% *vs* 62%). This evidence is very interesting and it correspond to data reported by Li *et al*[8] in which DASE was adopted not only for large stones but also for stones ≤ 12 mm difficult to remove at the first session.

In a large studied published in 1996[18], the overall complications rate of EST was up to 10%: Pancreatitis 5.4% (0.4% severe), haemorrhage 2% (0.5% severe), cholangitis/cholecystitis 1% (0.1% severe), perforation 0.3%. Since its introduction in clinical practice, endoscopic papillary balloon dilation was categorized as one of the important causes of pancreatitis as showed by Disario *et al*[10]. Nevertheless more recent studies disproved this evidence showing same rate of post-procedural pancreatitis comparing endoscopic papillary balloon dilation with EST[19]. Some studies, also, reported that the risk of post-ERCP pancreatitis was related to the final diameter of the balloon with lower pancreatitis risk using a balloon ≥ 12 mm than those using a balloon ≤ 10[20-23]. A randomized, controlled trial indicated that the pancreatitis risk for endoscopic papillary balloon dilation could be influenced by the dilation duration (a duration of 5 min is superior to the conventional 1-min duration)[24]. Interestingly in this study the observed pancreatitis risk and efficacy of 5-min endoscopic papillary balloon dilation were comparable with those of EST, and the authors proposed the possible use of endoscopic papillary balloon dilation not only in selected patients (*e.g.*, patients with coagulopathy) but also in routinely treatment of CBD stones. Concerning other complications, DASE was not related to an increased risk compared to EST alone[8]. In Li's study ascending cholangitis was < 1% and the risk of perforation or bleeding were comparable in those treated with EST alone than in those treated with DASE. A recent meta-analysis by Xu *et al*[25] confirmed a low rate of post-EPLBD bleeding compared to EST alone maybe because balloon compression of the sphincterotomy site during DASE can explain the low rate of bleeding.

In the current study the mean size of the balloon and the mean time of dilation were 16.7 mm and 51 s respectively with a final rate of post-ERCP pancreatitis or bleeding less than 9%. The majority of complications were immediate or early, and only 1 patient underwent surgery due to post-procedural perforation. No cholangitis/cholecystitis were recorded.

In our study elective ERCP, DASE as first approach and cannulation of major papilla followed by guidewire insertion, were related to low risk of complications. Pre-cut before DASE was related to an increased risk of complications. We can try to explain these findings: (1) patients treated electively are in better clinical condition compared to those treated as rescue therapy (*e.g.*, severe acute cholangitis increases the risk of bleeding); (2) DASE as first approach avoids "handling" of the CBD with retrieval balloon or Dormia basket reducing the risk of iatrogenic lesions or pancreatic injury; (3) cannulation of major papilla followed by guidewire insertion reduce the possibility of involuntary injection of contrast medium both in the Wirsung or submucosally in the papilla; and (4) pre-cut usually is reserved in those in which standard techniques of CBD cannulation failed so the risk of major papilla oedema or bleeding can increase.

No other variables were related to complications included ampullary/periampullary diverticulum confirming data reported in previous published studies[26].

The main limit of the current study, despite the interesting findings, is due to the retrospective design that can affect final results. As well know retrospective studies are typically constructed to search records that have already been collected and some data can be missing. Retrospective database would probably be less accurate and consistent than that achieved with a prospective cohort study design. In multicenter retrospective studies, also, many different healthcare professionals are involved in patient care with different endoscopic skills that can affect the final analysis.

In conclusion, DASE allowed a higher first-session success rate and can be consider a valid alternative to EST not only for bigger CBD stones. In experienced hands DASE is a safe procedure with acceptable rate of complications. In clinical practice DASE should be reserved to patients with "difficult" CBD stones and/or in those after failure of CBD clearance with retrieval balloon or Dormia basket. In patients with high risk of post-ERCP complications DASE could be used as first approach instead to second-line option after failure of

CBD. Further well-designed study are needed to assess the routinely use of DASE for CBD stone ⩽ 12 mm instead EST alone, and the advent of balloon-equipped sphincterotome could explore this aspect in the near future.

COMMENTS

Background

Endoscopic papillary large-balloon dilation after endoscopic sphincterotomy resulted effective for "difficult" common bile duct (CBD) stones treatment. This endoscopic technique has gradually spread to the current Dilation-Assisted Stone Extraction (DASE), in which balloon dilation was associated to a full or partial incision of the transverse fold, enhancing stones removal and reducing the risk of complications.

Research frontiers

In patients at risk for post-endoscopic retrograde cholangiopancreatography (ERCP) complication DASE could be used as first approach instead to second-line option after failure of CBD clearance with retrieval balloon or Dormia basket.

Innovations and breakthroughs

In this study DASE was useful to manage "difficult" CBD stones not only after failure of CBD clearance with retrieval balloon or Dormia basket but also as first approach in patients at risk for post-ERCP complication. After DASE in less than ¼ of patients a complication was recorded. The majority of complications occurred during the ERCP or within 24 h, and they were resolved conservatively or endoscopically in all patients but one (1 patient underwent surgery due to post-procedural perforation).

Applications

This study suggests that DASE allowed a higher first-session success rate and can be consider a valid alternative to EST not only for bigger CBD stones. DASE is a safe procedure in experienced hands.

Terminology

DASE: Dilation-Assisted Stone Extraction is a "combined" endoscopic technique in which balloon dilation was associated to a full or partial incision of the transverse fold after endoscopic sphincterotomy.

Peer-review

It is an interesting, well written manuscript from three referal centres including 120 patients with nice outcome. It gives a novel information as well as technical details.

REFERENCES

1 **Clayton ES**, Connor S, Alexakis N, Leandros E. Meta-analysis of endoscopy and surgery versus surgery alone for common bile duct stones with the gallbladder in situ. *Br J Surg* 2006; **93**: 1185-1191 [PMID: 16964628 DOI: 10.1002/bjs.5568]

2 **Kawai K**, Akasaka Y, Murakami K, Tada M, Koli Y. Endoscopic sphincterotomy of the ampulla of Vater. *Gastrointest Endosc* 1974; **20**: 148-151 [PMID: 4825160 DOI: 10.1016/s0015-5107(74)73914-1]

3 **Trikudanathan G**, Navaneethan U, Parsi MA. Endoscopic management of difficult common bile duct stones. *World J Gastroenterol* 2013; **19**: 165-173 [PMID: 23345939 DOI: 10.3748/wjg.v19.i2.165]

4 **Demling L**, Seuberth K, Riemann JF. A mechanical lithotripter. *Endoscopy* 1982; **14**: 100-101 [PMID: 7075559 DOI: 10.1055/s-2007-1021591]

5 **Maple JT**, Ikenberry SO, Anderson MA, Appalaneni V, Decker GA, Early D, Evans JA, Fanelli RD, Fisher D, Fisher L, Fukami N, Hwang JH, Jain R, Jue T, Khan K, Krinsky ML, Malpas P, Ben-Menachem T, Sharaf RN, Dominitz JA. The role of endoscopy in the management of choledocholithiasis. *Gastrointest Endosc* 2011; **74**: 731-744 [PMID: 21951472 DOI: 10.1016/j.gie.2011.04.012]

6 **Ersoz G**, Tekesin O, Ozutemiz AO, Gunsar F. Biliary sphincterotomy plus dilation with a large balloon for bile duct stones that are difficult to extract. *Gastrointest Endosc* 2003; **57**: 156-159 [PMID: 12556775 DOI: 10.1067/mge.2003.52]

7 **Heo JH**, Kang DH, Jung HJ, Kwon DS, An JK, Kim BS, Suh KD, Lee SY, Lee JH, Kim GH, Kim TO, Heo J, Song GA, Cho M. Endoscopic sphincterotomy plus large-balloon dilation versus endoscopic sphincterotomy for removal of bile-duct stones. *Gastrointest Endosc* 2007; **66**: 720-726; quiz 768, 771 [PMID: 17905013 DOI: 10.1016/j.gie.2007.02.033]

8 **Li G**, Pang Q, Zhang X, Dong H, Guo R, Zhai H, Dong Y, Jia X. Dilation-assisted stone extraction: an alternative method for removal of common bile duct stones. *Dig Dis Sci* 2014; **59**: 857-864 [PMID: 24254339 DOI: 10.1007/s10620-013-2914-4]

9 **Baron TH**, Harewood GC. Endoscopic balloon dilation of the biliary sphincter compared to endoscopic biliary sphincterotomy for removal of common bile duct stones during ERCP: a metaanalysis of randomized, controlled trials. *Am J Gastroenterol* 2004; **99**: 1455-1460 [PMID: 15307859 DOI: 10.1111/j.1572-0241.2004.30151.x]

10 **Disario JA**, Freeman ML, Bjorkman DJ, Macmathuna P, Petersen BT, Jaffe PE, Morales TG, Hixson LJ, Sherman S, Lehman GA, Jamal MM, Al-Kawas FH, Khandelwal M, Moore JP, Derfus GA, Jamidar PA, Ramirez FC, Ryan ME, Woods KL, Carr-Locke DL, Alder SC. Endoscopic balloon dilation compared with sphincterotomy for extraction of bile duct stones. *Gastroenterology* 2004; **127**: 1291-1299 [PMID: 15520997 DOI: 10.1053/j.gastro.2004.07.017]

11 **Staritz M**, Ewe K, Meyer zum Büschenfelde KH. Endoscopic papillary dilatation, a possible alternative to endoscopic papillotomy. *Lancet* 1982; **1**: 1306-1307 [PMID: 6123047 DOI: 10.1016/S0140-6736(82)92873-2]

12 **Kim HG**, Cheon YK, Cho YD, Moon JH, Park DH, Lee TH, Choi HJ, Park SH, Lee JS, Lee MS. Small sphincterotomy combined with endoscopic papillary large balloon dilation versus sphincterotomy. *World J Gastroenterol* 2009; **15**: 4298-4304 [PMID: 19750573 DOI: 10.3748/wjg.15.4298]

13 **Kim TH**, Oh HJ, Lee JY, Sohn YW. Can a small endoscopic sphincterotomy plus a large-balloon dilation reduce the use of mechanical lithotripsy in patients with large bile duct stones? *Surg Endosc* 2011; **25**: 3330-3337 [PMID: 21533521 DOI: 10.1007/s00464-011-1720-3]

14 **Tsuchida K**, Iwasaki M, Tsubouchi M, Suzuki T, Tsuchida C, Yoshitake N, Sasai T, Hiraishi H. Comparison of the usefulness of endoscopic papillary large-balloon dilation with endoscopic sphincterotomy for large and multiple common bile duct stones. *BMC Gastroenterol* 2015; **15**: 59 [PMID: 25980964 DOI: 10.1186/s12876-015-0290-6]

15 **Guo Y**, Li C, Lei S, Zhi F. Effects Comparison between Endoscopic Papillary Large Balloon Dilatation and Endoscopic Sphincterotomy for Common Bile Duct Stone Removal. *Gastroenterol Res Pract* 2015; **2015**: 839346 [PMID: 26351452 DOI: 10.1155/2015/839346]

16 **Jin PP**, Cheng JF, Liu D, Mei M, Xu ZQ, Sun LM. Endoscopic papillary large balloon dilation vs endoscopic sphincterotomy for retrieval of common bile duct stones: a meta-analysis. *World J Gastroenterol* 2014; **20**: 5548-5556 [PMID: 24833886 DOI: 10.3748/wjg.v20.i18.5548]

17 **Madhoun MF**, Wani S, Hong S, Tierney WM, Maple JT. Endoscopic papillary large balloon dilation reduces the need for mechanical lithotripsy in patients with large bile duct stones: a systematic review and meta-analysis. *Diagn Ther Endosc* 2014; **2014**: 309618 [PMID: 24729674 DOI: 10.1155/2014/309618]

18 **Freeman ML**, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, Moore JP, Fennerty MB, Ryan ME, Shaw MJ, Lande JD, Pheley AM. Complications of endoscopic biliary sphincterotomy. *N Engl J Med* 1996; **335**: 909-918 [PMID: 8782497 DOI: 10.1056/NEJM199609263351301]

19 **Lai KH**, Chan HH, Tsai TJ, Cheng JS, Hsu PI. Reappraisal of endoscopic papillary balloon dilation for the management of common bile duct stones. *World J Gastrointest Endosc* 2015; **7**: 77-86 [PMID: 25685263 DOI: 10.4253/wjge.v7.i2.77]

20 **Attasaranya S**, Cheon YK, Vittal H, Howell DA, Wakelin DE, Cunningham JT, Ajmere N, Ste Marie RW, Bhattacharya K, Gupta K, Freeman ML, Sherman S, McHenry L, Watkins JL, Fogel EL, Schmidt S, Lehman GA. Large-diameter biliary orifice balloon dilation to aid in endoscopic bile duct stone removal: a multicenter series. *Gastrointest Endosc* 2008; **67**: 1046-1052 [PMID: 18178208 DOI: 10.1016/j.gie.2007.08.047]

21 **Minami A**, Hirose S, Nomoto T, Hayakawa S. Small sphincterotomy combined with papillary dilation with large balloon permits retrieval of large stones without mechanical lithotripsy. *World J Gastroenterol* 2007; **13**: 2179-2182 [PMID: 17465497 DOI: 10.3748/wjg.v13.i15.2179]

22 **Youn YH**, Lim HC, Jahng JH, Jang SI, You JH, Park JS, Lee SJ, Lee DK. The increase in balloon size to over 15 mm does not affect the development of pancreatitis after endoscopic papillary large balloon dilatation for bile duct stone removal. *Dig Dis Sci* 2011; **56**: 1572-1577 [PMID: 20945093 DOI: 10.1007/s10620-010-1438-4]

23 **Li NP**, Liu JQ, Zhou ZQ, Ji TY, Cai XY, Zhu QY. Ampulla dilation with different sized balloons to remove common bile duct stones. *World J Gastroenterol* 2013; **19**: 903-908 [PMID: 23431070 DOI: 10.3748/wjg.v19.i6.903]

24 **Liao WC**, Lee CT, Chang CY, Leung JW, Chen JH, Tsai MC, Lin JT, Wu MS, Wang HP. Randomized trial of 1-minute versus 5-minute endoscopic balloon dilation for extraction of bile duct stones. *Gastrointest Endosc* 2010; **72**: 1154-1162 [PMID: 20869710 DOI: 10.1016/j.gie.2010.07.009]

25 **Xu L**, Kyaw MH, Tse YK, Lau JY. Endoscopic sphincterotomy with large balloon dilation versus endoscopic sphincterotomy for bile duct stones: a systematic review and meta-analysis. *Biomed Res Int* 2015; **2015**: 673103 [PMID: 25756050 DOI: 10.1155/2015/673103]

26 **Kim HW**, Kang DH, Choi CW, Park JH, Lee JH, Kim MD, Kim ID, Yoon KT, Cho M, Jeon UB, Kim S, Kim CW, Lee JW. Limited endoscopic sphincterotomy plus large balloon dilation for choledocholithiasis with periampullary diverticula. *World J Gastroenterol* 2010; **16**: 4335-4340 [PMID: 20818818 DOI: 10.3748/wjg.v16.i34.4335]

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ORIGINAL ARTICLE

Observational Study

Recommendations to quantify villous atrophy in video capsule endoscopy images of celiac disease patients

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Abstract

AIM

To quantify the presence of villous atrophy in endoscopic images for improved automation.

METHODS

There are two main categories of quantitative descriptors helpful to detect villous atrophy: (1) Statistical and (2) Syntactic. Statistical descriptors measure the small intestinal substrate in endoscope-acquired images based on mathematical methods. Texture is the most commonly used statistical descriptor to quantify villous atrophy. Syntactic descriptors comprise a syntax, or set of rules, for analyzing and parsing the substrate into a set of objects with boundaries. The syntax is designed to identify and distinguish three-dimensional structures based on their shape.

RESULTS

The variance texture statistical descriptor is useful to describe the average variability in image gray level representing villous atrophy, but does not determine the range in variability and the spatial relationships between regions. Improved textural descriptors will incorporate these factors, so that areas with variability gradients and regions that are orientation dependent can be distinguished. The protrusion syntactic descriptor is useful to detect three-dimensional architectural components, but is limited to identifying objects of a certain shape. Improvement in this descriptor will require incorporating flexibility to the prototypical

template, so that protrusions of any shape can be detected, measured, and distinguished.

CONCLUSION

Improved quantitative descriptors of villous atrophy are being developed, which will be useful in detecting subtle, varying patterns of villous atrophy in the small intestinal mucosa of suspected and known celiac disease patients.

Key words: Celiac disease; Endoscopy; Small intestine; Video capsule; Villous atrophy

Core tip: Celiac disease is a relatively common ailment throughout the world, affecting approximately 1% of the population. Yet, it is little known and rarely diagnosed. Untreated, it can lead to severe intestinal disturbance, cancer, neurological problems, fertility problems, and other disorders. Villous atrophy of the small intestine is often present in untreated celiac patients. Better quantitative image analysis is important to detect areas of pathology in the small intestine endoscopically. In this study the main approaches for automatically detecting villous atrophy by computerized means are described, which can be helpful to map areas of pathology and determine disease status.

Ciaccio EJ, Bhagat G, Lewis SK, Green PH. Recommendations to quantify villous atrophy in video capsule endoscopy images of celiac disease patients. *World J Gastrointest Endosc* 2016; 8(18): 653-662 Available from: URL: http://www.wjgnet.com/1948-5190/full/v8/i18/653.htm DOI: http://dx.doi.org/10.4253/wjge.v8.i18.653

INTRODUCTION

Celiac disease is prevalent throughout the entire world, though it varies in frequency, and averages about 1% of the population[1]. An important clinical problem is that the definitive diagnosis of celiac disease is difficult and requires serologic testing and endoscopy with biopsy, which is not available with accuracy in all areas of the world. Therefore geographic regions with lesser frequencies of celiac disease may simply be regions with a lack of experience in diagnosis and or areas without the facilities necessary for definitive diagnosis[2]. The presence of villous atrophy of the small intestinal mucosa, which is determined by examining biopsy slides under light microscopy[3], may not always be evident in untreated celiac disease patients. Present in the digitized biopsy slides are villous protrusion features, which are blunted in villous atrophy as compared to those found in healthy tissue[4]. Careful orientation of the biopsy on the slides and their proper examination is crucial, since off angle villi can erroneously appear blunted, mimicking villous atrophy[5]. Thus the experience of the pathologist is very important for accurate diagnosis of celiac disease.

Typically, villous atrophy is found in untreated celiac patients at the level of the duodenal bulb and the descending duodenum[6], but may also be present at the more distal regions of the small intestine, the jejunum and ileum, and be absent more proximally. The presence of villous atrophy tends to be patchy and is interspersed with regions of normal mucosa[7]. The mucosal abnormalities may be subtle or may even be lacking in images acquired with standard or video endoscopic techniques, due to the limits of resolution and the interpretation of microscopic changes of the intestinal villi, as manifested in the macroscopic image content. Though, more recently-developed high resolution endoscopes may overcome some problems with identification of mucosal structure[8].

During the last decade video capsule endoscopy has been used to image the entire small intestine with improved spatial resolution[9]. The video capsule is convenient to use for both adult and pediatric patients suspected of having celiac disease, because it is minimally invasive[10]. The capsule is swallowed and the video camera contained within the capsule snaps images at the rate of 2 per second or more[11]. The more recent video capsules have a variable frame rate, increasing in rate as the capsule motion increases, when presumably it is moving along the lumen at a faster rate, and decreasing when the capsule motion slows[12]. This ensures a more uniform frame rate per unit distance that the capsule travels. As the spatial and temporal resolution of recently commercially available video capsules has increased, it has been proposed that the series of video images can possibly be used to map the presence of villous atrophy all along the small intestinal length.

Prior research has suggested that there are differences in the video capsule endoscopy images of untreated celiac patients *vs* a control population[13-19]. Images from untreated celiac patients tend to be less structurally uniform both within a particular image, and across a series of images, as compared with control subjects[13-19]. In Figure 1, normal images at the top have uniform appearance and smooth folds. The celiac patient images at bottom were acquired from areas where villous atrophy was present, and have a mottled appearance, due to fissuring, and scalloping of the mucosal folds. These differences suggest the possibility that the presence of villous atrophy can be detected and mapped in a sequential series of video capsule images by computerized means. If areas of villous atrophy could be detected and mapped automatically all along the small intestinal tract, it would potentially be very helpful in the diagnosis of celiac disease. It would also be useful to monitor the progress in treatment of celiac disease. Currently, the only treatment is a lifelong gluten free diet[20], When the patient goes on the diet, the villi heal, albeit slowly[21]. Sometimes however, villous atrophy persists. Thus automated monitoring and mapping of

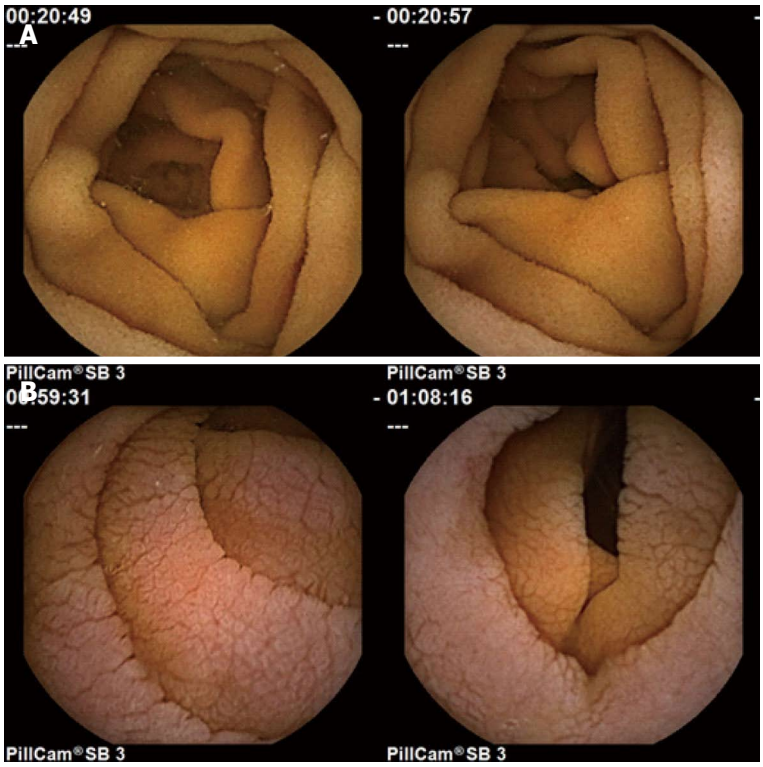

Figure 1 Normal (A) *vs* untreated celiac patient images (B). Note the presence of mucosal folds, a mottled appearance, and fissuring, in the images from untreated celiac patients (lower).

the location and severity of villous atrophy throughout the small intestine would be very useful. In this work, we describe the main modes of quantitative detection of villous atrophy from video capsule endoscopic images, and possible avenues to improve the detection rate and to better monitor the severity and types of pathology present in endoscopic images which are abnormal due to the presence of villous atrophy. The current detection of villous atrophy is determined by an experienced observer. This introduces bias based on observer experience and knowledge and possibly fatigue. These would be obviated by computerized techniques.

MATERIALS AND METHODS

Statement of the quantitative problem

For quantitative endoscopic image analysis in suspected or known celiac disease patients, it is important to detect areas of villous atrophy that may be present in the small intestinal mucosa. This is still mostly an unsolved problem. It is difficult to detect villous atrophy in part because the spatial resolution of the video capsule system from which discretized images are obtained is limited, and does not in every case clearly detect the individual villi in the small intestinal wall. The resolution in part depends on the video camera to intestinal wall distance, the camera lighting, and the camera angle, and is at best about 1 mm[17]. All of the factors for which resolution is determined are variable and tend to be random. Thus the identification of small intestinal villi, and the detection and quantification of villous atrophy, poses an important quantitative medical research problem, and a dilemma in terms of selecting the best method for recognition of the villi, and for estimation of whether or not there are normal or abnormal villi present in the image, as well as the degree and severity of areas of pathology.

Textural methods

To recognize abnormalities in endoscopic images, many investigators have used textural methods in part because of their simplicity and ease of use, as well as being a tried and true method of analysis[13-19]. Several helpful methods have been developed to describe the presence of villous atrophy as a set of textural features. Image textures can be measured locally using the wavelet operator and a local binary pattern[22]. It is possible to develop a set of scale invariant texture descriptors by utilizing wavelet analysis[23]. Over a series of images, texture can be defined by the presence of salient features that tend to reappear from one image to the next. This is illustrated in Figure 2. The panels are composed of basis images - images that contain the most salient features over a series of images acquired from the same patient. At bottom is shown four basis images from a patient with normal villi at the level of the duodenum. The appearance of these basis images is mostly smooth and uniform. The upper basis images were constructed from a series of images acquired from a celiac patient with villous atrophy. Sharp lines resembling actual fissures, as well as highly varied shading and texture is present in each of the basis images. The original images used to make the celiac basis images were highly varied in terms of the number and type of features with differing texture that were present.

For automation of textural properties and their locations in endoscopic images, texture can be defined

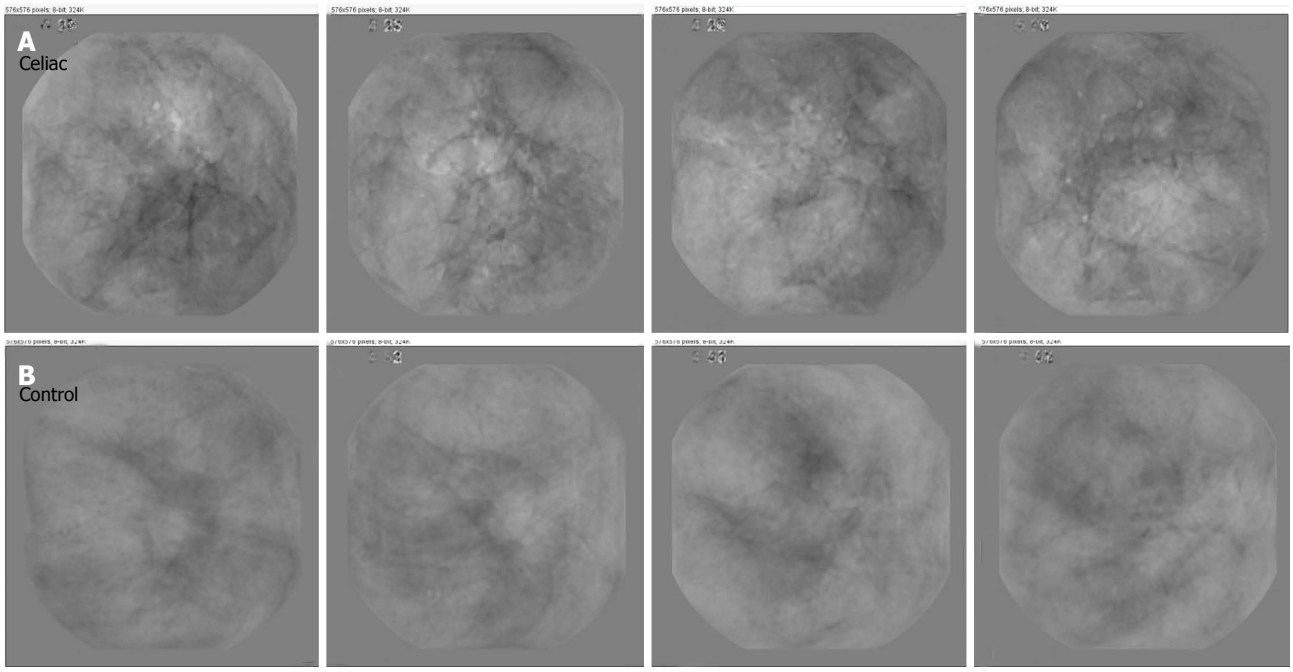

Figure 2 Evidence of more prominent fissuring is present in untreated control images (B) as compared with celiac basis images (A). The basis images are modified from a series of original endoscopic images so that salient features are enhanced.

quantitatively as the value of a statistical measurement of color or grayscale digital image level. For simplicity in initial prior investigations, endoscopic color images were typically reduced to gray level images, with the gray level ranging from 0 (black) - 255 (white)[13-19]. Values between 1 and 254 inclusive are successively brighter gray shades. For endoscopic image analysis, texture is then determined by measuring and quantifying the gray level of all pixels in an image, or of a subset of pixels in the image. All image pixels are analyzed as a group if one would like to make a broad statement about the image as a whole, and/or to compare successive image frames, *i.e.*, successive time epochs. For video capsule image analysis, successive frames will approximate the movement of the capsule along the gastrointestinal tract. However, because the capsule movement is passive and not likely to be at a constant rate, those successive images will likely represent uneven distances along the gastrointestinal system. The older imaging systems tended to have a fixed frame rate of 2 frames per second[24]. Newer systems having a variable frame rate[25] should be taken into account when considering successive image frames.

The simplest statistical measure of texture is the average or mean grayscale level (designated μ). To determine this value for the entire image, the gray-scale level of all pixels is averaged. A typical digital endoscopic image will have a size of 576 × 576 pixels = 331776 pixels[4]. Thus by summing the values of grayscale levels for all pixels and dividing by 331776, the mean level is obtained. The mean level of one image can have significance in several ways. Firstly it can be compared from one patient to another or from one level of the small intestine to another in the same patient. When the images are darker, it may signify the presence of darker structures in the substrate, though it can also be due to the presence of a darker shade in the mucosal wall. If darker structures are present in the substrate, these can represent a highly variable three-dimensional topography. For example, when villous atrophy is present, there tends to be fissuring of the small intestinal mucosa. The fissures appear as dark lines in the two-dimensional images, due to the fact that they are deeper within the mucosa and further from the video camera and its light source. The fissures can be variable in length, depth, and breadth (Figure 1, lower panels). They are often random in orientation. Their presence tends to render the image darker in overall gray level. Another phenomenon that tends to signify the presence of villous atrophy is a mottled appearance in the two-dimensional images (Figure 1, lower panels). The mottled appearance can result from the presence of mucosal protrusions of varying height. These protrusions have been proposed to be clumps of villi which have become atrophied and shortened in length[18,19]. Since the three-dimensional mucosal architecture is therefore uneven, camera and light source distance are important factors for imaging mucosal protrusions. Areas of lower elevation in the images will be partly obscured and shadowed by higher areas and thus appear substantially darker. The average grayscale level may thus decrease when there is mottling of the mucosal surface. Over a short succession of image frames, a high degree of variability in the mean grayscale level would likely indicate the presence of patchy villous atrophy[26], which is common in celiac disease patients. Lesser variability at more distal regions of the small intestine would be indicative of a lesser

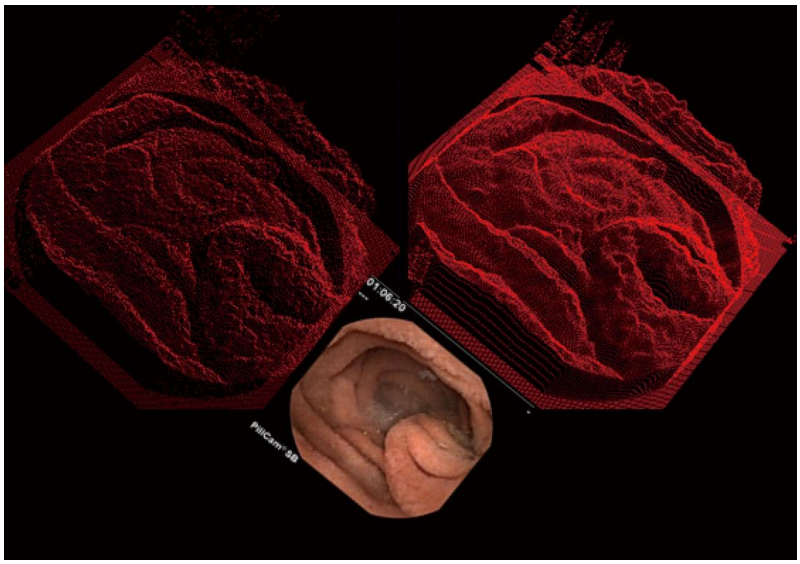

Figure 3 Shape-from-shading is used to render two-dimensional endoscopic images (lower panel) into three-dimensional constructs. First the color image is converted to grayscale. Then the degree of pixel brightness is linearly interpreted as depth in the constructs at top. Lighter areas in the lower image appear as taller protrusions in the images at top. Top left: Half resolution three-dimensional reconstruction; Top right: Full resolution three-dimensional reconstruction.

presence of villous atrophy and a more uniform, more normal mucosal surface, which is normally the case in untreated celiac disease patients. These patients tend to have the greatest presence of villous atrophy, which is patchy, at the level of the duodenal bulb and in the distal duodenum, and lesser degrees of villous atrophy in the jejunum and in the ileum[27]. When a comparison between celiac patients is made, darker mean grayscale level would be expected to indicate the presence of a greater degree of villous atrophy, though this hypothesis has yet to be proven. Likewise, when the same patient is compared at follow-up after starting the gluten free diet, it would be anticipated that a lighter average grayscale level would signify diminishing levels of villous atrophy.

A second main measure of image texture, and perhaps the most important to current systems used for quantitative analysis, is the second central moment, or variance (σ)[13,14]. Its positive square root is the standard deviation. This moment is a measure of the spread of the distribution of grayscale levels. A larger value of σ indicates greater range of gray shading about the mean level. The standard deviation or variance from the mean pixel level has been used as a textural feature to measure the variability in brightness of image features[13,14]. When more features are present with different brightness levels, for example when fissuring is evident as a series of many dark lines in the image, the standard deviation increases. Likewise, a mottled image appearance due to villous atrophy will cause an increase in the standard deviation of grayscale image brightness.

Although not currently implemented, higher-order textural measurements that are potentially useful for quantitative analysis of villous atrophy include the third central moment or skewness (γ) and the fourth central moment or kurtosis (κ). The skewness is an estimate of the degree of lopsidedness in the pixel graylevel distribution about the mean value. It can be helpful to detect spatial non-uniformity in the image brightness. For example if clumps of villi which have atrophied are present, they will be rendered as blunted protrusions, with a large darker surface area in the image[18]. This would skew the distribution toward the darker gray level pixel values. The kurtosis is a measure of the heaviness of the tail of the distribution, *i.e.*, how many very bright or very dark pixels are present in the image compared to the rest of the grayscale level values. The kurtosis measurement can therefore be assistive in detecting the presence of numerous very bright or very dark components of the endoscopic image space. These components can include small patches of normal tissue (bright) in areas of villous atrophy, and/or areas with fissuring (dark) among more normal villi.

Syntactic or structural methods

Syntactic methods are a way to model tissue structure based upon a set of prototypical or primitive features. For syntactic analysis, three-dimensional tissue structure should be generated, and can be studied by using shape-from-shading principles as shown in Figure 3. Areas of the original two-dimensional endoscopic image that are bright (lower panel) are converted into a height to render the object in three dimensions (top panels). It is evident in the top panels that the small intestinal mucosa consists of a series of mucosal protrusions. These mucosal protrusions can be modeled as a set of concentric, circular rings or squares (Figure 4). Using this syntactic model, a protrusion is detected when the average grayscale value within the ring or square is above a predefined threshold grayscale level. Based on shape-from-shading principles[18,19], the mucosal protrusion will appear as a bright spot in the endoscopic image. The outer edges of the spot will be a darker grayscale level, while the inner components will be manifested as progressively brighter pixels. At the pinnacle or center of the protrusion, the brightest grayscale level will occur. This phenomenon is based upon the camera light source to protrusion distance. The pinnacle of the protrusion extends furthest from the mucosal surface, and is therefore closest to the

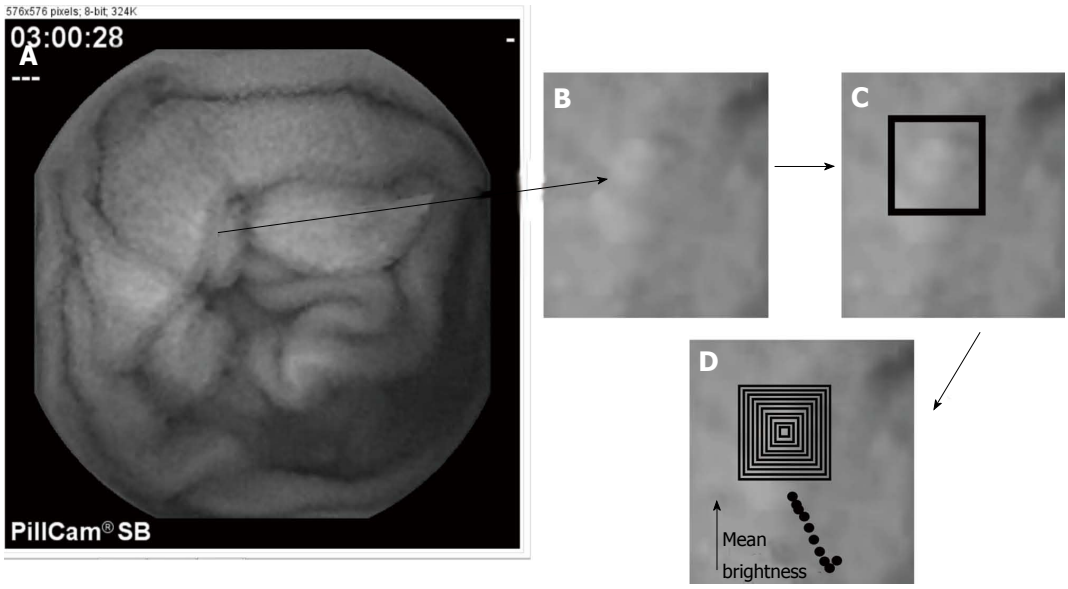

Figure 4 Example of the construction of a syntactic prototypical template. A: Video capsule endoscopic image in grayscale; B: Area with bright center is noted by the arrow; C: A square is used to identify the area of a protrusion; D: The series of concentric squares (rings) are used to determine the protrusion dimensions. The average pixel brightness diminishes from center square to outer square. The width and length of the protrusion is defined based on the outermost square, which is that square after which a larger concentric outer square would have an increased brightness. The height of the protrusion is the difference in brightness level from its center to its outermost concentric square.

video camera lens, which is constrained within the small intestinal lumen as it travels distally. The inverse square law of light states that the light intensity per unit area falling on the mucosal surface will vary in inverse proportion to the square of the distance from the light source. There are nonlinearities imposed on the model, but prior findings have suggested that the approximation is sufficiently accurate to render the two-dimensional image features as three-dimensional constructs which represent actual tissue structure[18,19]. Likewise, the base of the protrusion will appear darkest since it will be furthest from the camera lens. Taller protrusions will appear in endoscopic images as having brighter central regions due to the inverse square law, and *vice versa* for blunter protrusions. Wider protrusions will appear as image features having longer spatial gradients, from darker pixel areas in the outer portions to brighter pixel regions at the center area. Conversely, narrower protrusions will have sharper spatial gradients, from darker pixel regions at outer edge to the brighter central core in endoscopic images.

The evident three-dimensional mucosal protrusions (Figure 3) can be modeled in the two-dimensional endoscopic images based upon a fixed or flexible template (Figure 4). The simplest modeling method is to use a fixed template. For example, a protrusion can be modeled, and its architectural parameters can be determined, using a concentric series of square or circular shapes, or rings, as alluded to earlier in the text. The algorithm can be stated as follows. Each outlying shape can be made one pixel wide as a first approximation. The width of a mucosal protrusion would then be determined as follows. The average grayscale level of the image pixels overlapping each ring is first calculated. The brightest ring will be at the center of the protrusion, since it is highest and closest to the camera lens. Successive concentric rings in the outward direction will be darker in gray shade since the protrusion falls off in amplitude there and is further from the camera lens. The base of the protrusion is syntactically defined as the outermost ring that is still diminished in average grayscale level with respect to the adjacent, more inwardly located ring. Thus, the width of the protrusion is obtained, as is shown in Figure 4. To convert the protrusion width from pixels to millimeters would require knowing the camera lens to mucosal surface distance, which can be estimated. Alternatively, mucosal protrusion width can be measured in pixel units, which is the simplest form of this syntactic model. The height of the protrusion would be the difference in average grayscale levels from the innermost to the outermost ring defining the protrusion.

To better syntactically detect mucosal protrusions, a tolerance can be added so that architectures with slightly asymmetrical features, having a less rounded or square form, depending on the model being used, would still be detected as a protrusion. So for example, if an outer ring is only slightly brighter as compared to its inner neighbor, the base of the protrusion would not yet be considered to be reached. Subsequent outer rings would be counted as part of the mucosal protrusion, until arriving at a ring at which a sharp increase in average brightness is noted. Changing the tolerance would enable more or less candidate protrusions to be detected in the image, and with greater accuracy.

Once mucosal protrusions are detected, their statistics can be analyzed[18,19]. For example, the total number

of protrusions per endoscopic image can be calculated. The mean and variance in the width of the detected protrusions can be determined. And the mean and variance in the height of the detected protrusions can be computed. Greater variance in protrusion dimensions will likely indicate the presence of patchy villous atrophy. Decreased mean height and increased mean width would be suggestive of clumping of the villi, and therefore would be indicative of the presence of greater degrees of villous atrophy.

Another prominent macroscopic feature that is manifested when villous atrophy is present in the small intestinal mucosa that can be modeled syntactically is fissuring. Fissures are areas of the small intestinal mucosa that are devoid of villi. Thus architecturally, they can be described as valleys that are areas in the mucosa which are at greater depth with respect to camera lens location. They will appear in endoscopic images as dark lines of varying length and width[4,28]. Pixels of darker gray shading represent the fissured areas. One way to model the presence of fissures syntactically is to parse a linear region of darker pixels with a fixed length and width. As was described above for the modeling of mucosal protrusions, the fissures can be detected with the incorporation of a tolerance factor. The syntactic parameters in which a tolerance could be added would be the width, length, and brightness of each fissure. If the model parameters were say, width = 3 pixels, length = 10 pixels, and brightness = gray level 50/255, then tolerances could be imposed of for example ± 1 pixel and ± 10 grayscale levels. If the tolerance is made too small however, many actual fissures can be missed, and if the tolerance is made too large, structures that are not actually fissures may be detected.

Fissuring of the small intestinal mucosa due to villous atrophy does not appear to be dependent on factors such as muscle fiber orientation, and is more or less random[29]. Thus the fissure syntactic template, although it can be fixed for the length, width, and brightness parameters, needs to be flexible with respect to the orientation parameter. One way to implement this is simply to orient the model fissure at various predefined angles, at a particular location, and determine whether or not there is a satisfactory match of any orientation with the actual pixel content in the image. More orientations used for comparison would enable better detection of any fissure that is present, but at the expense of longer computation time. To reduce computation time, the image can be skeletonized. This is a standard processing technique in which image features are converted to a series of line structures which represent the central locations along each segment of the feature. The line structures in the skeletonized images can each be converted into a straight line approximation using linear regression analysis, and the angle of the straight line is then readily calculated. The prototypical template is then oriented according to the calculated angle of the structure, and a fissure is detected if the actual structure has similar length, width and brightness as the model, to within the specified tolerance.

Another structure that is often evident in images where villous atrophy is present, which can be modeled syntactically, is the scalloping of mucosal folds. This is a phenomenon in which the edges of the folds become scalloped - consisting of repeated structures with a rounded appearance, which are often of similar size[30,31]. To syntactically model the presence of scalloping, curved structures with similar brightness should be developed. The scalloping generally appears on edge as the camera viewing angle is toward distal regions along the small intestinal lumen. Thus the scalloped edges along each fold will appear to have similar brightness, as well as similar size and shape. The parameters for modeling the curved structure of each scallop would therefore be the width and height in terms of the number of pixels, and the degree of curvature.

The presence of a mottled appearance in endoscopic images can be modeled as a series of light and dark patches, with the length and width of the patches tailored to fit the observations of actual mottled areas found in exemplar images. It would be anticipated, as a first approximation, that the light and dark patches of mottled regions would be symmetric, and therefore have similar or the same length and width parameter values. The actual shape of each light and dark patch could be modeled as circular or square as a first estimate, with the use of tolerance to detect any mottled components with a more irregular shape. The construction of a small prototype would be useful to detected mottled regions, and by sliding this prototypical template about the image using a computer algorithm, and correlating template to image at each window location, the extent of the mottled region can then be determined.

RESULTS

In this work, several currently proposed methods were described for the detection and measurement of villous atrophy in the small intestinal mucosa by means of quantitative analysis of video capsule images. These methods can be subdivided into statistical and syntactic types of analyses. Both types of analyses seek to automatically detect abnormalities in the endoscopic images. The statistical methods are useful to analyze the entire image, or to analyze predefined portions of it, and to determine whether the statistics are substantially different with respect to control images. Statistical parameters can be compared from one segment, or subimage, to another in a particular endoscopic image, as well as from one endoscopic image to the next over a series of images, as they are obtained from the video capsule when it progresses along the small intestinal lumen. Using a threshold level for each statistical parameter, it is possible to automatically detect the presence of abnormal image regions and/or abnormal locations along the small intestinal lumen over a time lapse sequence of video capsule endoscopic images. Furthermore, the presence of gradients with varying

statistics, either along a single image or across a series of video capsule images, can possibly be detected and measured, though this must be shown in future work. Such gradients would be expected to be indicative of the presence of patchy villous atrophy in celiac patients. The resolution of the statistical measures is limited only by the video camera resolution, which has been steadily improving in recent years[32].

DISCUSSION

Summary

The advantages of syntactic or structural methods to detect the presence of villous atrophy were also described herein. Syntactic methods seek to model the structure of the small intestinal lumen based upon the presence of abnormal image features, which are indicative of pathology. Although actual villi located within the small intestine are difficult to detect at the current spatial resolution of video capsule camera systems, the manifestation of villous atrophy as structures in the small intestinal mucosa includes the presence of blunted protrusions, fissures, scalloped mucosal folds and a mottled or mosaic appearance of the mucosa. These structures are macroscopic, unlike the microscopic nature of the villi themselves, and can be detected by using appropriate prototypical templates. For simplicity, prototypical templates with fixed parameters can be used, with a tolerance added to all template parameters, so that features which are slightly out of proportion can still be detected. Once abnormal features are detected, they can be analyzed in terms of their density, shape and gray level characteristics, and gradients across individual endoscopic images and along a sequence of images can be determined.

Based on the above measures, automatic detection of regions with pathology indicative of villous atrophy in untreated celiac disease patients may soon be realized, even when the pathology is subtle or variable, and patchy in appearance. By mapping these structures, it would be possible to determine the extent of the pathology, and the change in pathologic region and content during the treatment of the disease.

Other methods

Although the methods described herein were limited to analysis of video capsule endoscopy images, other techniques can be used to potentially improve the detection of pathologic features. In the method of chromoendoscopy, dyes are sprayed onto the mucosal surface *via* a working channel of the endoscope to enable detailed evaluation of the mucosal surface at high magnification[33]. Fujinon intelligent chromoendoscopy assisted capsule endoscopy is useful to evaluate patients with obscure gastroenterology bleeding[34,35]. Furthermore, narrow-band imaging is capable of predicting the histological characteristics such as those present in gastric cancer lesions[36]. Optical coherence tomography has been found useful for noninvasive cross-sectional imaging in biological systems[37]. The water-immersion technique may be utilized to minimize patient discomfort and to minimize the need for sedation in children and adults[38]. Confocal laser endomicroscopy is a technique that involves a miniaturized confocal microscope, and was initially developed and integrated in the distal tip of a conventional colonoscope[39,40]. High-resolution magnification endoscopy can reliably identify normal *vs* atrophic mucosal regions[41]. I-scan technology consists of three types of algorithms: Surface enhancement, contrast enhancement, and tone enhancement, and can lead to easier detection, diagnosis and treatment of gastrointestinal diseases[42].

Limitations

Currently, video capsule endoscopic imaging is constrained in several respects. Firstly, the images depend upon camera angle with respect to the small intestinal lumen, as well as on the illumination by the camera light source. Poor camera angle can result in an incorrect interpretation of the presence and degree of pathology. Furthermore, for syntactic analysis, the rendering of two-dimensional endoscopic images as three-dimensional constructs depends upon the inverse square law for light illumination, but nonlinearities may be introduced during the process. The nonlinearities can distort the actual small intestinal features and their dimensions, as observed using shape-from-shading principles. The spatial resolution of each image depends on the camera lens to small intestinal mucosal surface distance, which is variable from image to image and even in a single image, whenever the camera angle to mucosal surface angle is not normal, *i.e.,* the light source is not pointed precisely perpendicular to the mucosal surface. For quantitative analysis, color images are typically converted to grayscale level for simplicity. For improved analysis, use of the tricolor image information may be helpful to detect subtle features of villous atrophy, a subject for future investigation.

COMMENTS

Background

This research is of potential importance to treat celiac disease, a common malady. The main symptom used to diagnose villous atrophy is the presence of villous atrophy in the small intestine. The villous atrophy can be subtle and patchy; therefore computerized means may be better at detecting and assessing the severity.

Research frontiers

Quantitative research on analysis of celiac disease using video capsule endoscopy is a new field. Only for the last 12 or so years has this technology been available. In recent versions, time and spatial resolution is markedly improving so that subtle details can be observed without the need for light microscopy.

Innovations and breakthroughs

The use of the video capsule is an improvement over standard endoscopy, because it travels throughout the gastrointestinal tract, not just at the proximal portions. It is also less invasive to the patient and can be used for pediatric patients.

Applications

This methodology could possibly be used with online video capsule software to detect villous atrophy as the capsule travels passively along the gastrointestinal tract. In future manifestations, should biopsy become available, a biopsy could be taken at each region in which villous atrophy is detected.

Terminology

Celiac disease is an autoimmune disease in which the patient is reactive to the protein gluten, which is found in wheat, rye, and barley grains. A video capsule is a device with camera which takes images at 2 frames or more per second and transmits them *via* radio link as it passes through the gastrointestinal tract.

Peer-review

This study was peer-reviewed by both clinical specialists and bioengineering specialists. The reviews were generally quite favorable. Improvements have been made in describing the data analysis and clinical setting.

REFERENCES

1 **Green PH**, Jabri B. Celiac disease. *Annu Rev Med* 2006; **57**: 207-221 [PMID: 16409146 DOI: 10.1146/annurev.med.57.051804.122404]

2 **Cataldo F**, Montalto G. Celiac disease in the developing countries: a new and challenging public health problem. *World J Gastroenterol* 2007; **13**: 2153-2159 [PMID: 17465493]

3 **Dickson BC**, Streutker CJ, Chetty R. Coeliac disease: an update for pathologists. *J Clin Pathol* 2006; **59**: 1008-1016 [PMID: 17021129 DOI: 10.1136/jcp.2005.035345]

4 **Ciaccio EJ**, Bhagat G, Tennyson CA, Lewis SK, Hernandez L, Green PH. Quantitative assessment of endoscopic images for degree of villous atrophy in celiac disease. *Dig Dis Sci* 2011; **56**: 805-811 [PMID: 20844959 DOI: 10.1007/s10620010137 16]

5 **Corazza GR**, Villanacci V, Zambelli C, Milione M, Luinetti O, Vindigni C, Chioda C, Albarello L, Bartolini D, Donato F. Comparison of the interobserver reproducibility with different histologic criteria used in celiac disease. *Clin Gastroenterol Hepatol* 2007; **5**: 838-843 [PMID: 17544877 DOI: 10.1016/j.cgh.2007.03.019]

6 **Gonzalez S**, Gupta A, Cheng J, Tennyson C, Lewis SK, Bhagat G, Green PH. Prospective study of the role of duodenal bulb biopsies in the diagnosis of celiac disease. *Gastrointest Endosc* 2010; **72**: 758-765 [PMID: 20883853 DOI: 10.1016/j.gie.2010.06.026]

7 **Lee SK**, Green PH. Endoscopy in celiac disease. *Curr Opin Gastroenterol* 2005; **21**: 589-594 [PMID: 16093775]

8 **Penny HA**, Mooney PD, Burden M, Patel N, Johnston AJ, Wong SH, Teare J, Sanders DS. High definition endoscopy with or without IScan increases the detection of celiac disease during routine endoscopy. *Dig Liver Dis* 2016; **48**: 644-649 [PMID: 26995214 DOI: 10.1016/j.dld.2016.02.009]

9 **Bouchard S**, Ibrahim M, Van Gossum A. Video capsule endoscopy: perspectives of a revolutionary technique. *World J Gastroenterol* 2014; **20**: 17330-17344 [PMID: 25516644 DOI: 10.3748/wjg.v20.i46.17330]

10 **Van Weyenberg SJ**, Smits F, Jacobs MA, Van Turenhout ST, Mulder CJ. Video capsule endoscopy in patients with nonresponsive celiac disease. *J Clin Gastroenterol* 2013; **47**: 393-399 [PMID: 23164686 DOI: 10.1097/MCG.0b013e31826bea12]

11 **Ibrahim M**, Van Gossum A. Novel imaging enhancements in capsule endoscopy. *Gastroenterol Res Pract* 2013; **2013**: 304-723 [PMID: 23878532 DOI: 10.1155/2013/304723]

12 **Fisher LR**, Hasler WL. New vision in video capsule endoscopy: current status and future directions. *Nat Rev Gastroenterol Hepatol* 2012; **9**: 392-405 [PMID: 22565098 DOI: 10.1038/nrgastro.2012.88]

13 **Ciaccio EJ**, Tennyson CA, Lewis SK, Krishnareddy S, Bhagat G, Green PH. Distinguishing patients with celiac disease by quantitative analysis of video capsule endoscopy images. *Comput Methods Programs Biomed* 2010; **100**: 39-48 [PMID: 20356648 DOI: 10.1016/j.cmpb.2010.02.005]

14 **Ciaccio EJ**, Tennyson CA, Bhagat G, Lewis SK, Green PH. Classification of video capsule endoscopy image patterns: comparative analysis between patients with celiac disease and normal individuals. *Biomed Eng Online* 2010; **9**: 44 [PMID: 20815911 DOI: 10.1186/1475925X944]

15 **Ciaccio EJ**, Tennyson CA, Bhagat G, Lewis SK, Green PH. Transformation of video capsule images to detect small bowel mucosal differences in celiac versus control patients. *Comput Methods Programs Biomed* 2012; **108**: 28-37 [PMID: 22284703 DOI: 10.1016/j.cmpb.2011.12.008]

16 **Ciaccio EJ**, Tennyson CA, Bhagat G, Lewis SK, Green PH. Quantitative estimates of motility from video capsule endoscopy are useful to discern celiac patients from controls. *Dig Dis Sci* 2012; **57**: 2936-2943 [PMID: 22644741 DOI: 10.1007/s1062001222251]

17 **Ciaccio EJ**, Lewis SK, Green PH. Detection of villous atrophy using endoscopic images for the diagnosis of celiac disease. *Dig Dis Sci* 2013; **58**: 1167-1169 [PMID: 23525733 DOI: 10.1007/s1062001326189]

18 **Ciaccio EJ**, Tennyson CA, Bhagat G, Lewis SK, Green PH. Use of shape-from-shading to estimate three-dimensional architecture in the small intestinal lumen of celiac and control patients. *Comput Methods Programs Biomed* 2013; **111**: 676-684 [PMID: 23816252 DOI: 10.1016/j.cmpb.2013.06.002]

19 **Ciaccio EJ**, Tennyson CA, Bhagat G, Lewis SK, Green PH. Implementation of a polling protocol for predicting celiac disease in video capsule analysis. *World J Gastrointest Endosc* 2013; **5**: 313-322 [PMID: 23858375 DOI: 10.4253/wjge.v5.i7.313]

20 **Lee AR**, Ng DL, Diamond B, Ciaccio EJ, Green PH. Living with coeliac disease: survey results from the U.S.A. *J Hum Nutr Diet* 2012; **25**: 233-238 [PMID: 22364496 DOI: 10.1111/j.1365277X.2012.01236.x]

21 **Lebwohl B**, Granath F, Ekbom A, Montgomery SM, Murray JA, Rubio-Tapia A, Green PH, Ludvigsson JF. Mucosal healing and mortality in coeliac disease. *Aliment Pharmacol Ther* 2013; **37**: 332-339 [PMID: 23190299 DOI: 10.1111/apt.12164]

22 **Vécsei A**, Amann G, Hegenbart S, Liedlgruber M, Uhl A. Automated Marsh-like classification of celiac disease in children using local texture operators. *Comput Biol Med* 2011; **41**: 313-325 [PMID: 21513927 DOI: 10.1016/j.compbiomed.2011.03.009]

23 **Hegenbart S**, Uhl A, Vécsei A, Wimmer G. Scale invariant texture descriptors for classifying celiac disease. *Med Image Anal* 2013; **17**: 458-474 [PMID: 23481171 DOI: 10.1016/j.media.2013.02.001]

24 **Fernandez-Urien I**, Carretero C, Borobio E, Borda A, Estevez E, Galter S, GonzalezSuarez B, Gonzalez B, Lujan M, Martinez JL, Martínez V, Menchén P, Navajas J, Pons V, Prieto C, Valle J. Capsule endoscopy capture rate: has 4 frames-per-second any impact over 2 frames-per-second? *World J Gastroenterol* 2014; **20**: 14472-14478 [PMID: 25339834 DOI: 10.3748/wjg.v20.i39.14472]

25 **Adler SN**, Bjarnason I. What we have learned and what to expect from capsule endoscopy. *World J Gastrointest Endosc* 2012; **4**: 448-452 [PMID: 23189215 DOI: 10.4253/wjge.v4.i10.448]

26 **Alaedini A**, Green PH. Narrative review: celiac disease: understanding a complex autoimmune disorder. *Ann Intern Med* 2005; **142**: 289-298 [PMID: 15710962]

27 **Kurien M**, Evans KE, Hopper AD, Hale MF, Cross SS, Sanders DS. Duodenal bulb biopsies for diagnosing adult celiac disease: is there an optimal biopsy site? *Gastrointest Endosc* 2012; **75**: 1190-1196 [PMID: 22624810 DOI: 10.1016/j.gie.2012.02.025]

28 **Ciaccio EJ**, Bhagat G, Lewis SK, Green PH. Quantitative image analysis of celiac disease. *World J Gastroenterol* 2015; **21**: 2577-2581 [PMID: 25759524 DOI: 10.3748/wjg.v21.i9.2577]

29 **Goenka MK**, Majumder S, Goenka U. Capsule endoscopy: Present status and future expectation. *World J Gastroenterol* 2014; **20**: 10024-10037 [PMID: 25110430 DOI: 10.3748/wjg.v20.i29.10024]

30 **Ianiro G**, Gasbarrini A, Cammarota G. Endoscopic tools for the diagnosis and evaluation of celiac disease. *World J Gastroenterol* 2013; **19**: 8562-8570 [PMID: 24379573 DOI: 10.3748/wjg.v19.i46.8562]

31 **Hegenbart S**, Uhl A, Vécsei A. Survey on computer aided decision support for diagnosis of celiac disease. *Comput Biol Med* 2015; **65**: 348-358 [PMID: 25770906 DOI: 10.1016/j.compbiomed.2015.02.007]

32 **Koprowski R**. Overview of technical solutions and assessment of

clinical usefulness of capsule endoscopy. *Biomed Eng Online* 2015; **14**: 111 [PMID: 26626725 DOI: 10.1186/s1293801501083]
33 **Jung M**, Kiesslich R. Chromoendoscopy and intravital staining techniques. *Baillieres Best Pract Res Clin Gastroenterol* 1999; **13**: 11-19 [PMID: 11030630]
34 **Pohl J**, May A, Rabenstein T, Pech O, NguyenTat M, Fissler-Eckhoff A, Ell C. Comparison of computed virtual chromoendoscopy and conventional chromoendoscopy with acetic acid for detection of neoplasia in Barrett's esophagus. *Endoscopy* 2007; **39**: 594-598 [PMID: 17611913 DOI: 10.1055/s2007966649]
35 **Gupta T**, Ibrahim M, Deviere J, Van Gossum A. Evaluation of Fujinon intelligent chromo endoscopy-assisted capsule endoscopy in patients with obscure gastroenterology bleeding. *World J Gastroenterol* 2011; **17**: 4590-4595 [PMID: 22147964 DOI: 10.3748/wjg.v17.i41.4590]
36 **Nakayoshi T**, Tajiri H, Matsuda K, Kaise M, Ikegami M, Sasaki H. Magnifying endoscopy combined with narrow band imaging system for early gastric cancer: correlation of vascular pattern with histopathology (including video). *Endoscopy* 2004; **36**: 1080-1084 [PMID: 15578298 DOI: 10.1055/s2004825961]
37 **Huang D**, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W, Hee MR, Flotte T, Gregory K, Puliafito CA. Optical coherence tomography. *Science* 1991; **254**: 1178-1181 [PMID: 1957169]
38 **Leung CW**, Kaltenbach T, Soetikno R, Wu KK, Leung FW, Friedland S. Water immersion versus standard colonoscopy insertion technique: randomized trial shows promise for minimal sedation. *Endoscopy* 2010; **42**: 557-563 [PMID: 20593332 DOI: 10.1055/s00291244231]
39 **Hoffman A**, Goetz M, Vieth M, Galle PR, Neurath MF, Kiesslich R. Confocal laser endomicroscopy: technical status and current indications. *Endoscopy* 2006; **38**: 1275-1283 [PMID: 17163333 DOI: 10.1055/s2006944813]
40 **Kiesslich R**, Goetz M, Neurath MF. Confocal laser endomicroscopy for gastrointestinal diseases. *Gastrointest Endosc Clin N Am* 2008; **18**: 451-466, viii [PMID: 18674696 DOI: 10.1016/j.giec.2008.03.002]
41 **Anagnostopoulos GK**, Yao K, Kaye P, Fogden E, Fortun P, Shonde A, Foley S, Sunil S, Atherton JJ, Hawkey C, Ragunath K. High-resolution magnification endoscopy can reliably identify normal gastric mucosa, Helicobacter pyloriassociated gastritis, and gastric atrophy. *Endoscopy* 2007; **39**: 202-207 [PMID: 17273960 DOI: 10.1055/s2006945056]
42 **Kodashima S**, Fujishiro M. Novel image-enhanced endoscopy with iscan technology. *World J Gastroenterol* 2010; **16**: 1043-1049 [PMID: 20205272 DOI: 10.3748/wjg.v16.i9.1043]

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ORIGINAL ARTICLE

Prospective Study

Prior minimal endoscopic sphincterotomy to prevent pancreatitis related to endoscopic balloon sphincteroplasty

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Author contributions: Kanazawa R and Sai JK contributed equally to this work; Kanazawa R collected and analyzed the data, and drafted the manuscript; Sai JK provided analytical oversightand designed and supervised the study; Watanabe S and Shiina S revised the manuscript for the important intellectual content; Ito T, Miura H, Ishii S, Saito H, Tomishima K, Shimizu R, Sato K and Hayashi M supported collecting the data; all authors have read and approved the final version to be published.

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Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at jinkans@juntendo.ac.jp. Participants gave informed consent was not obtained but the presented data are anonymized and risk of identification is low.

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Abstract

AIM

To investigate the efficacy of prior minimal endoscopic sphincterotomy (EST) to prevent pancreatitis related to endoscopic balloon sphincteroplasty (EBS).

METHODS

After bile duct access was gained and cholangiogram confirmed the presence of stones < 8 mm in the common bile duct at endoscopic retrograde cholangiography, patients were subjected to minimal EST (up to one-third of the size the papilla) plus 8 mm EBS (EST-EBS group). The incidence of pancreatitis and the difference in serum amylase level after the procedure were examined and compared with those associated with 8-mm EBS alone in 32 patients of historical control (control group).

RESULTS

One hundred and five patients were included in the EST-EBS group, and complete stone removal was accomplished in all of them. The difference in serum amylase level after the procedure was - 25.0 (217.9) IU/L in the EST-EBS group and this value was significantly lower than the 365.5 (576.3) IU/L observed in the control group (P < 0.001). The incidence of post-procedure pancreatitis was 0% (0/105) in the EST-EBS group and 15.6% (5/32) in the control group (P < 0.001).

CONCLUSION

Prior minimal EST might be useful to prevent the elevation of serum amylase level and the occurrence of pancreatitis related to EBS.

Key words: Choledocholithiasis; Adverse event; Pancreatitis; Endoscopic sphincterotomy; Endoscopic balloon sphincteroplasty

Core tip: We evaluated the efficacy of prior minimal endoscopic sphincterotomy (EST) to prevent pancreatitis related to endoscopic balloon sphincteroplasty (EBS). One hundred and five patients with bile duct stones < 8 mm were subjected to minimal EST (up to one-third of the size the papilla) plus 8 mm EBS (EST-EBS group). The incidence of pancreatitis and the difference in serum amylase level after the procedure were examined and compared with those associated with 8-mm EBS alone in 32 patients of historical control (control group). The difference in serum amylase level after the procedure in the EST-EBS group was significantly lower than that observed in the control group (P < 0.001). The incidence of post-procedure pancreatitis was 0% (0/105) in the EST-EBS group and 15.6% (5/32) in the control group (P < 0.001).

Kanazawa R, Sai JK, Ito T, Miura H, Ishii S, Saito H, Tomishima K, Shimizu R, Sato K, Hayashi M, Watanabe S, Shiina S. Prior minimal endoscopic sphincterotomy to prevent pancreatitis related to endoscopic balloon sphincteroplasty. *World J Gastrointest Endosc* 2016; 8(18): 663-668 Available from: URL: http://www.wjgnet.com/1948-5190/full/v8/i18/663.htm DOI: http://dx.doi.org/10.4253/wjge.v8.i18.663

INTRODUCTION

Preventing major adverse events related to endoscopic interventions to remove bile duct stones is a matter of great concern to endoscopists and patients. Endoscopic balloon sphincteroplasty (EBS) using a 6-8 mm balloon is associated with a lower frequency of hemorrhage and perforation compared with endoscopic sphincterectomy (EST)[1-4]. However, EBS alone is rarely performed these days because of the high risk of acute pancreatitis and concern for fatal pancreatitis[2,5,6]. Several studies have recently shown that EST plus large balloon sphincteroplasty (LBS) carries a low risk of post-procedure pancreatitis (0%-3%)[7,8], although there have been no comparative studies between LBS alone and EST followed by LBS.

In the present study, we investigated the efficacy of prior minimal EST (up to one third of the papilla) to prevent pancreatitis related to EBS by comparing a group subjected to EBS alone with another subjected to minimal EST followed by EBS.

MATERIALS AND METHODS

Patients

Between October 2010 and March 2014, patients aged 18 years or older were prospectively included in the current study after bile duct access was gained and cholangiogram confirmed the presence of bile duct stones (EST-EBS group). Patients were excluded if they had a history of EST or EBS, a choledochoduodenal fistula, concurrent hepatolithiasis, Billroth Ⅱ or Roux-en-Y anatomy, or a concomitant pancreatobiliary malignancy. Patients with conditions suggesting difficult bile duct cannulation, such as requirement of pancreatic guide-wire, pancreatic stent, precut sphincterotomy, pancreatic sphincterectomy or the Rendezvous technique for difficult bile duct access, were also excluded. Patients under anticoagulant therapy or with a coagulopathy (international normalized ratio > 1.3, partial thromboplastin time greater than twice that of control) and a platelet count of < 50000 × $10^3/\mu$L were excluded and subjected to EBS only. Patients with stones ⩾ 8 mm were subjected to limited EST (up to half of the papilla) plus LBS and excluded from the current study. The size of bile duct stones was measured on endoscopic retrograde cholangiopancreatography (ERCP) images corrected for magnification using the diameter of the endoscope as a reference.

As the historical control, 32 consecutive patients, who fulfilled the same inclusion criteria as the EST-EBS group and had undergone 8 mm EBS alone between November 2009 and December 2011, served as the control group.

Informed consent was obtained from all patients. The study was approved by the ethics committee of our institution.

Endoscopic procedure

ERCP was performed using a side-viewing duodenoscope (JF-240, JF-260V, TJF-260; Olympus, Tokyo, Japan). Electrocautery was carried out using a 120-watt endocut current (ERBE International, Erlangen, Germany)[9,10]. One of four trainees (> 100 ERCPs) accompanied by one specialist (> 10000 ERCPs) performed the procedures. Following preparation with pharyngeal anesthesia and intravenous injection of midazolam (0.06 mg/kg), ERCP was performed. After bile duct access

was gained and cholangiogram confirmed the presence of bile duct stones ≤ 8 mm, minimal EST followed by 8-mm EBS was performed. Minimal EST up to one third of the papilla was performed with a 30-mm-pull-type sphincterotome (Clever Cut 3; KD-V41M, Olympus) under the guidewire. EBS was performed with wire-guided hydrostatic balloon catheters (Eliminator, ConMed, NY; balloon length 3 cm, maximum inflated outer diameter 8 mm) placed across the papilla. The balloon was centered at the sphincter, and was dilated to the size of the lower bile duct or 8 mm, whichever was smaller. Inflation time was 30 s.

After the procedure, the stones were retrieved with an extraction balloon under the guidewire. When necessary, a mechanical lithotripter (Lithocrush, Olympus) was used to crush stones. An occlusion cholangiogram was obtained at the end of the procedure. Biliary stents or nasobiliary drains were placed when the stones were not completely removed. None of the patients had prophylactic pancreatic stents placed before or after the procedure.

Each patient was kept under fasting conditions after the procedure and was carefully monitored for the development of any adverse events. Physical examination and laboratory tests were performed daily after the procedure. Serum amylase was checked in all patients before and 24 h after the procedure. If the acute condition had settled and the serum concentration of amylase was below 375 IU/L (normal range: < 125 IU/L), the patient was allowed to take a meal.

Definitions of individual adverse events were similar to those given by Cotton *et al*[11]. The severity of adverse events was graded according to the length of hospitalization. Mild adverse events required 2 to 3 d of hospitalization; moderate adverse events required 4 to 10 d; and severe adverse events requiring more than 10 d of hospitalization[11,12]. Procedure-induced pancreatitis was defined as new or worsened abdominal pain associated with a serum concentration of amylase three or more times the upper limit of normal at 24 h after the procedure, requiring hospitalization or prolongation of planned admission[11,12]. Hemorrhage was considered clinically significant only if there was clinical evidence of bleeding, such as melena or hematemesis, with an associated decrease of at least 2 g per deciliter in hemoglobin concentration, or the need for a blood transfusion[11,12]. Cholangitis was diagnosed when there was right upper quadrant abdominal tenderness, body temperature of > 38 ℃, and elevated serum concentrations of liver enzymes. Acute cholecystitis was diagnosed based on suggestive clinical and radiographic signs. Perforation referred to retroperitoneal or bowel-wall perforation documented by any radiographic technique[11,12].

Outcome measurements

The incidences of procedure related pancreatitis and the differences in serum amylase levels from baseline at 24 h after the procedure were examined in both groups of patients. Secondary outcome measures included the stone clearance rate, and the number of ERCPs required for complete stone clearance. Complete stone clearance was defined as the absence of filling defects on the occlusion cholangiogram as noted by the endoscopists.

Statistical analysis

Statistical analyses were performed using statistical software (SPSS version 17.0 for Windows). Data were presented as the mean ± SD and were compared using paired *t* test. Mann-Whitney *U* test was used for comparing continuous data with skewed distribution in the two groups. A χ^2 test with Yate's correction was used to analyze gender. The difference in serum amylase level after the procedure and the incidence of post-procedure pancreatitis were compared using Wilcoxon signed-rank test. Statistical significance was defined as a P value < 0.05 (two tailed).

RESULTS

Among the 171 consecutive patients with choledocholithiasis who were enrolled in the current study, 8 patients were excluded for a history of EST and/or EBS, 1 was excluded for a choledochoduodenal fistula, 2 for concurrent hepatolithiasis, 6 for Billroth Ⅱ or Roux-en-Y anatomy, 2 for concomitant biliary malignancies, 13 were excluded for difficult bile duct canulation; besides, 8 patients who were under anticoagulant therapy or had a coagulopathy and 3 with a platelet count of < 50000 × 10^3/μL were also excluded. Twenty-three patients with stones larger than 8 mm were subjected to limited EST plus LBS (Figure 1).

Consequently, there were 105 patients in the EST-EBS group. The clinical characteristics of the patients in each group are shown in Table 1. The two groups were similar with respect to demographic features. Minimal EST plus 8 mm EBS was successfully performed in all patients. The waist of the balloon at the papilla was observed under fluoroscopic examination in both groups of patients during inflation of the balloon, and, after inflation, the waist remained in 9 (8.6%) patients of the EST-EBS group and 3 (8.7%) of the control group because of the stenosis or small diameter of the distal bile duct.

Complete duct clearance was accomplished in both groups of patients. The stones were completely removed in the first session in all patients of the EST-EBS group and in 27 (84.3%) of the control group (P < 0.001). The other 5 (15.7%) patients of the control group required 2 sessions. Mechanical lithotripsy was required in 2 (1.9%) patients of the EST-EBS group, and in one (4.3%) of the control group due to stenosis or small diameter of the distal bile duct (Table 2).

The mean (SD) serum amylase levels before and after the procedure were 148.2 (301.6) IU/L and 123.3 (138.7) IU/L in the EST-EBS group, and 164.5 (136.3)

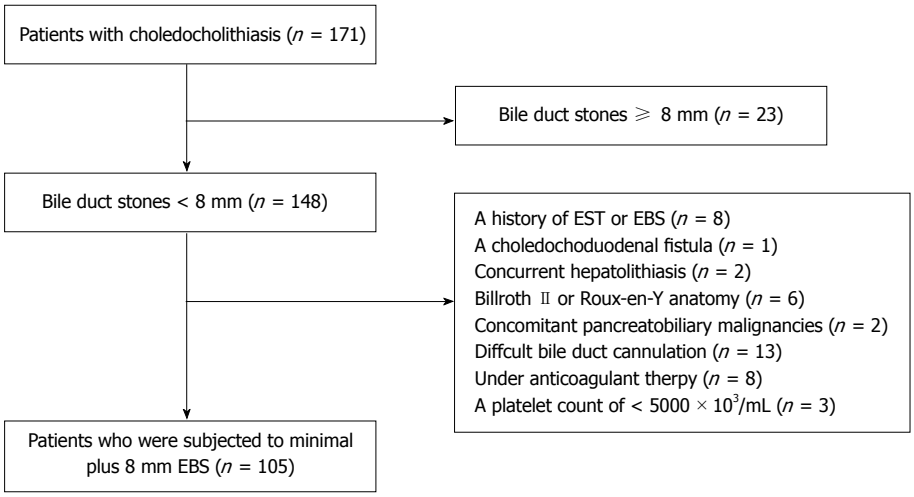

Figure 1 Flow chart of patients in this study. EST: Endoscopic sphincterotomy; EBS: Endoscopic balloon sphincteroplasty.

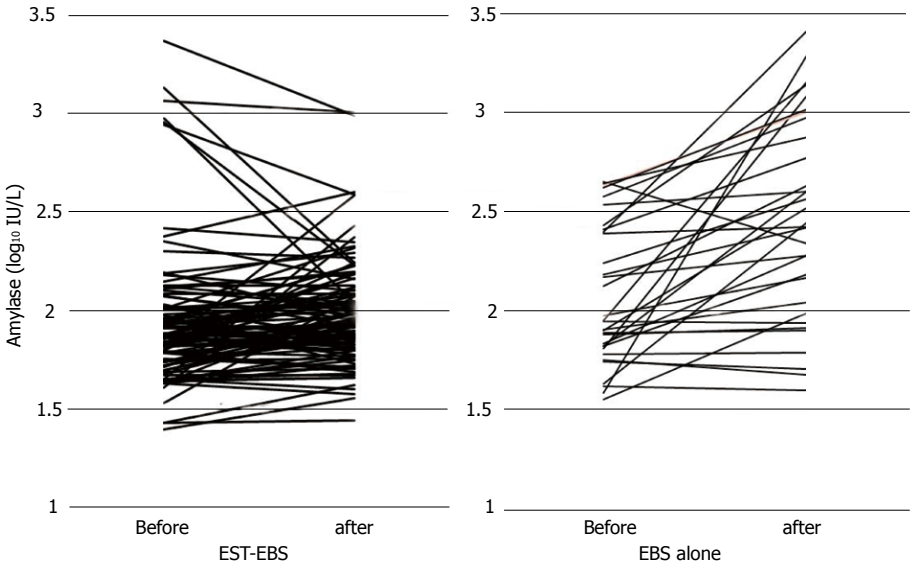

Figure 2 Difference in serum amylase level after the procedure in both groups of patients. The difference in control group was significantly higher than that in EST-EBS group ($P < 0.001$). EST: Endoscopic sphincterotomy; EBS: Endoscopic balloon sphincteroplasty.

IU/L and 530.4 (604.4) IU/L in the control group. The difference in serum amylase level after the procedure was - 25.0 (217.9) IU/L in the EST-EBS group and 365.5 (576.3) IU/L in the control group ($P < 0.001$) (Figure 2). The incidence of post-procedure pancreatitis was 0% (0/105) in the EST-EBS group and 15.6% (5/32) in the control group ($P < 0.001$). Cholangitis occurred in 3.1% (1/32) of the patients in the control group. None of the other patients in either group experienced any adverse event such as hemorrhage, perforation or cholecystitis within 7 d after the procedure.

DISCUSSION

EBS using a 6- to 8-mm balloon is associated with a lower frequency of hemorrhage and perforation compared with EST[1,2], and allows preservation of sphincter of Oddi function[3,4]. However, EBS alone has been associated with a high risk of acute pancreatitis[2,5,6]. In the study by Disario *et al*[6], pancreatitis occurred in 17.9% of patients subjected to EBS and in 3.3% of those subjected to EST; besides, 2 (1.7%) patients in the EBS group died because of severe pancreatitis. In addition, in five prospective randomized controlled trials of EBS *vs* EST[5,6,13-15], the incidence of pancreatitis after EBS varied between 4.9% and 20%. Furthermore, EBS was identified as an independent risk factor of post-ERCP pancreatitis in a large prospective multicenter study, including one death related to pancreatitis after EBS[16]. Therefore, it is necessary to modify the EBS technique to reduce the risk of pancreatitis.

EST plus LBS for the extraction of large bile duct stones has shown a low incidence of pancreatitis (0%-4.0%) in large-scale studies[8,9,17], although pancreatitis was thought to be closely related to balloon sphincteroplasty. Attasaranya *et al*[8]. suggested that

Table 1 Baseline characteristics of the patients

	EST-EBS (n = 105)	EBS alone (n = 32)	P value
Sex (female/male)	61/44	17/15	NS
Age (yr)	70.2 (29-83)	71.4 (28-88)	NS
Maximum CBD diameter (mm)	8.1 ± 4.5	7.7 ± 3.9	NS
Maximum stone diameter (mm)	6.6 ± 1.9	4.9 ± 1.8	NS
Stone number	2.1 ± 1.4	2.3 ± 1.7	NS
Serum amylase (IU/L)	148.2 ± 301.6	164.5 ± 136.3	NS
Periampullary diverticulum, n (%)	41 (32.5)	10 (31.7)	NS
Acute cholangitis before ERCP, n (%)	44 (16.6)	6 (21.8)	NS
Acute cholecystitis before ERCP, n (%)	3 (2.8)	1 (3.1)	NS

NS: Not significant; ERCP: Endoscopic retrograde cholangiopancreatography; EST: Endoscopic sphincterotomy; EBS: Endoscopic balloon sphincteroplasty; CBD: Common bile duct.

Table 2 Results of stone retrieval

	EST-EBS (n = 105)	EBS alone (n = 32)	P value
n (%) sessions required			
1	105 (100)	27 (84.3)	< 0.001
2		5 (15.7)	
Complete removal, n (%)	105 (100)	32 (100)	NS
Mechanical lithotripsy, n (%)	2 (1.9)	1 (4.3)	NS
Pancreatogram, n (%)	34 (32.7)	10 (31.2)	NS
Serum amylase (IU/L)	-25.0 ± 217.9	365.5 ± 576.3	< 0.001
Post procedure pancreatitis	0 (0)	5 (15.6)	< 0.001

NS: Not significant; EST: Endoscopic sphincterotomy; EBS: Endoscopic balloon sphincteroplasty.

EST performed before LBS may result in a separation between the pancreatic and biliary orifices, and balloon dilation forces that are exerted away from the pancreatic duct might lead to a lower risk of postprocedure pancreatitis compared with EBS alone.

In the current study, we performed minimal EST before 8-mm EBS in 105 patients with bile duct stones ⩽ 8 mm in diameter. We successfully extracted the stones in all the patients with none of them experiencing post-procedure pancreatitis. Furthermore, in this group the difference in serum amylase level between the baseline value and that after the procedure was significantly lower and the incidence of post-procedure pancreatitis was significantly lower compared with the control group subjected to EBS alone. The objective of minimal EST was to separate the pancreatic orifice from the biliary orifice to prevent pancreatitis related to EBS, and to avoid bleeding and perforation related to standard EST. The objective of EBS after EST was to maximize the biliary sphincterotomy orifice and thereby enable free access of a retrieval balloon catheter or basket to the common channel. Actually, all patients in the current study showed a waist at the papilla during balloon dilation after minimal EST, and if the sphincter is not dilated by a balloon, resistance may occur at the biliary outlet during retrieval of the stone using a basket or retrieval balloon catheter; besides papillary edema or spasm may obstruct the flow of pancreatic juice and the pancreas would be injured as a result of these manipulations[18].

There are some limitations in comparing the current data with previous data from the viewpoint of efficacy and safety. First, the procedure for endotherapy of bile duct stones may depend on the endoscopist, although a trainee attempted the procedure and was supported by an expert on each occasion in our study. Second, our series included patients with a mean age of 70 years, whereas the median age was 49 years in the prospective multicenter trial done in the United States that showed a higher rate of pancreatitis after EBS[6]. Therefore the risk associated with minimal EST plus EBS in younger patients was not fully estimated in the current study. Third, the true advantage of one technique over the other can only be assessed in a randomized controlled trial, while the current study was conducted prospectively and the results were compared with a historical control. Fourth, although minimal EST plus 8-mm EBS resulted in a high cost due to the use of a balloon catheter and a sphincterotomy knife, preventing post-procedure pancreatitis was undoubtedly worth the higher cost. Fifth, long-term adverse events including cholangitis, recurrence of bile duct stones, and cholecystitis are an important problem and should be assessed in future studies.

In conclusion, prior minimal EST is expected to significantly reduce the risk of pancreatitis related to EBS for the treatment of patients with bile duct stones. Further studies involving a larger series of patients are required to confirm the reliability of the present results.

COMMENTS

Background

Endoscopic balloon sphincteroplasty (EBS) is associated with lower frequency of bleeding and perforation compared with endoscopic sphincterotomy (EST), as well as preservation of sphincter of Oddi function. But, EBS has a higher risk of acute pancreatitis and concern for fatal pancreatitis. It is necessary to modify the EBS technique to reduce the risk of pancreatitis.

Innovations and breakthroughs

Prior minimal EST is expected to significantly reduce the risk of pancreatitis related to EBS for the treatment of patients with bile duct stones.

Applications

The paper may interest readers because prior minimal EST might be useful to prevent the elevation of serum amylase level and the occurrence of pancreatitis related to EBS.

Terminology

The objective of minimal EST was to separate the pancreatic orifice from the biliary orifice to prevent pancreatitis related to EBS, and to avoid bleeding and perforation related to standard EST. The objective of EBS after EST was to maximize the biliary sphincterotomy orifice and thereby enable free access of a retrieval balloon catheter or basket to the common channel.

Peer-review

In this article, the authors found that the prior minimal EST might be useful to prevent the elevation of serum amylase level and the occurrence of pancreatitis.

This new method would maybe reduce the risk of post ERCP pancreatitis. This is a well-written paper containing interesting results which merit publication.

REFERENCES

1 **Staritz M**, Ewe K, Meyer zum Büschenfelde KH. Endoscopic papillary dilation (EPD) for the treatment of common bile duct stones and papillary stenosis. *Endoscopy* 1983; **15** Suppl 1: 197-198 [PMID: 6872989 DOI: 10.1055/s-2007-1021507]

2 **Baron TH**, Harewood GC. Endoscopic balloon dilation of the biliary sphincter compared to endoscopic biliary sphincterotomy for removal of common bile duct stones during ERCP: a metaanalysis of randomized, controlled trials. *Am J Gastroenterol* 2004; **99**: 1455-1460 [PMID: 15307859 DOI: 10.1111/j.1572-0241.2004.30151.x]

3 **Yasuda I**, Tomita E, Enya M, Kato T, Moriwaki H. Can endoscopic papillary balloon dilation really preserve sphincter of Oddi function? *Gut* 2001; **49**: 686-691 [PMID: 11600473 DOI: 10.1136/gut.49.5.686]

4 **Sato H**, Kodama T, Takaaki J, Tatsumi Y, Maeda T, Fujita S, Fukui Y, Ogasawara H, Mitsufuji S. Endoscopic papillary balloon dilatation may preserve sphincter of Oddi function after common bile duct stone management: evaluation from the viewpoint of endoscopic manometry. *Gut* 1997; **41**: 541-544 [PMID: 9391256 DOI: 10.1136/gut.41.4.541]

5 **Fujita N**, Maguchi H, Komatsu Y, Yasuda I, Hasebe O, Igarashi Y, Murakami A, Mukai H, Fujii T, Yamao K, Maeshiro K. Endoscopic sphincterotomy and endoscopic papillary balloon dilatation for bile duct stones: A prospective randomized controlled multicenter trial. *Gastrointest Endosc* 2003; **57**: 151-155 [PMID: 12556774 DOI: 10.1067/mge.2003.56]

6 **Disario JA**, Freeman ML, Bjorkman DJ, Macmathuna P, Petersen BT, Jaffe PE, Morales TG, Hixson LJ, Sherman S, Lehman GA, Jamal MM, Al-Kawas FH, Khandelwal M, Moore JP, Derfus GA, Jamidar PA, Ramirez FC, Ryan ME, Woods KL, Carr-Locke DL, Alder SC. Endoscopic balloon dilation compared with sphincterotomy for extraction of bile duct stones. *Gastroenterology* 2004; **127**: 1291-1299 [PMID: 15520997 DOI: 10.1053/j.gastro.2004.07.017]

7 **Ersoz G**, Tekesin O, Ozutemiz AO, Gunsar F. Biliary sphincterotomy plus dilation with a large balloon for bile duct stones that are difficult to extract. *Gastrointest Endosc* 2003; **57**: 156-159 [PMID: 12556775 DOI: 10.1067/mge.2003.52]

8 **Attasaranya S**, Cheon YK, Vittal H, Howell DA, Wakelin DE, Cunningham JT, Ajmere N, Ste Marie RW, Bhattacharya K, Gupta K, Freeman ML, Sherman S, McHenry L, Watkins JL, Fogel EL, Schmidt S, Lehman GA. Large-diameter biliary orifice balloon dilation to aid in endoscopic bile duct stone removal: a multicenter series. *Gastrointest Endosc* 2008; **67**: 1046-1052 [PMID: 18178208 DOI: 10.1016/j.gie.2007.08.047]

9 **Maydeo A**, Bhandari S. Balloon sphincteroplasty for removing difficult bile duct stones. *Endoscopy* 2007; **39**: 958-961 [PMID: 17701853 DOI: 10.1055/s-2007-966784]

10 **Mariani A**, Di Leo M, Giardullo N, Giussani A, Marini M, Buffoli F, Cipolletta L, Radaelli F, Ravelli P, Lombardi G, D'Onofrio V, Macchiarelli R, Iiritano E, Le Grazie M, Pantaleo G, Testoni PA. Early precut sphincterotomy for difficult biliary access to reduce post-ERCP pancreatitis: a randomized trial. *Endoscopy* 2016; **48**: 530-535 [PMID: 26990509 DOI: 10.1055/s-0042-102250]

11 **Cotton PB**, Lehman G, Vennes J, Geenen JE, Russell RC, Meyers WC, Liguory C, Nickl N. Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 1991; **37**: 383-393 [PMID: 2070995 DOI: 10.1016/S0016-5107(91)70740-2]

12 **Freeman ML**, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, Moore JP, Fennerty MB, Ryan ME, Shaw MJ, Lande JD, Pheley AM. Complications of endoscopic biliary sphincterotomy. *N Engl J Med* 1996; **335**: 909-918 [PMID: 8782497 DOI: 10.1056/NEJM199609263351301]

13 **Bergman JJ**, Rauws EA, Fockens P, van Berkel AM, Bossuyt PM, Tijssen JG, Tytgat GN, Huibregtse K. Randomised trial of endoscopic balloon dilation versus endoscopic sphincterotomy for removal of bileduct stones. *Lancet* 1997; **349**: 1124-1129 [PMID: 9113010 DOI: 10.1016/S0140-6736(96)11026-6]

14 **Vlavianos P**, Chopra K, Mandalia S, Anderson M, Thompson J, Westaby D. Endoscopic balloon dilatation versus endoscopic sphincterotomy for the removal of bile duct stones: a prospective randomised trial. *Gut* 2003; **52**: 1165-1169 [PMID: 12865276 DOI: 10.1136/gut.52.8.1165]

15 **Arnold JC**, Benz C, Martin WR, Adamek HE, Riemann JF. Endoscopic papillary balloon dilation vs. sphincterotomy for removal of common bile duct stones: a prospective randomized pilot study. *Endoscopy* 2001; **33**: 563-567 [PMID: 11473325 DOI: 10.1055/s-2001-15307]

16 **Freeman ML**, DiSario JA, Nelson DB, Fennerty MB, Lee JG, Bjorkman DJ, Overby CS, Aas J, Ryan ME, Bochna GS, Shaw MJ, Snady HW, Erickson RV, Moore JP, Roel JP. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. *Gastrointest Endosc* 2001; **54**: 425-434 [PMID: 11577302 DOI: 10.1067/mge.2001.117550]

17 **Heo JH**, Kang DH, Jung HJ, Kwon DS, An JK, Kim BS, Suh KD, Lee SY, Lee JH, Kim GH, Kim TO, Heo J, Song GA, Cho M. Endoscopic sphincterotomy plus large-balloon dilation versus endoscopic sphincterotomy for removal of bile-duct stones. *Gastrointest Endosc* 2007; **66**: 720-726; quiz 768, 771 [PMID: 17905013 DOI: 10.1016/j.gie.2007.02.033]

18 **Jeong S**, Ki SH, Lee DH, Lee JI, Lee JW, Kwon KS, Kim HG, Shin YW, Kim YS. Endoscopic large-balloon sphincteroplasty without preceding sphincterotomy for the removal of large bile duct stones: a preliminary study. *Gastrointest Endosc* 2009; **70**: 915-922 [PMID: 19647241 DOI: 10.1016/j.gie.2009.04.042]

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CASE REPORT

Same site submucosal tunneling for a repeat per oral endoscopic myotomy: A safe and feasible option

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Author contributions: Wehbeh AN and Mekaroonkamol P conducted the literature review; Wehbeh AN, Mekaroonkamol P and Cai Q drafted and edited the manuscript, and approved the final version submitted; Cai Q captured the images and is the guarantor of the article.

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Informed consent statement: Patient gave informed consent prior to getting the procedure done.

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Abstract

Per oral endoscopic myotomy (POEM) is a novel endoscopic procedure for achalasia treatment. Due to its novelty and high success rates, a repeat procedure is usually not warranted, making the feasibility and safety of such approach unknown. We report the first case of a successful repeat POEM done at the same site of a previously uncompleted POEM. An 84-year-old female with type 2 achalasia presented for a POEM procedure. The procedure was aborted at the end of tunneling and before myotomy due to hypotension, which later resolved spontaneously. POEM was re-attempted at the same site of the original tunnel 1 year afterward, and surprisingly we didn't encounter any submucosal fibrosis. The procedure felt similar to a native POEM and a myotomy was performed uneventfully. Our case is the first to suggest that submucosal tunneling during a repeat POEM can be done at the same site. Hypotension during POEM is a rare complication that should be recognized as a potential result of tension capnothorax, it can however, be managed with close supportive care.

Key words: Per oral endoscopic myotomy; Achalasia; Myotomy; Submucosal tunnel; Repeat procedure; Submucosal fibrosis

Core tip: Per oral endoscopic myotomy (POEM) is a novel method of treating achalasia. More is being learnt about potential complications as it increases in popularity. This is the first case of a repeat submucosal tunneling done at the same site of a prior POEM

attempt which was aborted just before myotomy. No complications or difficulties were encountered during the second attempt. This may suggest that submucosal tunneling does not cause fibrosis, and that repeat POEM after a technically unsuccessful attempt could be done at the same site and orientation of the original tunnel.

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INTRODUCTION

Per oral endoscopic myotomy (POEM) is a novel endoscopic procedure for achalasia treatment. The principle techniques involve endoscopic submucosal tunneling followed by a myotomy[1]. Overall, it has success rates reportedly ranging between 82% to 100% and can be safely performed with a small number of reported major complications[1-3]. However, one of the complications that can occur is hemodynamic instability, which has been reported in up to 20% of patients in one study[4]. Due to its novelty and the high success rates, repeat procedure is rarely warranted, making the feasibility and safety of such approach unknown. Here, we report the first case of a repeat submucosal tunneling successfully performed at the same site of a previous POEM procedure.

CASE REPORT

An 84-year-old female presented with progressive dysphagia to both solids and liquids and failure to thrive over several months. Her other medical problems included gastroesophageal reflux disease, hypertension, deep vein thrombosis, severe osteoarthritis of both hips, lower extremities contracture, and chronic low back pain. Initial laboratory work up was essentially unrevealing. Manometry study confirmed severe achalasia type 2. The decision was made to proceed with POEM procedure. During endoscopy, she was placed in supine position which was standard practice at our institution. Incision site was first injected with a premixed solution of saline and methylene blue (5 mL/500 mL) followed by careful dissection to the submucosal layer using a triangle-tip knife. A submucosal tunnel was being made from the incision site to 2 cm distal to the cardia, but after a complete submucosal tunneling process just before myotomy (Figure 1), she developed severe hypotension and bradycardia. Consequently, the procedure was aborted. Chest X-ray revealed left apical pneumothorax, pneumomediastinum, pneumoperitoneum, and extensive subcutaneous emphysema. Her hypotension resolved with supportive care within minutes of aborting the procedure. A gastrografin swallow study was obtained which did not show any evidence of contrast leakage, but it demonstrated a grossly dilated esophagus consistent with achalasia, and postoperative edema with slow emptying at the gastroesophageal junction (Figure 2). Thereafter, she underwent an upper endoscopy with Botulinum injection every 2-3 mo but eventually her symptoms stopped responding to botulinum treatment. Repeat POEM was thus performed 1 year later. She was placed in the same supine position due to her medical comorbidities. A severely dilated sigmoid esophagus was observed (Figure 3A). The GE junction was tight, and some pressure was required to traverse the endoscope, consistent with known achalasia. Due to great difficulty orienting the endoscope on a different plane, submucosal incision was made at the exact same site (Figure 3C) of the original tunnel, and surprisingly we did not encounter any submucosal fibrosis or technical challenges. The repeat tunneling at the same submucosal plane was successfully completed and felt similar to a native POEM (Figure 4). A myotomy was quickly and uneventfully performed followed by mucosal closure with hemostatic clips (Figure 3). The length of the myotomy was 8 cm, which is the standard at our institution. At 4-wk follow up her symptoms remarkably improved, as shown by a decreased Eckhardt score from 9 to 4. Her reflux symptoms also remained stable on the same dose of omeprazole.

DISCUSSION

Our case is the first to highlight the feasibility and safety of performing a repeat POEM at a location where submucosal tunneling was previously performed. As discussed above, there are limited scenarios where repeat POEM would be considered. They include intra-procedural complications resulting in incomplete procedure, insufficient symptomatic relieve, and recurrent symptoms after an initial improvement[5]. The question remains as whether it is feasible to repeat a POEM procedure, and if so what would the best approach be.

POEM on a site of prior endoscopic mucosal resection is considered relatively contraindicated due to fear of encountering fibrosis[2]. Recent report on repeat POEM procedures opted to create submucosal tunnel at the opposite side of the scarred mucosectomy area due to concern for an obliterated submucosal space[5]. However, this did not apply to our case, meaning that submucosal fibrosis does not necessarily result from a first POEM attempt. Although theoretically myotomy may lead to fibrosis, but this hasn't been confirmed in the literature. In addition, myotomy is performed from 3 cm proximal to gastroesophageal junction and is therefore unlikely to impact the development of submucosal fibrosis in the proximal tunnel.

Moreover, the opposite site approach may not always be feasible due to different patient position and endoscopic orientation as in our case where patient position is very limited. Therefore, we opted for the

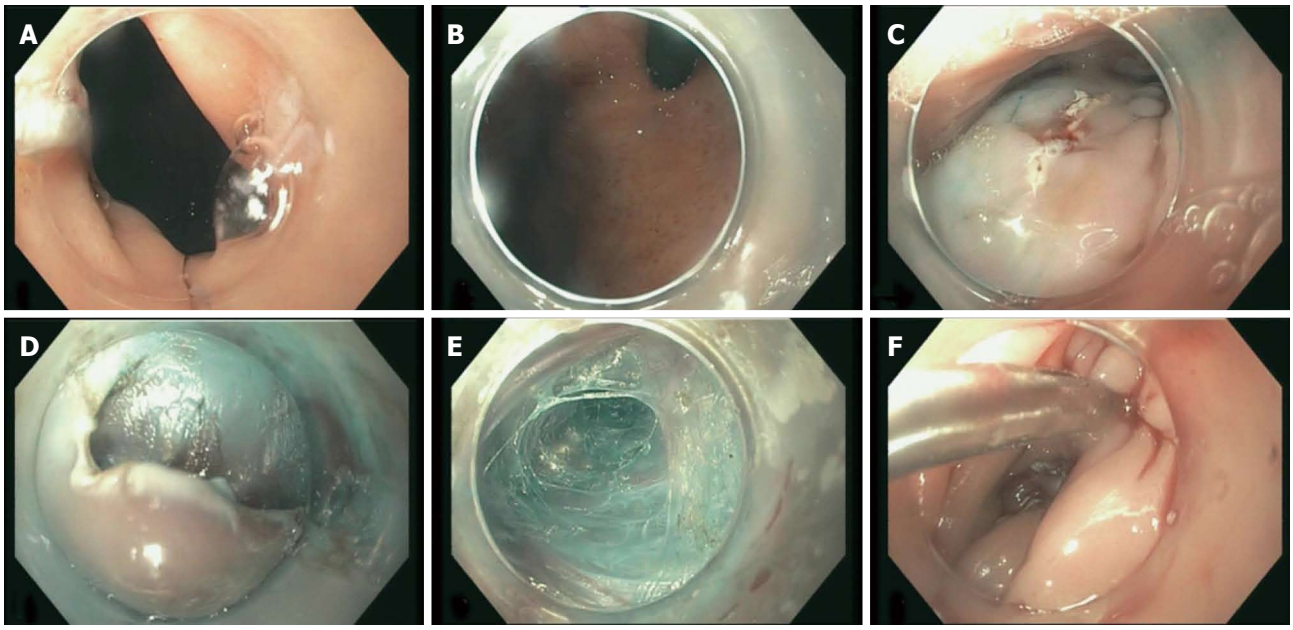

Figure 1 Endoscopic pictures from the first per oral endoscopic myotomy attempt showing: Gastroesophageal junction (A), cardia before myotomy (B), mucosotomy site (C), initial dissection site (D), creating the submucosal tunnel (E), and closure of mucosotomy (F).

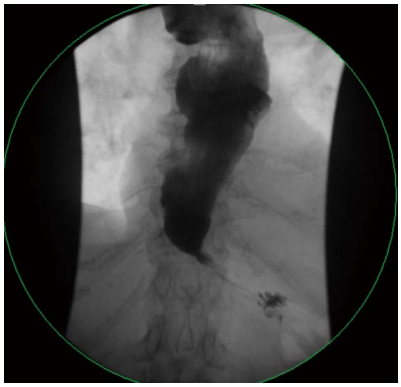

Figure 2 Gastrografin swallow study obtained after the index per oral endoscopic myotomy attempt showing a grossly distended esophagus consistent with achalasia, and postoperative edema with slow emptying at the gastroesophageal junction. No evidence of contrast leakage is seen.

same posterior approach as it allowed most flexible endoscopic maneuverability. Same site repeat POEM also preserves the opposite side of the esophagus for other potential procedures. Similar to our findings, double POEM was recently reported whereby tunneling was done more proximal to original tunnel to extend the myotomy[6].

Hypotension during POEM is a rare complication that should be recognized as a potential sign of tension capnothorax; it can however, be managed with close supportive care[7,8]. Other commonly reported physical findings include subcutaneous emphysema, mediastinal emphysema, and pneumoperitoneum without hemodynamic instability, all of which are believed to be normal physiologic reaction to the procedure[9].

In summary, this report suggests that should POEM need to be re-attempted, same site operation, including incision, submucosal tunneling and myotomy, is a viable method.

COMMENTS

Case characteristics

An 84-year-old female with progressive dysphagia to both solids and liquids and failure to thrive.

Clinical diagnosis

She had severely dilated sigmoid esophagus and tight gastroesophageal junction upon passing gastroscope, consistent with manometry-proven achalasia type 2.

Differential diagnosis

Differential includes esophageal cancer causing pseudoachalasia, stricture, extrinsic compressive mass, and esophagogastric junction outflow obstruction.

Laboratory diagnosis

Laboratory testing on initial presentation was essentially unremarkable.

Imaging diagnosis

No imaging was required to make the diagnosis. Manometry study revealed panesophageal pressurization and elevated integrated resting pressure, diagnostic of achalasia type 2.

Pathological diagnosis

Biopsy was not required to establish the diagnosis.

Treatment

Per oral endoscopic myotomy (POEM) was performed twice: the first submucosal tunneling was completed without myotomy due to hemodynamic instability. The second attempt was successfully performed *via* the same site tunneling.

Related reports

Only 2 other reports on repeat POEM were found, but neither of them reports on performing repeat submucosal tunneling on the same site and orientation of the original tunnel.

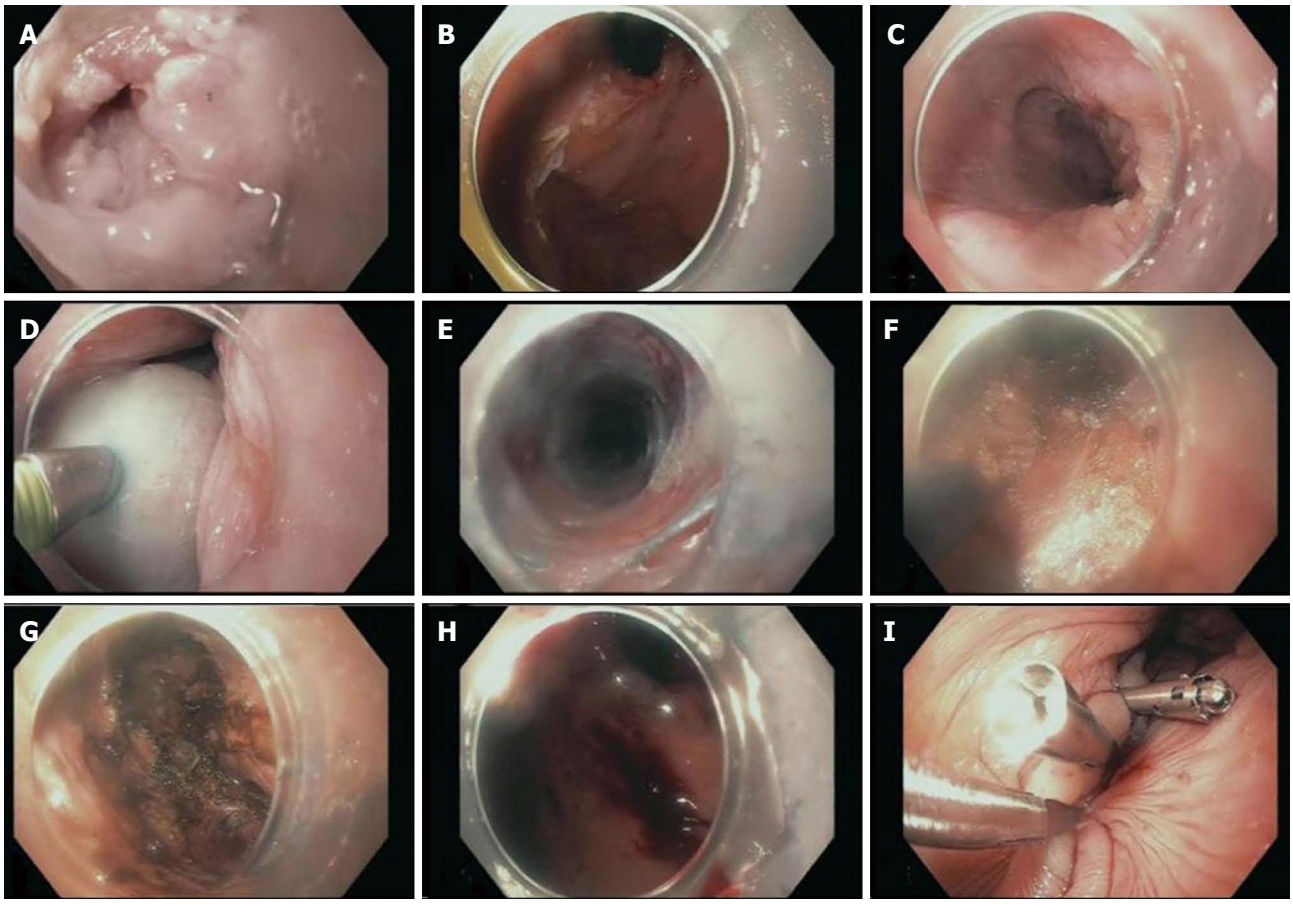

Figure 3 Endoscopic pictures taken from the repeat per oral endoscopic myotomy showing: sigmoid esophagus (A), cardia before myotomy (B), mucosa of previous dissection site (C), Mucosal bleb (D), submucosal tunneling (E), initial myotomy (F), completed myotomy (G), cardia after submucosal tunnneling (H), closure of mucosotomy (I).

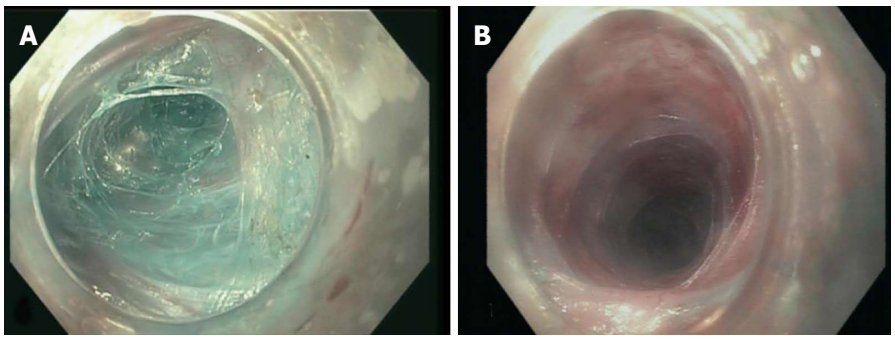

Figure 4 Comparison of submucosal tunnel of the index (A) and repeat (B) per oral endoscopic myotomy.

Peer-review

POEM has been demonstrated to be safe and effective for treating achalasia, regardless of the previous treatment history, including previous POEM therapy. Generally, the opposite site approach was recommended to avoid the potential fibrosis. In the present case, POEM was performed at exactly the same site of a previous POEM procedure.

REFERENCES

1 **Bechara R**, Ikeda H, Inoue H. Peroral endoscopic myotomy: an evolving treatment for achalasia. *Nat Rev Gastroenterol Hepatol* 2015; **12**: 410-426 [PMID: 26035678 DOI: 10.1038/nrgastro.2015.87]

2 **Stavropoulos SN**, Modayil RJ, Friedel D, Savides T. The International Per Oral Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global POEM experience. *Surg Endosc* 2013; **27**: 3322-3338 [PMID: 23549760 DOI: 10.1007/s00464-013-2913-8]

3 **Talukdar R**, Inoue H, Nageshwar Reddy D. Efficacy of peroral endoscopic myotomy (POEM) in the treatment of achalasia: a systematic review and meta-analysis. *Surg Endosc* 2015; **29**: 3030-3046 [PMID: 25539695 DOI: 10.1007/s00464-014-4040-6]

4 **Kurian AA**, Dunst CM, Sharata A, Bhayani NH, Reavis KM, Swanström LL. Peroral endoscopic esophageal myotomy: defining the learning curve. *Gastrointest Endosc* 2013; **77**: 719-725 [PMID: 23394838 DOI: 10.1016/j.gie.2012.12.006]

5 **Li QL**, Yao LQ, Xu XY, Zhu JY, Xu MD, Zhang YQ, Chen WF, Zhou PH. Repeat peroral endoscopic myotomy: a salvage option

for persistent/recurrent symptoms. *Endoscopy* 2016; **48**: 134-140 [PMID: 26349067 DOI: 10.1055/s-0034-1393095]
6 **Kumbhari V**, Tieu AH, Azola A, Saxena P, Ngamruengphong S, El Zein MH, Khashab MA. Double peroral endoscopic myotomy for achalasia. *Gastrointest Endosc* 2015; **82**: 953 [PMID: 26119650 DOI: 10.1016/j.gie.2015.05.036]
7 **Phillips S**, Falk GL. Surgical tension pneumothorax during laparoscopic repair of massive hiatus hernia: a different situation requiring different management. *Anaesth Intensive Care* 2011; **39**: 1120-1123 [PMID: 22165368]
8 **Tang A**, Huddleston P, Attaluri P, Cruz A, Joseph S, Lavy D. Clinical cases of nonsurgical pneumoperitoneum: categorizing the disease and treatment options. *Am Surg* 2015; **81**: E206-E208 [PMID: 25975311]
9 **Ren Z**, Zhong Y, Zhou P, Xu M, Cai M, Li L, Shi Q, Yao L. Perioperative management and treatment for complications during and after peroral endoscopic myotomy (POEM) for esophageal achalasia (EA) (data from 119 cases). *Surg Endosc* 2012; **26**: 3267-3272 [PMID: 22609984 DOI: 10.1007/s00464-012-2336-y]

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CASE REPORT

Plexiform angiomyxoid myofibroblastic tumor of stomach: A rare case

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Author contributions: Jonaitis L carried out the investigations, medical therapy and follow-up of the patient; Kiudelis M performed the surgery; Poskienė L made histological examination; Jonaitis L, Slepavicius P prepared the manuscript; all authors were involved in drafting and revising the manuscript.

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Abstract

Plexiform angiomyxoid myofibroblastic tumor (PAMT) is a rare benign mesenchymal tumor of stomach. Rarity of this kind of tumors and scarce review articles may cause underrecognition of this entity and pose a real diagnostic challenge to gastroenterologists, pathologists and surgeons when encountering such patients and differentiating PAMT from other gastric intramural tumors. We report a case of 28-year-old woman, who presented with epigastric pain after meals, iron-deficiency anaemia and weight loss. Upper gastrointestinal endoscopy revealed submucosal tumor-like elevated lesion in the anterior wall of the antrum with intact overlying mucosa. Endoscopic ultrasound showed a 3-cm hypoechoic homogenous mass, originating from the third layer of the gastric wall. Endoscopic ultrasound-guided fine needle aspiration was not informative. Endoscopic buttonhole biopsy was performed to obtain specimens. Following this, the unexpected prolapse of the tumor occurred into the lumen of the stomach, causing gastric outlet obstruction - the biopsy was obtained. Pathomorphological features suggested the diagnosis of PAMT. Gastric resection of the Billroth I type was performed. Diagnosis was confirmed by histological analysis of the surgical specimen.

Key words: Plexiform angiomyxoid myofibroblastic tumor; Intramural; Mesenchymal; Submucosal; Antrum

Core tip: Plexiform angiomyxoid myofibroblastic tumor is a rare benign mesenchymal tumor of stomach. Rarity of this kind of tumors and scarce review articles may cause underrecognition of this entity and pose a real diagnostic challenge, when differentiating between various intramural lesions. Clinical signs and symptoms are nonspecific or absent, radiological features often overlap, upper gastrointestinal endoscopy has a limited role because of intramural location. Endoscopic ultrasound yields opportunity to visualize and biopsy the tumor. Definite diagnosis requires histological and immunohistochemical analysis.

Jonaitis L, Kiudelis M, Slepavicius P, Poskienė L, Kupcinskas L. Plexiform angiomyxoid myofibroblastic tumor of stomach: A rare case. *World J Gastrointest Endosc* 2016; 8(18): 674-678 Available from: URL: http://www.wjgnet.com/1948-5190/full/v8/i18/674.htm DOI: http://dx.doi.org/10.4253/wjge.v8.i18.674

INTRODUCTION

Plexiform angiomyxoid myofibroblastic tumor (PAMT) is a benign mesenchymal tumor of stomach. To date, only 19 immunohistochemically confirmed cases have been reported in the literature. We report a case of 28-year-old woman with submucosal tumor in the anterior wall of the antrum. After repeated biopsies pathomorphological features of the specimen suggested the diagnosis of PAMT. Gastric resection of the Billroth I type was performed and diagnosis of PAMT was confirmed.

CASE REPORT

A 28-year-old previously healthy Caucasian female was ivestigated due to epigastric pain, associated with meals, iron-deficiency anaemia and lost 8 kg of weight during the preceding six months. Her previous medical history was unremarkable. Outpatient upper gastrointestinal endoscopy revealed submucosal tumor-like elevated lesion in the anterior wall of the antrum with intact overlying mucosa (Figure 1). Histology from that mucosa showed active chronic Helicobacter pylori-positive gastritis with reactive lymphoid hyperplasia.

The endoscopic ultrasound was used to assess the tumor: It showed a 3-cm hypoechoic homogenous mass, originating from the third layer of the gastric wall. Endoscopic ultrasound-guided fine needle aspiration was performed to obtain specimens, but histopathological findings were not informative. Therefore endoscopic buttonhole biopsy was performed, but results were not informative again. After this procedure the patient was discharged home, but hospitalized again 7 d later due to vomiting, nausea and discomfort in the upper abdomen. The endoscopy revealed that submucosal mass protruded into the gastric lumen and caused gastric outlet obstruction (Figure 2). The biopsies were taken from protruded mass.

This time microscopic features suggested the diagnosis of PAMT. The partial gastrectomy of the Billroth I type has been performed.

Histological examination of resected tumor confirmed the diagnosis: Microscopically, gastric wall showed involvement of submucosa and muscularis propria by a tumor comprising plexiform islands of monomorphic spindle cells accompanied by abundant myxoid stroma, that was rich in small vessels. The surface of tumor was ulcerated with hyperplastic changes found in adjacent mucosa. On immunohistochemical staining, the tumor cells were positive for smooth muscle actin and negative for desmin, CD34 and S100 protein. Mitoses were rarely seen (< 1/50 HPF). The vascular endothelial Ki-67 labeling index was approximately 40% (Figure 3).

Recovery after operation was complicated by gastroduodenal anastomositis, which was managed successfully with conservative measures.

We plan to make the follow-up investigations (upper gastrointestinal endoscopy and abdominal ultrasound) for the possible recurrence of tumor after 6 mo and then once a year.

DISCUSSION

PAMT also known as plexiform fibromyxoma of stomach, is an unique benign mesenchymal gastric tumor, originating within the muscularis propria[1-6]. To date, only 19 immunohistochemically confirmed cases have been reported in the medical literature[7-9]. According to the reported cases of PAMT, the estimated frequency of this gastric mesenchymal tumor is less than 1/150 compared with that of gastric gastrointestinal stromal tumor (GIST). The patients' ages range from 7 to 75 years (mean, 43 years) and approximate male-to-female ratio is 1:1[10-13].

The representative signs and symptoms include abdominal pain and discomfort, nausea, vomiting, and weight loss (caused by pyloric obstruction), hematemesis and anemia (associated with upper gastrointestinal bleeding caused by ulceration), palpable abdominal mass. Cystic degeneration, fistulating abscess formation and perforation were also reported[1,2,12].

Endoscopically, PAMT appears as submucosal mass, which ranges from 1.9 cm to 15 cm (mean, 6.3 cm)[14]. Tumor is always located in gastric antrum (there are presumptions about the possible origin from cells specifically distributed at this location of muscularis propria layer) though it can extend to the pylorus and duodenal bulb[15]. The overlying mucosa is often ulcerated.

On computed tomography (CT) scan, the tumor appears relatively small (found in the gastric antrum). There is strong and heterogeneous internal enhancement effect. Small nodules show a strong enhancement

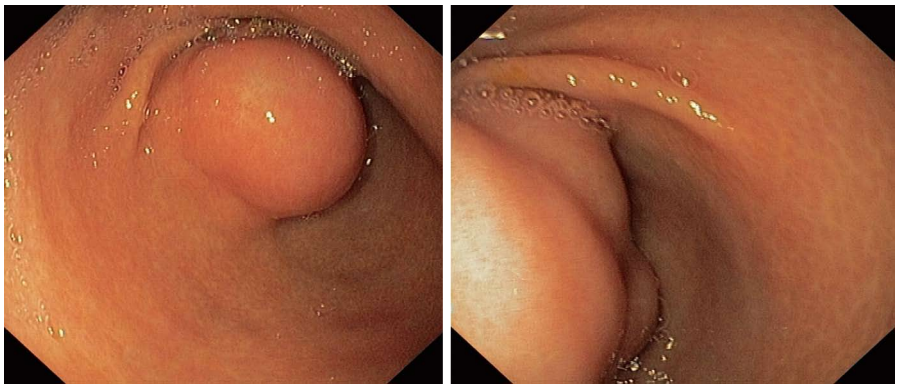

Figure 1 Images from outpatient upper gastrointestinal endoscopy. Submucosal tumor with intact overlying mucosa is located in the anterior wall of the antrum. It partially obstructs the gastric outlet.

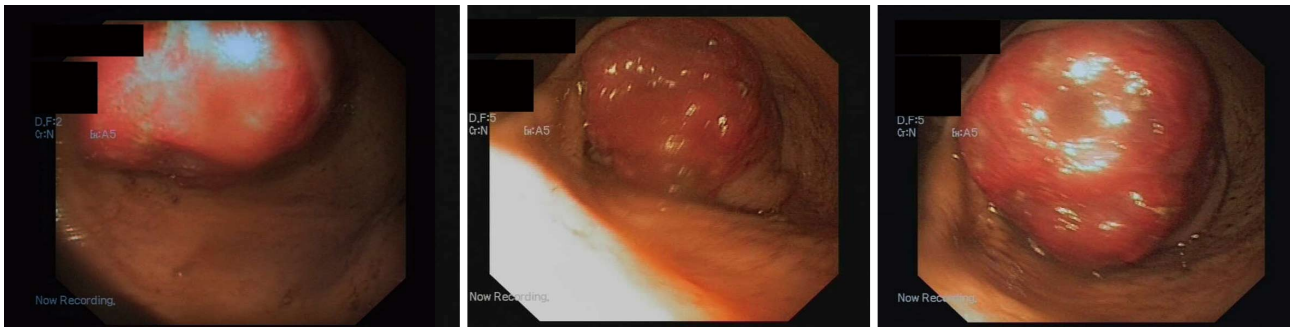

Figure 2 Endoscopic images from our case of plexiform angiomyxoid myofibroblastic tumor show multinodular tumor-like mass protruding into the gastric lumen after performed buttonhole biopsy. This mass blocks the pylorus resulting in the stasis of gastric content.

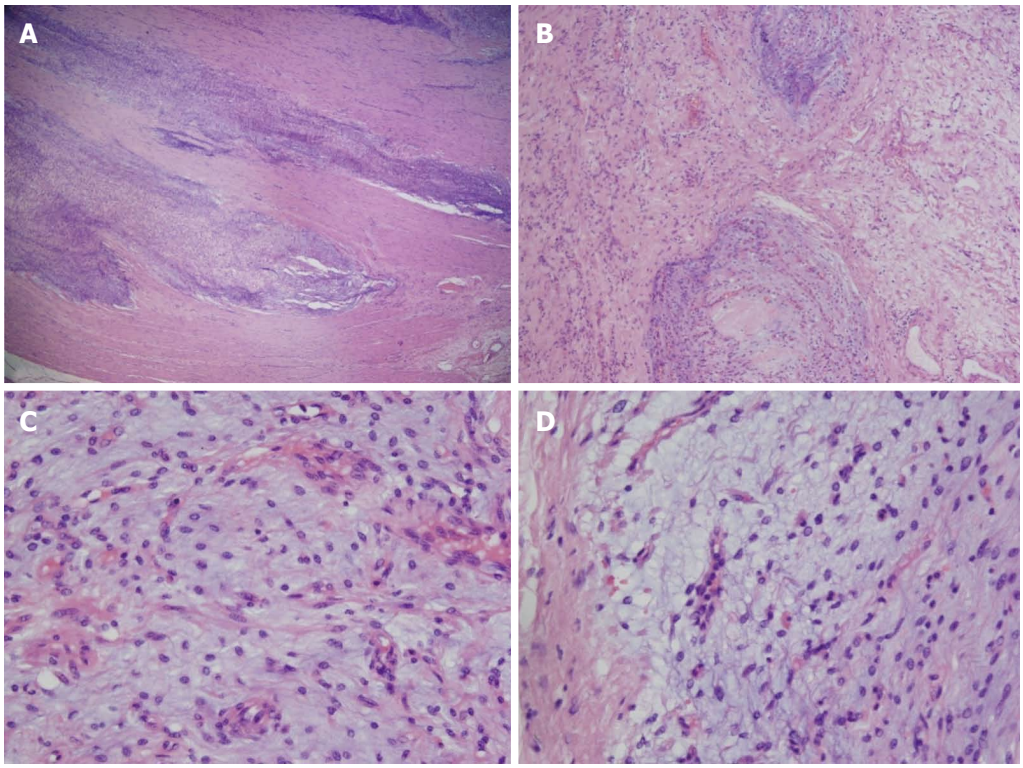

Figure 3 Multinodular plexiform growth pattern (A, B) and monomorphic spindle cells (C, D) accompanied by abundant myxoid stroma.

effect in the rim[10]. The tumor also shows areas of low attenuation (because of the presence of myxoid tissue) and foci of vascularity. Magnetic resonance (MR) images demonstrate the myxoid stroma as T2-hyperintense lesion with persistent enhancement after administration of contrast material[3,5].

Histologically, PAMT is characterized by multinodular plexiform growth pattern (except for the extragastric tumor components). Tumor originates within the third layer of stomach wall - the muscularis propria - and may extend into the submucosa and mucosa, causing ulceration (furthermore, gastric content particles may impact into the fistulated tumor, resulting in abscess and pseudocyst formation). Bland-looking spindle tumor cells are separated by an abundant myxoid or fibromyxoid matrix, rich in capillaries. Nuclei of the tumor cells are oval or plump-shaped and cytoplasm is slightly eosinophilic. Nucleoli are small and inconspicious. Mitoses are rare (usually 0-4/50 HPF). The stroma is positive for Alcian blue stain, occasional collagenization may be observed. Immunohistochemical analysis of PAMT cells shows positivity for actin and vimentin, and negativity for CD34, S100P, KIT, DOG1, cytokeratin, neurofilament, epithelial membrane antigen, ALK. Tumor cells are mostly positive for α-smooth muscle actin (up to 80%), while positivity for desmin, CD10 and caldesmon is variable. Ki-67 usually demonstrates a very low proliferation index (1%-2%). Genetic studies show no mutations in KIT and PDGFRA[1,2,6,7,9,14].

Differential diagnoses of PAMT include GIST, which accounts for the majority of intramural gastric tumors, also inflammatory fibroid polyp, plexiform neurofibroma, myxoid leiomyoma, leiomyosarcoma, desmoid fibromatosis, gastric schwannoma, solitary fibrous tumor, inflammatory myofibroblastic tumor[4,8].

As mentioned before, differentiating between various intramural lesions may be difficult - clinical signs and symptoms are nonspecific or absent, radiological features often overlap, upper gastrointestinal endoscopy has a limited role because of intramural location. Endoscopic ultrasound yields opportunity to visualize and biopsy the tumor. Definite diagnosis requires histological and immunohistochemical analysis[11,16]. According to the described cases PAMT has good prognosis, no cases of local recurrence or metastasis had been reported.

As gastric PAMT is so rare in clinical practice, special attention is necessary to recognise this entity and avoid misdiagnosis. Although absence of confirmed recurrences or metastases suggests that PAMT of stomach is benign[12], larger number of cases must be reported and analysed in order to specify it's clinical significance, outcome and prognosis.

COMMENTS

Case characteristics

A 28-year-old previously healthy Caucasian female presented with epigastric pain, associated with meals, iron-deficiency anaemia and loss of weight during the preceding six months.

Clinical diagnosis

Submucosal tumor-like elevated lesion in the anterior wall of the antrum.

Differential diagnosis

Gastrointestinal stromal tumor, inflammatory fibroid polyp, plexiform neurofibroma, myxoid leiomyoma, leiomyosarcoma, desmoid fibromatosis, gastric schwannoma, solitary fibrous tumor, inflammatory myofibroblastic tumor.

Laboratory diagnosis

Iron-deficiency anaemia.

Imaging diagnosis

The endoscopic ultrasound showed a 3-cm hypoechoic homogenous mass, originating from the third layer of the gastric wall.

Pathological diagnosis

Plexiform angiomyxoid myofibroblastic tumor (PAMT).

Treatment

Partial gastrectomy of the Billroth I type.

Related reports

PAMT also known as plexiform fibromyxoma of stomach, is an unique benign mesenchymal gastric tumor, originating within the muscularis propria. To date, only 19 immunohistochemically confirmed cases have been reported in the medical literature.

Experiences and lessons

Differentiating between various intramural lesions may be difficult - clinical signs and symptoms are nonspecific or absent, radiological features often overlap, upper gastrointestinal endoscopy has a limited role because of intramural location. Definite diagnosis requires histological and immunohistochemical analysis.

Peer-review

The paper Plexiform angiomyxoid myofibroblastic tumor of stomach: A rare case is an interesting description of a rare condition of tumor. The case presented here shows that surgical intervention under is successful.

REFERENCES

1 **Takahashi Y**, Suzuki M, Fukusato T. Plexiform angiomyxoid myofibroblastic tumor of the stomach. *World J Gastroenterol* 2010; **16**: 2835-2840 [PMID: 20556828 DOI: 10.3748/wjg.v16.i23.2835]

2 **Lee PW**, Yau DT, Lau PP, Chan JK. Plexiform fibromyxoma (plexiform angiomyxoid myofibroblastic tumor) of stomach: an unusual presentation as a fistulating abscess. *Int J Surg Pathol* 2014; **22**: 286-290 [PMID: 23794494 DOI: 10.1177/1066896913492198]

3 **Kang HC**, Menias CO, Gaballah AH, Shroff S, Taggart MW, Garg N, Elsayes KM. Beyond the GIST: mesenchymal tumors of the stomach. *Radiographics* 2013; **33**: 1673-1690 [PMID: 24108557 DOI: 10.1148/rg.336135507]

4 **Stanford Medicine**. Gastric Plexiform Fibromyxoma. Differential Diagnosis. Available from: URL:http//surgpathcriteria.stanford.edu/gitumors/gastric-plexiform-fibromyxoma/differential-diagnosis.html

5 **Sakamoto K**, Hirakawa M, Atsumi K, Mimori K, Shibata K, Tobo T, Yamamoto H, Honda H. A case of gastric plexiform fibromyxoma: radiological and pathological findings. *Jpn J Radiol* 2014; **32**: 431-436 [PMID: 24744134 DOI: 10.1007/s11604-014-0315-z]

6 **Miettinen M**, Makhlouf HR, Sobin LH, Lasota J. Plexiform fibromyxoma: a distinctive benign gastric antral neoplasm not to be confused with a myxoid GIST. *Am J Surg Patho l*2009; **33**: 1624-1632 [PMID: 19675452 DOI: 10.1097/PAS.0b013e3181ae666a]

7 **Wang FH**, Chen ZR, Niu HL, Zeng RX, Xia JQ. Plexiform fibromyxoma of stomach: a distinctive benign tumor of gastric antrum.

Zhonghua Binglixue Zazhi 2012; **41**: 190-191 [PMID: 22800485]
8 **Sing Y**, Subrayan S, Mqadi B, Ramdial PK, Reddy J, Moodley MS, Bux S. Gastric plexiform angiomyxoid myofibroblastic tumor. *Pathol Int* 2010; **60**: 621-625 [PMID: 20712648 DOI: 10.1111/j.1440-1827.2010.02569.x]
9 **Lu B**, Ye W, Liu H. A Rare Gastric Tumor in a Young Woman. Gastric Plexiform Angiomyxoid Myofibroblastic Tumor. *Gastroenterology*2015; **149**: 294-295 [PMID: 26119799 DOI: 10.1053/j.gastro.2015.03.050]
10 **Ikemura M**, Maeda E, Hatao F, Aikou S, Seto Y, Fukayama M. Plexiform angiomyxoid myofibroblastic tumor (PAMT) of the stomach. A case report focusing on its characteristic growth pattern. *Int J Clin Exp Pathol* 2014; **7**: 685-689 [PMID: 24551290]
11 **Rau TT**, Hartmann A, Dietmaier W, Schmitz J, Hohenberger W, Hofstaedter F, Katenkamp K. Plexiform angiomyxoid myofibroblastic tumour: differential diagnosis of gastrointestinal stromal tumour in the stomach. *J Clin Pathol* 2008; **61**: 1136-1137 [PMID: 18820104 DOI: 10.1136/jcp.2008.059162]
12 **Schulz T**, Drgac J, Chmelar C, Höhler T, Agaimy A, Vieth M. Plexiform angiomyxoid myofibroblastic tumour of the stomach. *Pathologe* 2012; **33**: 65-69 [PMID: 22293792 DOI: 10.1007/s00292-011-1548-6]
13 **Kim A**, Bae YK, Shin HC, Choi JH. Plexiform angiomyxoid myofibroblastic tumor of the stomach: a case report.*J Korean Med Sci* 2011; **26**: 1508-1511 [PMID: 22065909 DOI: 10.3346/jkms.2011.26.11.1508]
14 **Li P**, Yang S, Wang C, Li Y, Geng M. Presence of smooth muscle cell differentiation in plexiform angiomyxoid myofibroblastic tumor of the stomach: a case report. *Int J Clin Exp Pathol* 2014; **7**: 823-827 [PMID: 24551311]
15 **Banerjee N**, Gupta S, Dash S, Ghosh S. Plexiform angiomyxoid myofibroblastic tumour of the duodenum: a rare entity. *BMJ Case Rep* 2015; **2015**: pii: bcr2015210004 [PMID: 26216925 DOI: 10.1136/bcr-2015-210004]
16 **Wang LM**, Chetty R. Selected unusual tumors of the stomach: a review. *Int J Surg Pathol* 2012; **20**: 5-14 [PMID: 22134628 DOI: 10.1177/1066896911429300]

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CASE REPORT

Balloon-assisted enteroscopy for suspected Meckel's diverticulum and indefinite diagnostic imaging workup

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Author contributions: Gomes GF, Bonin EA and Bartholomei TF acquired the data and wrote and revised the manuscript; Noda RW and Cavazzola LT contributed to writing and revising the manuscript.

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Informed consent statement: The patients involved in this study gave written informed consent authorizing use and disclosure of their protected health information.

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Abstract

Meckel's diverticulum (MD) is estimated to affect 1%-2% of the general population, and it represents a clinically silent finding of a congenital anomaly in up to 85% of the cases. In adults, MD may cause symptoms, such as overt occult lower gastrointestinal bleeding. The diagnostic imaging workup includes computed tomography scan, magnetic resonance imaging enterography, technetium 99m scintigraphy (99mTc) using either labeled red blood cells or pertechnetate (known as the Meckel's scan) and angiography. The preoperative detection rate of MD in adults is low, and many patients ultimately undergo exploratory laparoscopy. More recently, however, endoscopic identification of MD has been possible with the use of balloon-assisted enteroscopy *via* direct luminal access, which also provides visualization of the diverticular ostium. The aim of this study was to review the diagnosis by double-balloon enteroscopy of 4 adults with symptomatic MD but who had negative diagnostic imaging workups. These cases indicate that balloon-assisted enteroscopy is a valuable diagnostic method and should be considered in adult patients who have suspected MD and indefinite findings on diagnostic imaging workup, including negative Meckel's scan.

Key words: Double-balloon enteroscopy; Meckel's diverticulum; Diagnosis

Core tip: Meckel's diverticulum (MD) is estimated to affect 1%-2% of the general population and has 4%-6%

risk of causing symptoms during a lifetime. In adults, it may cause occult massive bleeding and the preoperative detection rate is low; patients with undiagnosed MD ultimately undergo exploratory laparoscopy. More recently, however, endoscopic identification of MD has been possible with the use of balloon-assisted enteroscopy *via* direct luminal access, providing visualization of the diverticular ostium. We report here the use of double-balloon enteroscopy for diagnosing 4 adults with symptomatic MD who had negative diagnostic imaging workup.

Gomes GF, Bonin EA, Noda RW, Cavazzola LT, Bartholomei TF. Balloon-assisted enteroscopy for suspected Meckel's diverticulum and indefinite diagnostic imaging workup. *World J Gastrointest Endosc* 2016; 8(18): 679-683 Available from: URL: http://www.wjgnet.com/1948-5190/full/v8/i18/679.htm DOI: http://dx.doi.org/10.4253/wjge.v8.i18.679

INTRODUCTION

Meckel's diverticulum (MD) is a congenital true diverticulum that develops from a patent omphalo-mesenteric duct[1]. It is estimated to affect 1%-2% of the general population and has 4%-6% risk of causing symptoms during a lifetime[2,3]. Surgical resection is not mandatory for cases of MD that are found incidentally. Any MD > 2 cm in length and with palpable abnormal tissue within the diverticulum, however, is associated with a higher lifetime risk for complication for male patients of ages under 50 years[4], and should be considered for resection. Although MD represents a clinically silent finding of a congenital anomaly in up to 85% of cases[4], patients who develop a complication may suffer from the lack of diagnosis and subsequent delayed initiation of appropriate treatment. When symptoms occur, they usually include melena/hematochezia from a bleeding vessel or abdominal pain from intussusception or adhesions. Confirmation of MD relies on identifying a true diverticulum, usually located within 100 cm from the ileocecal valve. Rarely, a source of bleeding, such as an ulcer, can be found inside its lumen.

In adults, any patient presenting with documented bleeding in the lower gastrointestinal tract and negative findings on upper endoscopy and colonoscopy should be suspected of having a symptomatic MD. The routine diagnostic imaging workup includes computed tomography (CT) scan, magnetic resonance imaging (MRI) enterography, technetium 99m scintigraphy (99mTc) using either labeled red blood cells or pertechnetate (known as the Meckel's scan) and angiography. More recently, however, endoscopic identification of MD has been possible with the use of balloon-assisted enteroscopy *via* direct luminal access, providing visualization of the diverticular ostium[5].

Herein, we report the use of double-balloon enteroscopy (DBE) for diagnosing 4 adults with symptomatic MD who had negative diagnostic imaging workup.

CASE REPORT

Between January 2007 and December 2015, 114 patients underwent DBE at Nossa Senhora das Graças Hospital (Curitiba, Brazil). For most patients, the indication for DBE was obscure gastrointestinal bleeding. All patients underwent clinical evaluation by the examiner before the procedure. MD was clinically suspected in young patients with episodes of overt rectal bleeding and negative diagnostic imaging workup. MD was found in 4 patients with obscure gastrointestinal bleeding, including overt rectal bleeding in 3 and with abdominal pain in 1. The patients included 3 males and 1 female, ranging in age from 16-year-old to 45-year-old (mean, 22-year-old).

MD diagnosis was made by retrograde (per anus) DBE for all 4 patients, with 1 of the patients having first undergone an unsuccessful approach by anterograde (per mouth). The typical endoscopic feature of MD in these cases was diverticular ostium and lumen in the ileum, found after exhaustive active search (Figure 1). All diverticula were located between 70 cm and 90 cm from the ileocecal valve, and none had stigmata of recent or active bleeding. All patients underwent endoscopic submucosal ink injection (tattooing) of the peridiverticular region, which facilitated a later elective laparoscopic resection (Figure 2).

The equipment used was the Fujinon EN-450P DBE system (Fuji, Tokyo, Japan). All procedures were performed under deep sedation that was established using intravenous propofol.

Cases 1 and 2

These two patients had similar symptoms, and as such will be described jointly. Diagnosis occurred at 17-years-old (case 1) and 27-years-old (case 2). Both patients had history of multiple episodes of bleeding with hematochezia, melena and blood transfusion. In both patients, upper and lower endoscopy and red blood cell-labeled scintigraphy gave negative findings. Both patients also had a previous negative Meckel's scan. Case 2 had experienced an episode of hematochezia with hemodynamic instability, for which an angiography was performed but did not reveal a source of bleeding. Both patients underwent a retrograde DBE, which revealed MD in the ileum.

Case 3

This 17-year-old male presented to our institution with a history of three episodes of hematochezia, each requiring blood transfusion. He underwent upper endoscopy and colonoscopy, which showed blood clots in the colon but revealed no source of bleeding. A subsequent upper and lower endoscopy, followed by Meckel's scan and small bowel video capsule exam, provided no additional findings. At admission, hemoglobin and hematocrit

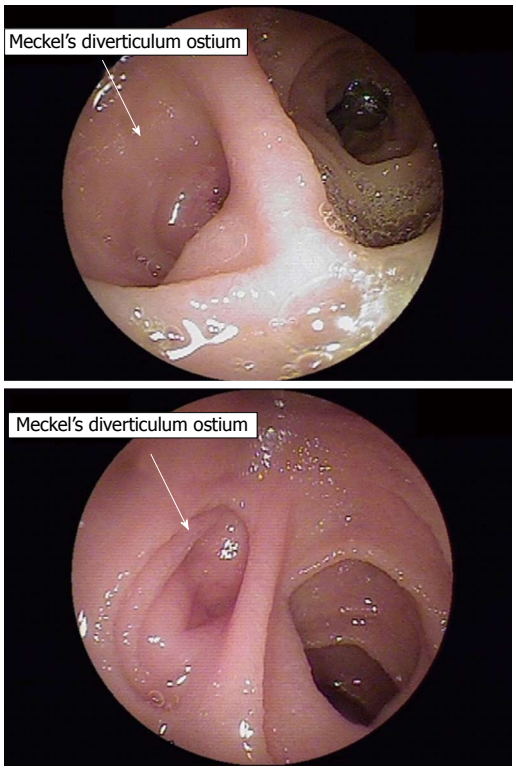

Figure 1 The typical endoscopic feature of Meckel's diverticulum in these cases was diverticular ostium and lumen in the ileum, found after exhaustive active search. The two images represent the different depths of the Meckel's diverticulum in different cases.

were within normal range. Three weeks later, the patient had a new episode of rectal bleeding and was re-hospitalized. A DBE was performed orally until the jejuno-ileal region was reached, which showed normal findings. We then decided to carry out another DBE, this time rectally, and MD was visualized in the ileum at 90 cm from the ileocecal valve. There was no evidence of active bleeding or ulcers around the diverticulum.

Case 4

This 45-year-old female presented with severe abdominal pain associated with bloating. She had been hospitalized twice within a 2-wk period, and presented clinically with abdominal distension; however, no abdominal mass was palpable. White and red blood cell counts and platelets were normal. An abdominal CT scan was performed and demonstrated thickening of the distal ileum region of about 10 cm in length, which was suspected as obstructive inflammatory bowel disease. A DBE was then performed and showed MD, with no signs of ulceration or obstruction. The patient underwent laparoscopy, which showed MD attached to a mesodiverticular band and determined obstruction of the ileum, located approximately 80 cm from the ileocecal valve.

Treatment

All patients underwent elective laparoscopic resection

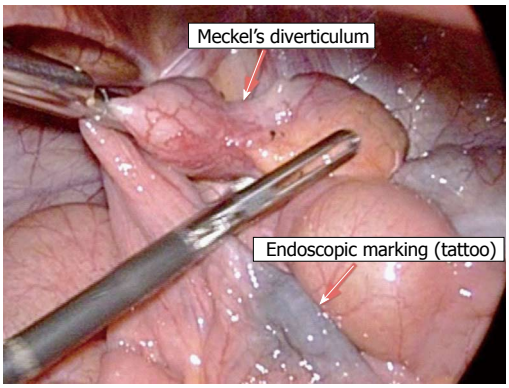

Figure 2 All patients underwent endoscopic submucosal ink injection (tattooing) of the peridiverticular region, which facilitated a later elective laparoscopic resection.

of a segment of the small bowel that contained the diverticulum, with end-to-end anastomosis. The treatment was successful in all cases.

DISCUSSION

MD is considered a true diverticulum, which by definition contains all layers of the intestinal wall. It is located in the ileum, with reported average distances from the ileocecal valve varying according to age: 34 cm in children > 2-year-old; 46 cm in patients between 3-year-old and 21-year-old; 67 cm in adults 21-year or older[6]. MD may have gastric, duodenal, colon, mucosal and pancreatic rests, which originate from multipotent cells within the omphalo-mesenteric duct wall.

A wide array of imaging techniques are available for detecting MD, such as Meckel's scan, balloon-assisted enteroscopy, capsule endoscopy, CT scan (with or without enterography), MRI enterography and mesenteric catheter angiography. MD diagnosis is more difficult in adults, for whom Meckel's scan MD's most accurate diagnostic modality is less accurate, as compared to children[1]. In adults, MD should be suspected in cases of occult gastrointestinal bleeding with no evidence of vascular malformation or of unexplained abdominal pain with an abnormal imaging finding in the ileum. In cases of occult bleeding, the preoperative detection rate is low; adult patients may end up having undiagnosed MD and ultimately undergo exploratory laparoscopy[1].

CT scan is considered the first-line diagnostic method for any adult patient with suspected MD. The sensitivity of CT scan for diagnosing MD has increased over the years, owing to development of the multidetector scan technique (MDCT). This technology provides visualization of the small bowel in various planes, and adding oral contrast (enterography) improves MD imaging[7]. Furthermore, CT is very useful in diagnosing and assessing complications associated with MD, particularly for intra-abdominal abscess formation, obstruction, perforation and associated tumors, which is crucial in acute abdomen cases. MDCT may also detect

active extravasation of intravenous contrast medium in cases with active intestinal hemorrhage.

Meckel's scan is a valuable non-invasive test, in which radioactive tracers are used to locate the presence of functioning ectopic gastric mucosa. In children, it has a sensitivity of 80%-90%, specificity of 95% and accuracy of 90%[2]. In contrast, in adults, the sensitivity is 62.5%, specificity is 9% and accuracy is 46%[8]. According to the guideline recently published by the Society of Nuclear Medicine and Molecular Imaging[8], "the indication for Meckel scintigraphy is to localize ectopic gastric mucosa in a Meckel diverticulum as the source of unexplained gastrointestinal bleeding. Meckel scintigraphy should be used when the patient is not actively bleeding… Even in young children, active bleeding is best studied by radiolabeled red blood cell scintigraphy". False-positive results are due to the presence of ectopic gastric mucosa elsewhere in the gastrointestinal tract, to enteric duplication and to inflammatory processes. A false-negative result may occur in cases of brisk gastrointestinal bleeding, small gastric ectopic mucosa (< 1.8 cm^2) and a "wandering diverticulum". In our series, all patients had a negative Meckel's scan. Despite its low accuracy in adults, though, it remains widely used for confirming MD in our geographic region, given its nature of being a non-invasive diagnostic method.

Mesenteric catheter angiography is another diagnostic modality, but it is useful only in cases of ongoing bleeding and for patients with counterindications to a Meckel's scan. The usual minimum required bleeding rate is of 0.5 mL/min; however, lower bleeding rates can be detected when the digital subtraction angiography technique is applied. This procedure can be useful in locating an overt bleeding vessel and applying embolization treatment; however, it may require superselective catheterization of the mid- and distal ileal arteries[9].

Diagnosis of small bowel diseases has evolved dramatically over the past decade, particularly since the advent of capsule endoscopy and balloon-assisted enteroscopy. Both procedures enable endoscopic access to the entire small bowel. Capsule endoscopy is a simple, non-invasive technique to examine the small bowel by ingesting a wireless "pill" camera. Although capsule endoscopy has been used for diagnosing MD, its diagnostic yield is limited and there is a risk of capsule retention within the diverticulum[10]. For these reasons, we tend not to use capsule endoscopy for patients with suspected MD.

Balloon-assisted enteroscopy consists of using a single- or a double-balloon method for inserting a flexible endoscope for visualization, biopsy and treatment of the entire small bowel. The first case of MD that was diagnosed by DBE was described in 2005, and since then it has been considered a safe and effective method for diagnosing MD, with a low complication rate in adults[5]. In a recent study by He *et al*[11], the overall diagnostic yield of DBE for MD before surgery was 86%, which was significantly higher compared to that of capsule endoscopy. Compared to Meckel's scan, its accuracy is higher for adult patients with suspected symptomatic MD. Admittedly, such results are based upon limited data, but it seems that DBE is becoming a pivotal diagnostic modality for confirming suspected MD in adults. Fukushima *et al*[5], based on their experience with 10 patients, recommends that dynamic MDCT scan followed by retrograde DBE be applied to stable patients to perform the initial diagnostic workup in adults with suspected MD. In addition, anterograde DBE is recommended as the initial approach for patients with overt, ongoing bleeding, and capsule endoscopy and mesenteric angiography are also suggested for such cases.

DBE offers some advantages over other methods for allowing direct observation of the diverticular ostium, access to the entire small bowel, repeated examinations of the region and intraluminal therapy (*i.e.* injection, coagulation)[12,13]. Finding another potential source of bleeding may aid in establishing the correct diagnosis, since MD may coexist with several other lesions. Endoscopic tattooing is advised for locating the site of the lesion, whenever an endoscopic revision is needed. In our case series, tattooing also aided in locating the affected segment laparoscopically for subsequent resection. DBE may also reveal unusual MD presentations, such as an inverted MD - a rare condition in which the diverticulum is completely inverted intraluminally and mimics a large subepithelial lesion[12]. Intradiverticular polyps and tumors can be also found through direct visualization inside the MD lumen[5].

Apart from diagnosis, DBE can also provide a minimally invasive endoscopic approach for treatment of symptomatic MD[13,14]. Identifying and treating a bleeding vessel within the MD using DBE[13] can help to avoid an emergency operation. Bleeding control can be accomplished by endoscopic injection, coagulation and clipping. Since rebleeding is a concern, it is advised in such cases to proceed to elective MD resection. Successful cases of intradiverticular MD polypectomy and resection of an inverted MD through DBE have also been reported[14].

In our experience, DBE has emerged over the years as a useful diagnostic modality of adult patients with suspected MD and indefinite findings on diagnostic imaging workup.

COMMENTS

Case characteristics

The authors describe 4 cases of Meckel's diverticulum being diagnosed using double-balloon enteroscopy.

Clinical diagnosis

Adult patients presenting with overt rectal bleeding or abdominal pain and without diagnosis despite extensive imaging workup.

Differential diagnosis

Gastrointestinal vascular malformations.

Laboratory diagnosis
Anemia due to bleeding.

Imaging diagnosis
Findings from upper endoscopy, lower endoscopy, Meckel's scan and computed tomography scan were all negative for source of symptoms.

Pathological diagnosis
Meckel's diverticulum.

Treatment
Complete laparoscopic surgical excision of the diverticulum.

Related reports
Meckel's diverticulum may cause occult massive bleeding in adult patients and the preoperative detection rate is low. Endoscopic identification of Meckel's diverticulum is possible with the use of balloon-assisted enteroscopy *via* direct luminal access, providing visualization of the diverticular ostium.

Term explanation
Meckel's diverticulum is the most common congenital anomaly of the gastrointestinal tract. It is estimated to affect 1%-2% of the general population and has 4%-6% risk of causing symptoms during a lifetime. Double-balloon enteroscopy is an endoscopic procedure that allows investigation and treatment of small bowel lesions.

Experiences and lessons
Balloon-assisted enteroscopy is a valuable diagnostic method and should be considered for use in adult patients with suspected Meckel's diverticulum and indefinite diagnostic imaging workup, including negative technetium 99^{m} pertechnetate scintigraphy (known as the Meckel's scan).

Peer-review
The manuscript is well written. The most common cause of obscure gastrointestinal bleeding is gastrointestinal vascular malformation. Meckel's diverticulum, however, is a clinically important condition. Of 114 patients who underwent double-balloon enteroscopy, 4 cases of Meckel's diverticulum were diagnosed and are described by this study.

REFERENCES

1 **Sagar J**, Kumar V, Shah DK. Meckel's diverticulum: a systematic review. *J R Soc Med* 2006; **99**: 501-505 [PMID: 17021300 DOI: 10.1258/jrsm.99.10.501]

2 **Soltero MJ**, Bill AH. The natural history of Meckel's Diverticulum and its relation to incidental removal. A study of 202 cases of diseased Meckel's Diverticulum found in King County, Washington, over a fifteen year period. *Am J Surg* 1976; **132**: 168-173 [PMID: 952346 DOI: 10.1016/0002-9610(76)90043-X]

3 **Cullen JJ**, Kelly KA, Moir CR, Hodge DO, Zinsmeister AR, Melton LJ. Surgical management of Meckel's diverticulum. An epidemiologic, population-based study. *Ann Surg* 1994; **220**: 564-568; discussion 568-569 [PMID: 7944666]

4 **Park JJ**, Wolff BG, Tollefson MK, Walsh EE, Larson DR. Meckel diverticulum: the Mayo Clinic experience with 1476 patients (1950-2002). *Ann Surg* 2005; **241**: 529-533 [PMID: 15729078 DOI: 10.1097/01.sla.0000154270.14308.5f]

5 **Fukushima M**, Kawanami C, Inoue S, Okada A, Imai Y, Inokuma T. A case series of Meckel's diverticulum: usefulness of double-balloon enteroscopy for diagnosis. *BMC Gastroenterol* 2014; **14**: 155 [PMID: 25175823 DOI: 10.1186/1471-230X-14-155]

6 **Ymaguchi M**, Takeuchi S, Awazu S. Meckel's diverticulum. Investigation of 600 patients in Japanese literature. *Am J Surg* 1978; **136**: 247-249 [PMID: 308325]

7 **Paulsen SR**, Huprich JE, Fletcher JG, Booya F, Young BM, Fidler JL, Johnson CD, Barlow JM, Earnest F. CT enterography as a diagnostic tool in evaluating small bowel disorders: review of clinical experience with over 700 cases. *Radiographics* 2006; **26**: 641-657; discussion 657-662 [PMID: 16702444 DOI: 10.1148/rg.263055162]

8 **Spottswood SE**, Pfluger T, Bartold SP, Brandon D, Burchell N, Delbeke D, Fink-Bennett DM, Hodges PK, Jolles PR, Lassmann M, Maurer AH, Seabold JE, Stabin MG, Treves ST, Vlajkovic M. SNMMI and EANM practice guideline for meckel diverticulum scintigraphy 2.0. *J Nucl Med Technol* 2014; **42**: 163-169 [PMID: 24948825 DOI: 10.2967/jmnt.113.136242]

9 **Kotha VK**, Khandelwal A, Saboo SS, Shanbhogue AK, Virmani V, Marginean EC, Menias CO. Radiologist's perspective for the Meckel's diverticulum and its complications. *Br J Radiol* 2014; **87**: 20130743 [PMID: 24611767 DOI: 10.1259/bjr.20130743]

10 **Tanaka Y**, Motomura Y, Akahoshi K, Nakama N, Osoegawa T, Kashiwabara Y, Chaen T, Higuchi N, Kubokawa M, Nishida K, Yukaya T, Oya M, Nakamura K. Capsule endoscopic detection of bleeding Meckel's diverticulum, with capsule retention in the diverticulum. *Endoscopy* 2010; **42** Suppl 2: E199-E200 [PMID: 20845270 DOI: 10.1055/s-0030-1255696]

11 **He Q**, Zhang YL, Xiao B, Jiang B, Bai Y, Zhi FC. Double-balloon enteroscopy for diagnosis of Meckel's diverticulum: comparison with operative findings and capsule endoscopy. *Surgery* 2013; **153**: 549-554 [PMID: 23305600 DOI: 10.1016/j.surg.2012.09.012]

12 **Huang TY**, Liu YC, Lee HS, Chu HC, Chen PJ, Weng JW, Fu CK, Hsu KF. Inverted Meckel's diverticulum mimicking an ulcerated pedunculated polyp: detection by single-balloon enteroscopy. *Endoscopy* 2011; **43** Suppl 2 UCTN: E244-E245 [PMID: 21837594 DOI: 10.1055/s-0030-1256603]

13 **Olafsson S**, Yang JT, Jackson CS, Barakat M, Lo S. Bleeding Meckel's diverticulum diagnosed and treated by double-balloon enteroscopy. *Avicenna J Med* 2012; **2**: 48-50 [PMID: 23210023 DOI: 10.4103/2231-0770.99166]

14 **Fukushima M**, Suga Y, Kawanami C. Successful endoscopic resection of inverted Meckel's diverticulum by double-balloon enteroscopy. *Clin Gastroenterol Hepatol* 2013; **11**: e35 [PMID: 23022701 DOI: 10.1016/j.cgh.2012.09.023]

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