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EDITORIAL

Utilisation of magnets to enhance gastrointestinal endoscopy

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Abstract

Methods to assess, access and treat pathology within the gastrointestinal tract continue to evolve with video endoscopy replacing radiology as the gold standard. Whilst endoscope technology develops further with the advent of newer higher resolution chips, an array of adjuncts has been developed to enhance endoscopy in other ways; most notable is the use of magnets. Magnets are utilised in many areas, ranging from endoscopic training, lesion resection, aiding manoeuvrability of capsule endoscopes, to assisting in easy placement of tubes for nutritional feeding. Some of these are still at an experimental stage, whilst others are being increasingly incorporated in our everyday practice.

Key words: Magnet; Endoscopy; Training; Therapeutic; Capsule; Nutrition; Child; Paediatric; Colonoscopy; Imaging

Core tip: Magnetic technology is being incorporated into many aspects of endoscopy from diagnostic procedures to assisting in therapeutic interventions. Here we summarise some of the more exciting innovations and the potential future roles magnets will play in this field.

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INTRODUCTION

Magnets were traditionally viewed with great scepticism by the endoscopy community due to the potentially hazardous consequence that ingestion of this material

led to. However the property of magnets, notably the ability to be sensed and also exert a force from a distance, began to be recognised as a solution to many emerging problems faced by an endoscopist. Magnetic technology is now incorporated within many areas of endoscopy.

Endoscopic training

Colonoscopy is undertaken worldwide, with variations in reported caecal intubation rates. Although there are several reasons for this, a common factor elucidated in quality assurance audits is the consequence of recurrent colonic looping leading to a consequent lack of advancement of the endoscope tip, and subsequent patient discomfort[1]. Measures to appreciate colonoscopic positioning in the past required fluoroscopy, however, its use was cumbersome and posed a radiation risk[2,3]. In 1993, the technique of magnetic endoscopic imaging (MEI) of the colonoscope was described by Bladen *et al*[4]. This was then further developed by Olympus® into a mobile unit known as "Scopeguide". This technology provides a real time three-dimensional image of the colonoscope as it passes through the colon. The basic principle relies on the generation of pulsed low intensity magnetic fields generated from electromagnetic generator coils positioned at regular intervals within the colonoscope. This is then picked up by a receiver dish which allows calculation of the precise position and orientation of the colonoscope. It enables loops to be visualised and loop resolution to be performed under direct vision as well as assisting in identifying the location of the tip of the scope.

It has been proposed that this device can improve caecal intubation rates, times and patient comfort. This was demonstrated in the first randomized controlled trial (RCT) of MEI on colonoscopy performance in adults[5]. However, more recent studies have demonstrated conflicting results in those with enough statistical power to show a difference in the two groups. Two studies have shown higher caecal intubation rates, one study has shown shorter intubation times and two showed patient comfort scores were better with MEI, although one of the latest studies looking into its role in unsedated colonoscopy failed to show any statistical difference in any of these outcome measures[5-8]. The largest RCT on MEI to date (n = 810) did however reveal that in less experienced endoscopists the performance, measured by caecal intubation rate, was significantly better than with standard colonoscopy without MEI[9]; also demonstrated by Chen *et al*[10] in a meta-analysis collating 8 RCT. This may lead to the conclusion that the benefit of the device may be more of a training tool for trainee endoscopist through identification of loops, as shown by similar performance improvements in this group in other cohort studies[11-13].

These devices are not in general routine practice on all endoscopy sessions, in part because they are expensive to purchase and require the use of Olympus® equipment. However, what studies have not recorded is the current trainee and trainer satisfaction with this equipment. As the dynamics of the colon can be visualised, there can be a more logical discussion between the trainer and trainee, to resolve an issue of lack of tip advancement or patient discomfort. In practice, trainees appear to be more satisfied with the use of MEI during colonoscopy. One explanation for this is that it allows the trainer to explain the decision making required to facilitate tip advancement without taking the colonoscope over from the trainee. With the growing pressure to train a greater number of generic healthcare endoscopists, the additional cost may thus be justified. With other endoscope manufacturers, such as Pentax®, incorporating MEI into their equipment in the near future it is likely this technology becomes increasingly embedded in day to day colonoscopy practice.

Therapeutic endoscopy

Going beyond the realms of basic diagnostic endoscopy, into an era where the endoscopist has now developed the proficiency to undertake therapy, comes an explosion of technology. Endoscopic polypectomy has evolved since its first undertaking by Hiromi Shinya in 1969, from the basic "lassoing" of a polyp to endoscopic mucosal resection (EMR) to endoscopic submucosal dissection (ESD) which allows en-bloc resection of large lesions[14]. ESD is however a technically demanding procedure with relatively longer procedure times compared with EMR, and significant complication rates with perforation risk as high as 18% in some series[15]. A common reason for this difficulty is the limited field within which the endoscopist, with his "one handed knife", is operating in. Current standard technique requires the use of a combination of submucosal fluid injection and utilisation of gravity. However, these methods often lead to difficulty in maintaining a safe field of dissection due to a lack of elevation to expose the submucosal plane. To overcome this issue, Gotoda *et al*[16] designed a magnetic anchor device to apply counter-traction. The anchor consisted of a small magnetic weight that was attached to an endoclip with a thread. Once the standard circumferential incision had been made for ESD, the anchor, which was loaded on the end of a standard endoscope, was deployed by attaching the clip to one end of the flap of the lesion[16]. Initially, an extracorporeal magnetic control system of a C-arm type was used to attract the anchor away from the lesion to allow sufficient counter-traction of the flap by the endoclip, which behaved as micro-forceps. The external magnet has since been miniaturised by other investigators to a smaller hand held magnet which is positioned over the torso of the patient. This method has been shown to be feasible as well as reduce procedural times, with no reported complications on 25 gastric lesions[17,18]. This is a promising method and adds to the arsenal of ways to allow possible endoluminal triangulation.

At a more endoscopic surgical level, the use of magnets has been used to create suture free anastomoses. The concept relies on a pair of identical magnetic rings being applied to each end of the intestinal segments to be joined.

When they are then brought into close proximity, the magnets align and mate together. Over a period of about 5 d the inner area necroses off while the surrounding non compressed tissue heals and remodels itself. The coupled magnets then fall off into the created lumen leaving a magnetic compression anastomosis. Initial animal model experiments have shown encouraging safety and efficacy. But unfortunately this did not transpire into the clinical setting, with reports of serious adverse events[19-21]. Further disadvantages in this technique were the inevitable delay in anastomotic formation as well as a restriction on the circumference of the anastomosis due to the initial fixed size magnets used. To get over this drawback, more recent research has looked into using "nano-magnets" delivered *via* an endoscopic catheter device. These self-assemble at the two opposing desired sites to occupy a larger perimeter. The lumen of the anastomosis is then created with the aid of a needle knife. An early proof of concept studys on live porcine models, as well as a human cadaver, has shown the successful formation of gastro-jejunostomies[22]. Although currently not commercially available, magnetic compression anastomosis seems a viable option to aid in the formation of a secure gastro-enteric anastomosis during future natural orifice transluminal endoscopic surgery, replacing the standard methods of suturing or stapling which has its associated complications of leakage and stricture formation.

Capsule endoscopy

The demand for capsule endoscopes has grown exponentially, and it is unlikely that even Paul Swain when he took it upon himself to swallow this first "pill" in 1999 would have envisaged that over 2 million of these would have been ingested worldwide subsequently. The market is well established in the small bowel, and beginning to grow in force progressively for the colon. The upper GI tract seemed to have eluded this technology, firstly due to the speed of travel down the oesophagus and secondly because the larger more capacious stomach really necessitated capsule maneuverability. This has led to several investigators trialling various methods for capsule control, with magnetic assisted capsule endoscopy (MACE) being the most promising. Four systems have been developed, all of which have incorporated magnetic inclusion bodies into the capsule endoscope and controlled externally either by a magnetic field generated by a guidance system or more simply by a fixed magnet on a hand held device. The largest comparative trial to date (n = 189) comparing MACE to standard upper GI endoscopy was undertaken in France using a system developed jointly by Olympus® and Siemens®. The mean examination time was 11 min compared to the 6 min for standard gastroscopy, with the specificity and sensitivity of 94% and 62% respectively for major lesions[23]. However, the magnetic guidance system was similar in size to that of an MRI scanner and was limited to the examination of the stomach.

A simpler system which utilises a hand held magnet has recently been developed by Intromedic Ltd®, the MiroCam-Navi, and which for the first time was capable of exploring the entire upper GI tract. Although awaiting a randomised comparison trial the first feasibility study undertaken on volunteers showed promising visualisation of all the landmarks of the upper GI tract from the GOJ, cardia, fundus, body, incisura, antrum and pylorus of 92%, 88%, 100%, 96%, 96% and 100% respectively[24]. This system even has the possibility to aid in small bowel examination by reducing gastric transit time, through manoeuvring the capsule across the pylorus. Due to the simplicity of its use and high patient acceptance this technology certainly seems a true prospect for the future of upper GI tract examination, with the possibility of accurate capsule localisation and even targeted drug delivery being a distinct likelihood in the future[25,26]. The opportunity to support a community based screening programme, if one was to ever occur for upper GI tract pathology, is an attractive proposition with this technology. This MACE system would not require the expensive set-up costs or decontamination equipment needed with standard endoscopy. However, the current cost of this capsule would need to drop considerably, which should be within the realms of the manufacturers should mass use occur.

Nutritional feeding

In recent times there has been a growing demand for endoscopically placed naso-gastric/jejunal tubes largely due to increase demand for enteral feeding in those unable to maintain an adequate oral intake[27,28]. Jejunal tube placement is often undertaken at the bedside blindly, although this approach is associated with a significant failure rate. The alternative of direct endoscopic or radiological placement requires significantly resources. To attempt to solve these issues, two "bedside magnetic" devices have been developed; the Syncro-Blue tube and the Cortrak system. The Syncro-Blue tube uses a magnetic stylet placed at the end of the feeding tube which is then maneuvered into position *via* attraction of a hand held magnet. This system was evaluated in a case series of 288 critically ill patients, with successful post pyloric placement in 89% and a mean procedure time of 15 min[29]. Each tube costs approximately 95 dollars, which is likely to be cost saving given the associated expense of endoscopic or radiologically placed tubes. The more widely used Cortrak system, which has an electromagnetic transmitting stylet and a receiver placed in the epigastrium, allows real time tracking of the feeding tube as it is passed down the upper GI tract to its desired position. Although the Cortrak system does not allow external control, a recent systematic review has shown that procedure times as well as tube related adverse events are significantly lower compared to endoscopy with similar successful insertion rates[30]. The advantage of this system over the former is that it does not need X-ray imaging to confirm its position, with studies demonstrating 99.5% correlation with X-ray positioning[31]. In addition, there is the benefit of re-inserting the tube if accidental

dislodgement to the stomach was to occur.

CONCLUSION

So it seems that magnets are truly an ally to GI endoscopy, with several establishing methods. Those that are in an experimental stage are growing in momentum with even newer concepts being conceived. With more and more collaborations being undertaken between scientists, physicians and surgeons this seems to be an innovating field and the application of magnets is and will remain an attractive proposition enhancing endoscopy.

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MINIREVIEWS

Endoscopic options for treatment of dysplasia in Barrett's esophagus

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Abstract

Recent advances in the endoscopic treatment of dysplasia in Barrett's esophagus (BE) have allowed endoscopists to provide effective and durable eradication therapies. This review summarizes the available endoscopic eradication techniques for dysplasia in patients with BE including endoscopic mucosal resection, endoscopic submucosal dissection, photodynamic therapy, argon plasma coagulation, radiofrequency ablation and cryotherapy.

Key words: Dysplasia; Barrett's esophagus; Endoscopic therapy; Endoscopic mucosal resection; Radiofrequency ablation; Endoscopy; Photodynamic therapy

Core tip: Endoscopic treatment of high-grade dysplasia in Barrett's esophagus (BE) has become the standard of care for patients with this premalignant condition. In this review, we highlight the efficacy, durability and safety of the available endoscopic therapies for BE with high-grade dysplasia.

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INTRODUCTION

Barrett's esophagus (BE) is defined by the "American Gastroenterological Association" (AGA) as "a condition in which any extent of metaplastic columnar epithelium that predisposes to cancer development replaces the stratified squamous epithelium that normally lines the distal esophagus", (Figure 1)[1]. The existence of intestinal metaplasia (IM) in the esophagus predisposes to development of esophageal adenocarcinoma and BE

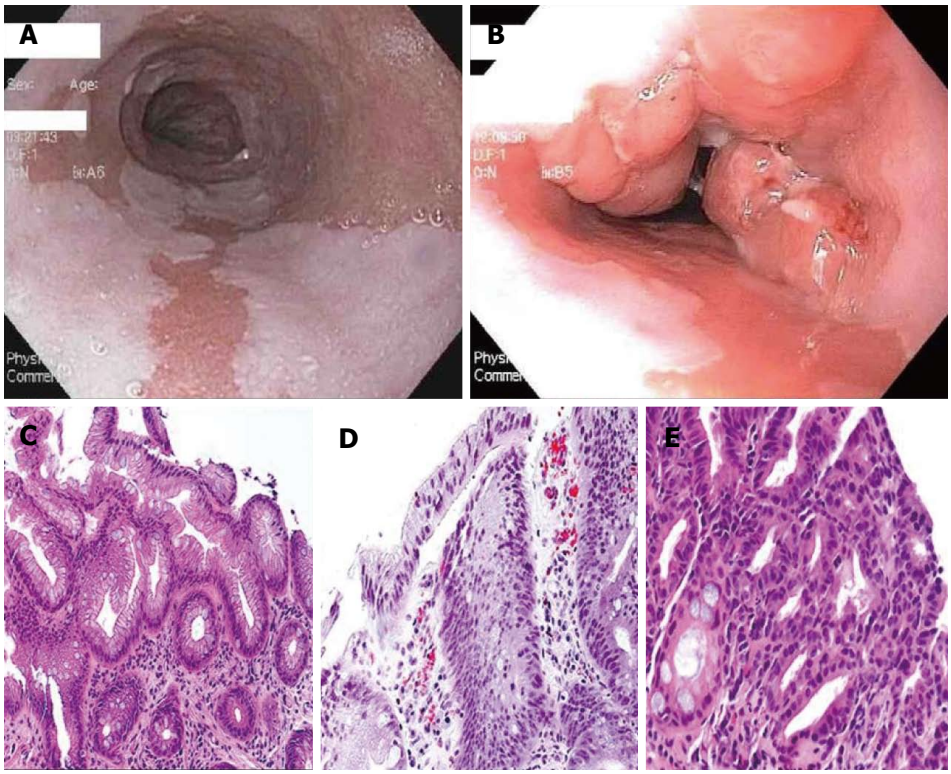

Figure 1 Histopathology pictures. A: White-light endoscopic image of long segment BE; B: White-light endoscopic image of BE with nodular mucosa found to be HGD; C: Hematoxylin and eosin (HE) stain of Barrett's mucosa; D: HE of Barrett's mucosa with LGD; E: Barrett's mucosa with HGD. Histopathology pictures courtesy of Purva Gopal, MD, Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas. HGD: High-grade dysplasia; LGD: Low-grade dysplasia; BE: Barrett's esophagus.

has become a well-recognized and treatable condition. The estimates of progression of non-dysplastic BE to adenocarcinoma are variable but uniformly low, ranging from 0.12% to as high as 2.9% per year, with more recent studies reporting lower rates of progression, generally less than 0.5% per year[2,3]. However, the incidence of progression to adenocarcinoma in patients with BE with dysplasia is up to five times as high as in non-dysplastic BE[2]. The presence of high-grade dysplasia (HGD, Figure 1) in BE portends a significant risk of progression to adenocarcinoma, calculated to be up to a 6% annual risk in one meta-analysis[3].

The need for non-invasive strategies to treat dysplasia in patients with BE has become an impetus for gastrointestinal endoscopists to develop new and effective endoscopic techniques. In this paper, we review the different options for treatment of dysplasia in BE, with a focus on endoscopic treatment of HGD.

SURGICAL TREATMENTS

In the past, the gold standard of therapy for HGD was esophagectomy, a procedure with well-recognized morbidity and perioperative mortality as high as 10%[4,5]. More recently, laparoscopic approaches and techniques such as the transhiatal esophagectomy have become more common. These techniques have lower morbidity than some of the older surgical techniques, including reduced hospital length of stay, fewer major complications, and less post-operative dumping syndrome[6,7]. Surgical therapy is a valid curative option for patients in whom there is suspicion of cancer invading the submucosa or if lymph node metastases are present. In patients with early esophageal adenocarcinoma, up to 20% of patients with cancer involving the submucosa will have lymph node metastases, with the risk increasing further with growth of the tumor into the deeper submucosa. In contrast, the risk of lymph node metastases in patients with intramucosal adenocarcinoma (*i.e.*, not invading the submucosa) is much lower at less than 2%[8].

While endoscopic therapy of HGD has become increasingly common, esophagectomy is still an option for patients. The AGA and American Society of Gastrointestinal Endoscopists (ASGE) still acknowledge esophagectomy as a therapeutic option in appropriate patients with BE and HGD, while the American College of Gastroenterology (ACG) guidelines on BE state that esophagectomy is no longer the necessary treatment response to HGD[1,9,10].

ENDOSCOPIC TREATMENTS

For patients with HGD limited to the esophageal mucosa, endoscopic eradication has become the mainstay of therapy. Multiple modalities compatible with endoscopy have been studied including both mechanical removal of tissue and ablative techniques. Methods that involve tissue resection include endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD).

The ablative techniques include several older techniques such as photodynamic therapy (PDT), laser therapy with Nd:YAG (neodymium-doped yttrium aluminum garnet; Nd:$Y_3Al_5O_{12}$) or potassium titanyl phosphate (KTP) lasers, multipolar electrocoagulation (MPEC), argon plasma coagulation (APC), and newer techniques such as cryotherapy and radiofrequency ablation (RFA). These therapies are tailored to the type of HGD present, specifically whether the dysplasia is visible, raised, discolored or nodular; features which have been associated with higher rates of malignancy compared to flat mucosa[11]. It is important to note that all the endoscopic treatments described below require acid suppression therapy for success, namely proton pump inhibitor (PPI) therapy.

EMR AND ESD

EMR, initially developed in Japan for treatment of superficial squamous cell esophageal carcinoma, is now the treatment of choice for nodular HGD in the esophagus[12]. It is also considered helpful diagnostic tool to evaluate for adenocarcinoma invading the submucosa, as well as to determine whether mucosal nodules harbor dysplasia. EMR is useful in staging, as illustrated by Wani *et al*[13]'s study which found that in patients with BE and dysplasia or early cancer, EMR resulted in upstaging of the diagnosis in 10% of patients and downgrading of the diagnosis in 21%. The two main EMR techniques are use of an endoscopic resection cap (ER-cap) (Olympus, Tokyo, Japan), which varies in terms of shape and texture and a multi-band ligator (Wilson-Cook, Indianapolis, United States) used for multiband mucosectomy (MBM). A diathermic snare is used for resection in both techniques. A submucosal lift with saline or a more viscous solution such as hydroxypropyl methylcellulose (artificial tears) can also be employed prior to resection when using the ER-cap method and is sometimes used with MBM. Pouw *et al*[14] performed a randomized controlled trial comparing of ER-cap and MBM and found that MBM was less costly and resulted in fewer acute complications without any significant difference in the depth of tissue resected.

EMR has been shown to be safe and effective as monotherapy for eradication of HGD in several studies. The reported rates of remission from HGD after EMR range from 87%-96% with median follow-up of 22-28 mo[15-17]. The long term remission rate and the durability of EMR as a solo modality for treatment are not currently known; therefore, these patients should be maintained in a surveillance endoscopy program. Complications of EMR include bleeding, perforation, and most commonly stricture formation. The frequency of stricture development reported in EMR studies varies widely, from 12.5% to 88%, depending on the extent of EMR and number of sessions[15-17]. For the majority of patients, post-EMR strictures are easily treated with endoscopic dilation techniques. In general, the smaller the area of resection, the lower the likelihood of stricture formation[17].

ESD is a safe and effective therapy for early gastric cancers and large dysplastic colon polyps[18,19]. Technically, the procedure differs from EMR in that a specialized ESD knife is used to access the submucosal space and dissect the superficial lesion away from the submucosa. As with EMR, a cushion of fluid is first injected to lift the lesion of interest and protect the esophageal wall from deeper penetration of the ESD knife. This fluid typically contains a viscous agent to allow for a sustained lift and a dye to help identify tissue planes for appropriate dissection[20]. The rationale for using ESD is that this technique can allow for a larger and more precise area of dysplastic tissue removal than EMR can safely target.

ESD has recently been evaluated in the management of BE with HGD and early adenocarcinoma. A German group reported a 77% curative resection rate in a small group of patients with a recurrence rate of 5.9% in two years follow-up. The complication rate was 27% for this group of patients and included one perforation and three strictures[21]. A retrospective analysis of 70 Belgian patients who underwent ESD reported a curative resection rate of 64% for patients with HGD and 85% for patients with early adenocarcinoma. At a median follow-up of 20 mo, 92% of patients retained remission from neoplasia. Strictures formed in 60% of patients and these were managed endoscopically[22]. The technique of ESD requires specific training and is only safe in qualified hands in high volume centers. At this time, the ASGE is the only major United States GI society that recognizes ESD as a potential treatment for visible HGD[10].

PDT

PDT is a technique for endoscopic ablation using either 5-aminolevulinic acid or porfimer sodium as a photosensitizing agent followed by exposure to laser light, which causes a photochemical reaction, damaging both mucosal and deeper tissues. The largest study of PDT was a randomized clinical trial evaluating PDT plus omeprazole *vs* omeprazole alone, which showed that patients treated with PDT had a HGD eradication rate of 77% compared to 39% in the omeprazole-alone group. With 5-year follow-up 15% of patients treated with PDT had progressed to cancer, compared to 29% in the omeprazole group[23]. In one longer-term follow-up study of 66 patients with HGD and early adenocarcinoma who underwent PDT, in the calculated 5-year survival was 97% in patients with HGD and 80% in those with early adenocarcinoma without significant long-term complications[24]. Currently, all three major United States societies mention PDT as an option for ablating HGD in BE[1,9,10].

LASER THERAPIES

Nd:YAG and KTP laser-derived thermal therapies have also been evaluated as a treatment tool for HGD in BE. Both Nd:YAG and KTP are crystals that when used in lasers produce wavelengths of light that can damage

tissue, such as dysplastic BE. These lasers have typically been studied in tandem with one another or combined with another mode of therapy. Sharma *et al*[25] reported a series of seven patients with BE and HGD who were not surgical candidates who underwent combination therapy with Nd:YAG laser and monopolar electrocautery. The dysplasia was eradicated in all seven with only residual metaplasia in three patients over a mean follow-up of 3.4 years. Nd:YAG-enhanced KTP laser was also shown to be safe and effective in pilot study of 10 patients with 100% eradication of dysplasia on follow-up esophageal biopsies and no recurrence on average follow-up of 10 mo[26]. Laser treatment is rarely used at this time as other therapies have become more popular.

APC AND MULTIPOLAR ELECTROCOAGULATION

APC is another form of endoscopic thermal therapy using the medium of argon gas to conduct electrical current leading to tissue destruction. The therapy is performed *via* a catheter that fits through the endoscope working channel. MPEC utilizes electrical current through an endoscopic catheter to cause localized tissue destruction. One prospective trial compared APC and MPEC for treatment of dysplastic BE and found no statistical difference in either endoscopic or histologic eradication of dysplasia[27]. However, MPEC required significantly fewer endoscopic therapy sessions with a trend toward better histologic eradication. There were no serious adverse events but 8% of patients treated with MPEC and 13% of patients treated with APC experienced transient upper GI symptoms. While APC is not typically used as a solo modality for treatment of BE and dysplasia, APC can be used to treat small areas of residual BE. In one study of patient with BE and HGD who underwent mucosectomy, treatment of residual disease with APC was found to prolong recurrence-free survival[28].

CRYOTHERAPY

The goal of this endoscopic therapy is to use freeze-thaw cycles for the destruction of tissue. Cryotherapy is performed using low-pressure liquid nitrogen (CSA Medical, Maryland, United States) or carbon dioxide (GI Supply, Pennsylvania, United States) delivered *via* spray catheter. One of the earlier prospective studies of cryotherapy found a 94% eradication rate for HGD with complications including chest pain and dysphagia, as well as one gastric perforation[29]. Recently, a prospective cohort study of 96 patients (two-thirds of whom had HGD) underwent cryotherapy, resulting in a complete eradication rate of 81% for HGD. Only three patients developed a stricture in the 37 mo of follow-up[30]. The durability of cryotherapy in preventing disease recurrence has come into question. Halsey *et al*[31] published data suggesting that up to 30% of patients treated with cryotherapy experienced disease recurrence at a median of 6.5 mo, and 10% had a second recurrence. However, a more recent single center retrospective cohort reported a HGD eradication rate of 100% with sustained remission in 97% of patients with previous HGD over a range of 24-57 mo[32]. At this time, only in the ASGE guidelines is cryotherapy specifically mentioned as a treatment option for dysplasia in BE[10].

RFA

RFA has emerged as the ablative technique of choice for BE with HGD because of the quality of evidence to support the ease of its administration, its efficacy, and safety profile. The procedure involves the direct application of radiofrequency energy to the esophageal mucosa, using either a balloon for circumferential treatment and more focal treatment through an attachment to the end of the endoscope or a small catheter that can pass through the working channel (Barxx/Covidien, Dublin, Ireland). With these tools, RFA can be applied to the mucosa circumferentially or focally. In the landmark multicenter sham-controlled randomized controlled trial by Shaheen *et al*[33], RFA resulted in eradication of dysplasia in 81% of patients with HGD. The treatment also decreased the progression of dysplasia to cancer. Complications were rare in this study, with only a 6% rate of stricture formation over 12 mo of follow-up[33]. RFA has also been shown to be successful in eradicating persistent dysplasia after initial therapy with PDT. In one study, RFA used as rescue therapy after PDT treatment successfully eradicated residual HGD in 86% of patients[34].

For some patients with BE, multiple endoscopic therapies are required for treatment. RFA is most effective on smooth BE mucosa, and is not adequate treatment for nodular dysplasia. As a result, endoscopists have been combining endoscopic eradication therapies, most commonly EMR and RFA. With combination therapy, visible or nodular dysplasia can be precisely removed with EMR, and any residual dysplasia or metaplasia can be systematically treated with RFA, typically performed after the EMR site has healed. One retrospective study of combination therapy reported an 86% complete eradication rate of HGD, but complete eradication of only 62% of nondysplastic intestinal metaplasia[35]. More recently, a multicenter prospective trial in Europe (EURO Ⅱ) evaluated the efficacy and safety of such a treatment strategy. EMR was performed on visible abnormalities within the BE segment and the remaining visible Barrett's mucosa was treated with RFA 6 wk later. Patients underwent a median of two RFA sessions. This combination of procedures achieved a 92% complete eradication rate for HGD and neoplasia and complete eradication of intestinal metaplasia in 87% of patients. At 36 mo of follow-up, only 4% of patients had recurrence of neoplasia. There were no major complications from the procedures and the rate of esophageal stenosis rate was 6%[36].

The existing evidence for treatment of low-grade dysplasia (LGD, Figure 1) in BE (most often with RFA) is

less abundant than studies of patients with BE and HGD. However, a recent randomized clinical trial (the SURF trial) showed a significantly lower rate of progression of LGD to either HGD or adenocarcinoma over three years after RFA[37]. Complicating the decision to ablate LGD is the fact that there is significant disagreement between pathologists on the definition of LGD. Several studies have highlighted the discrepancy in pathologist interobserver agreement when evaluating specimens with LGD. In one such study, expert pathologist confirmed only 15% of previously diagnosed LGD[38]. The AGA recommends RFA as therapy for BE with LGD based on high quality evidence while the ASGE dictates that RFA should be considered as therapy for LGD, and ACG acknowledges the effectiveness of RFA for LGD[1,9,10].

RISK OF RECURRENCE AFTER ENDOSCOPIC THERAPY

Recurrence after endoscopic therapy is a concern for gastroenterologists treating patients with dysplastic BE and the rates of recurrence vary widely depending on the study. Gupta *et al*[39] noted that IM returned in up to 33% of patients at 2 years after endoscopic therapy including RFA. A smaller percentage of recurrent IM was dysplastic (22%). The investigators were unable to identify any predictors for recurrence in this particular population of patients[39]. Other groups have tried to define predictors for recurrence of IM after definitive ablative therapy. In one recent large retrospective analysis, researchers found a slightly lower recurrence rate of 20% at 2.4 years for either IM or dysplasia. These investigators were able to identify risk factors for recurrence of BE and neoplasia, which included a worse pre-treatment histology, older age, and longer BE segments[40]. A single-center retrospective analysis of patients who achieved complete eradication of both IM and dysplasia with RFA found the one-year recurrence rate of IM to be 25% while dysplasia recurred in 8.5% of patients[41]. In contrast, a systematic review and meta-analysis of prospective and retrospective studies of RFA found that recurrence of dysplasia and IM was much lower after RFA treatment, with a 0.9% pooled recurrence rate for dysplasia and a 13% rate of recurrence for IM with an average follow-up of 1.5 years. There was wide range of IM recurrence rates reported in this study, ranging from 8% to 21%[42].

ENDOSCOPIC THERAPY OF NON-DYSPLASTIC BE

The debate rages on in the world of BE whether ablation of non-dysplastic Barrett's esophagus (NDBE) should be performed. Endoscopists advocating ablation of NDBE extrapolate the success of RFA in patients with HGD and LGD, applying these findings to non-dysplastic metaplasia. Another argument favoring ablation of NDBE is the lack of randomized controlled trials showing that surveillance of BE reduces mortality from esophageal adenocarcinoma, and thus other interventions should be considered[43,44]. Endoscopists who argue against ablation of NDBE focus on the lack of high quality evidence available to support such a notion and the very low rates of progression to cancer reported for non-dysplastic BE. Other issues proposed in the argument against ablation of nondysplastic BE include issues related to subjecting large numbers of patients to multiple endoscopic procedures, and the associated costs of the procedures and risk of complications[45]. One other argument against ablation of non-dysplastic BE is the possibility of missing subtle nodularity or mucosal changes that would be optimally treated with EMR, and instead burying it with suboptimal RFA therapy[45,46]. More prospective randomized controlled trials are needed to study the utility of RFA and other endoscopic therapies to treat NDBE. The AGA and ASGE mention that RFA could be considered for selected patients with NDBE thought to be at increased risk of progression to HGD and cancer[1,10].

CONCLUSION

The treatment options for HGD in BE have evolved into less-invasive therapies. There are now highly effective endoscopic therapies that are less morbid than esophagectomy. Most patients are treated with a combination of endoscopic resection and RFA with good outcomes. However, it is the job of the gastrointestinal endoscopist to be vigilant in surveillance for possible dysplasia recurrence in these patients. We have not yet reached the point where a patient can be told he or she has experienced complete eradication with no possibility of recurrence, and all patients should remain in surveillance. Until that time comes, we will continue to sharpen the endoscopic tools that will help us along the way to a durable cure.

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Endoscopic incisional therapy for benign esophageal strictures: Technique and results

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Abstract

Benign esophageal strictures refractory to the conventional balloon or bougie dilatation may be subjected to various adjunctive modes of therapy, one of them being endoscopic incisional therapy (EIT). A proper delineation of the stricture anatomy is a prerequisite. A host of electrocautery and mechanical devices may be used, the most common being the use of needle knife, either standard or insulated tip. The technique entails radial incision and cutting off of the stenotic rim. Adjunctive therapies, to prevent re-stenosis, such as balloon dilatation, oral or intralesional steroids or argon plasma coagulation can be used. The common strictures where EIT has been successfully used are Schatzki's rings (SR) and anastomotic strictures (AS). Short segment strictures (< 1 cm) have been found to have the best outcome. When compared with routine balloon dilatation, EIT has equivalent results in treatment naïve cases but better long term outcome in refractory cases. Anecdotal reports of its use in other types of strictures have been noted. Post procedure complications of EIT are mild and comparable to dilatation therapy. As of the current evidence, incisional therapy can be used for management of refractory AS and SR with relatively short stenosis (< 1 cm) with good safety profile and acceptable long term patency.

Key words: Endoscopic incisional therapy; Esophageal strictures; Anastomotic strictures; Needle knife; Radial incision and cutting

Core tip: Benign esophageal strictures refractory to conventional balloon or bougie dilatation can be subjected to endoscopic incisional therapy. The technique entails the use of needle knife or scissors for radial incision and cutting off of the stenotic rim. Adjunctive therapies with balloon dilatation or intralesional steroids may be needed for prevention of re-stenosis. Current evidence suggests use of incisional therapy for refractory short segment (< 1 cm) anastomotic strictures and Schatzki's rings with good safety profile and acceptable long term patency.

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INTRODUCTION

Benign esophageal strictures are a frequent challenge for the endoscopist. Peptic injury secondary to chronic acid exposure accounts for 80% of all benign esophageal strictures[1]. However, the remaining 20%-30% may be associated with Schatzki's rings (SR), esophageal webs, post radiation injury, anastomotic strictures (AS) and caustic ingestion. Based on anatomical complexity the strictures are classified as either simple or complex[2]. Simple are those with short, straight strictures, usually allowing passage of normal diameter endoscopes and are easy to treat (webs, rings and peptic strictures). The difficult to treat complex strictures are longer (> 2 cm), angulated or with severely stenosed lumen, a consequence of fibrosis with cicatricial narrowing. AS, caustic strictures and radiation strictures are known to be complex strictures[2]. Dilatation by bougie or balloon dilators has been the age old technique for management of benign esophageal strictures and generally the simple ones respond adequately to 1-3 dilatations[3]. The more difficult ones require more sessions of dilatations or the need for additional modes of treatment. Henceforth, Kochman *et al*[4] have defined strictures as: (1) refractory, when there was a persisting dysphagia score of 2 or more, as a result of inability to successfully achieve a diameter of 14 mm over 5 sessions at 2 wk intervals; and (2) recurrent, when there was inability to maintain a satisfactory luminal diameter for 4 wk once the target diameter of 14 mm had been achieved.

Although dilatation is a time tested, safe and effective mode of therapy for esophageal strictures, 10% of patients may require repeated dilatations[4,5] and 90% of those who have a single recurrence will eventually develop further recurrence. Moreover, dilatation failure group will require adjunctive modes of therapy. The various endoscopic options (Table 1) besides dilatation are intralesional steroid injection[6-8] or topical mitomycin C[9,10], esophageal stenting (self-expanding metal stents[11-13], self-expanding plastic stents[14,15] and biodegradable stents[16-19]), rendezvous procedure (antegrade and retrograde dilatation)[20,21] and incisional therapy.

Limited literature exists on endoscopic incisional therapy (EIT) and this review will deal with indications, techniques and the outcome of this modality in the management armamentarium of benign esophageal strictures.

DESCRIBED USES OF EIT

After the first description of its utility by Raskin *et al*[22] for Schatzki's ring in 1985, incisional therapy has been found to be useful in a number of other causes such as AS[23-25], strictures after esophageal endoscopic sub mucosal dissection (ESD) or endoscopic mucosal resection (EMR)[26,27], corrosive strictures[28], upper esophageal webs[29] and a host of other benign strictures.

Table 1 Endoscopic options of esophageal stricture management

Dilatation
Balloon
Bougie
Dilatation with injection therapy
Intralesional triamcinolone
Topical mitomycin C
Incisional therapy
Stent placement
SEMS
SEPS
Biodegradable stents
Rendezvous procedure

SEMS: Self expanding metal stents; SEPS: Self expanding plastic stents.

TECHNICAL DETAILS OF INCISIONAL THERAPY

Pre procedure assessment

Before subjecting a patient to EIT a proper assessment of the indication, the suitability of the procedure and the safety of the patient has to be done. The baseline symptom profile including the grade of dysphagia has to be recorded. Usually, strictures refractory to conventional modes of therapy are subjected to EIT as use of EIT for naive strictures (without prior dilatation therapy) has not been found to be superior to the conventional dilatation[30]. Active inflammation or underlying malignancy has to be ruled out with histology. Contrast esophagography and cross sectional imaging are needed for proper delineation of the stricture anatomy. The diameter of the stricture can be roughly estimated on endoscopy as: (1) size of 10 mm or more if a standard endoscope tip can be passed (GIF-H180 with insertion tube diameter of 9.8 mm; Olympus Medical Systems, Tokyo, Japan); (2) size of 5-10 mm if standard ultrathin scope can be passed (GIF-N180 with insertion tube diameter of 4.9 mm); (3) size of 2-5 mm if the ultrathin scope cannot be passed; and (4) less than 2 mm (pin point strictures) if the outer sheath of the needle-knife catheter (1.7-mm needle diameter) (Wilson Cook Medical Inc, Winston-Salem, NC) can just be passed or not pass through. The depth of the lesion is assessed by comparing with the length of the needle knife (approximately 4 mm). This documentation will help in outcome assessment post therapy. Finally, patients with bleeding diathesis, respiratory failure, severe or unstable cardiac disease and anastomotic leakage or infection need correction of these risk factors before therapy.

Instruments required

EIT has been carried with a host of electrocautery and mechanical devices including polypectomy snares and

Table 2 Instruments for incisional therapy

	Distal tip outer diameter (Fr)	Knife length (mm)	Knife diameter (mm)	Min. channel size (mm)	Working length (cm)
Needle knives					
Olympus (Tokyo, Japan)					
Triple lumen needle knife	5	5	0.2	2.8	195
Hook knife	Hook length 1.3 mm	4.5	0.4	2.8	165/230
Needle knife (require handle)					
KD-10Q-1.B	NA	3	0.4	2.0	195
KD-11Q-1.B	NA	3	0.7 (flat)	2.0	195
IT-Knife-L	Ceramic tip with diameter 2.2 mm	4	0.4	2.6	
Boston scientific (Natick, Mass)					
RX needle knife	5.5	5			200
Microknife™XL triple lumen knife	7-5.5				200
Cook medical (Winston Salem, NC)					
Fusion needle knife	6	4		4.2	200
Zimmon needle	5	7		2.0	200/320
Scissors					
Surgical scissors FS-3L-1 (Olympus): Min. channel size - 2.8 mm Working length - 165 cm					
Heiss-Device flexible endoscopic scissors (Telemed Systems, Hudson, Mass): 1.7 mm blade diameter × 2.5 mm blade length 1.7 mm shaft diameter 180 cm shaft length Single-action blade					
SB knife Jr (Sumitomo Bakelite Co., Tokyo, Japan): Width 4.4 mm × Length 3.5 mm Rotatable monopolar scissors					

Fr: French; NA: Not applicable; IT knife: Insulated tip knife.

argon plasma coagulation[31]. However, the most widely used are the needle knives that are nothing but "naked" diathermy wires[32]. The standard needle knife designed for endoscopic retrograde cholangio-pancreaticography is a diathermy wire that protrudes out of the catheter sheath by a handle mechanism and electrocautery is done powered by electrosurgical generators. This free hand technique is a cause of concern for fear of perforation. To minimize this risk, a modification has been made with the addition of an insulated ceramic tip (insulated tip needle knife, IT knife) allowing only cutting at the side. Other modifications such as the hook tip knife can also be used[32].

Mechanical devices that have been used are the Heiss-Device flexible endoscopic scissors (Telemed Systems, Hudson, Mass) and the FS-3L-1, endoscopic suture scissors (Olympus America Corp, Melville, NY).

A combined mechanical and electrocautery device, originally devised for ESD, known as SB Knife Jr (Sumitomo Bakelite Co., Tokyo, Japan) has also been used. It is a scissor-type knife with rotatable monopolar scissors and insulated coating for enhanced incision power while protecting surrounding tissues. A comprehensive table of the various instruments with their specifications has been depicted in Table 2 and Figure 1.

The technique

First applied to SR, the most commonly used incisional therapy is the needle knife electroincision and will be dealt with in detail here. Although most commonly the standard needle knife is used, with the advent of various modifications, the IT-knife is preferred for short strictures[32]. The basic principle of this modality is the same as dilatation, *i.e.*, disruption or displacement of the fibrotic tissue to help restore a satisfactory lumen diameter and prevent the reorganization of the fibrotic tissue.

The electroincision requires use of radial incisions with the knife attached to an electrosurgical unit such as UES-30 generator (Olympus, Tokyo, Japan) or more commonly ERBE generator (Elektromedizin GmbH, Tübingen, Germany) with software controlled fractionated cuts either in the pure cut or blended cut modes.

The technique used has been essentially the application of radial incision of the stricture area and was rechristened with the term of "radial incision and cutting" (RIC) method by Muto *et al*[25] RIC is carried out in the following steps (Figure 2): (1) The stricture area is incised under direct vision with the needle knife in a radial fashion parallel to the longitudinal axis of the esophagus. Usually a virtual line connecting the cranial and the caudal sides of the lumen is presumed and the incision line is guided accordingly. Precise movement is imperative for appropriate use of needle knife and can be achieved better with the endoscope tip movement rather than the needle itself; (2) The length and the number of incisions are guided by the need to completely remove the rim of stenosis. On an average, 8-12 radial incisions are needed[24]. The incision depth is assessed using the needle-knife length as a comparator; (3) While for short segment strictures, the

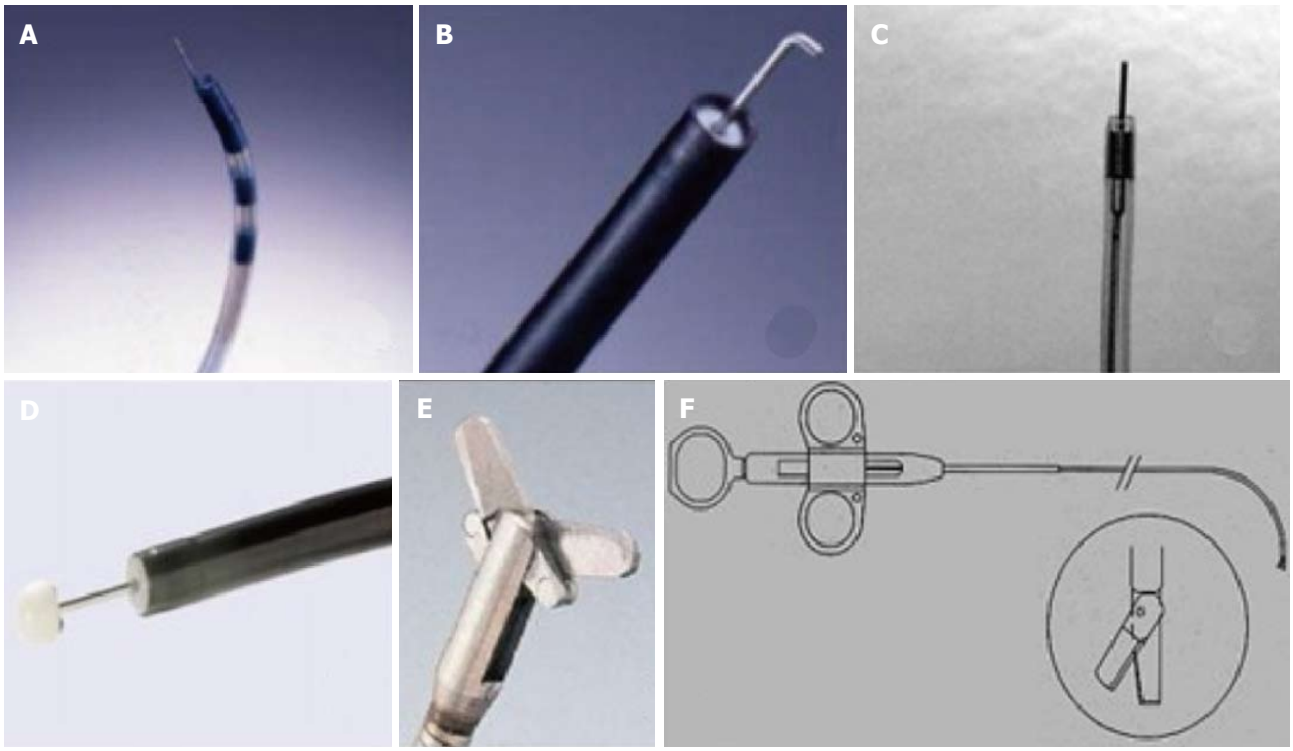

Figure 1 Accessories for incisional therapy. A: Triple lumen needle knife; B: Hook knife; C: Needle knife (KD 10Q); D: Insulated tip knife; E: Endoscopic surgical scissors (Image courtesy of Olympus); F: Heiss-Device flexible endoscopic scissors (image courtesy of Telemed systems).

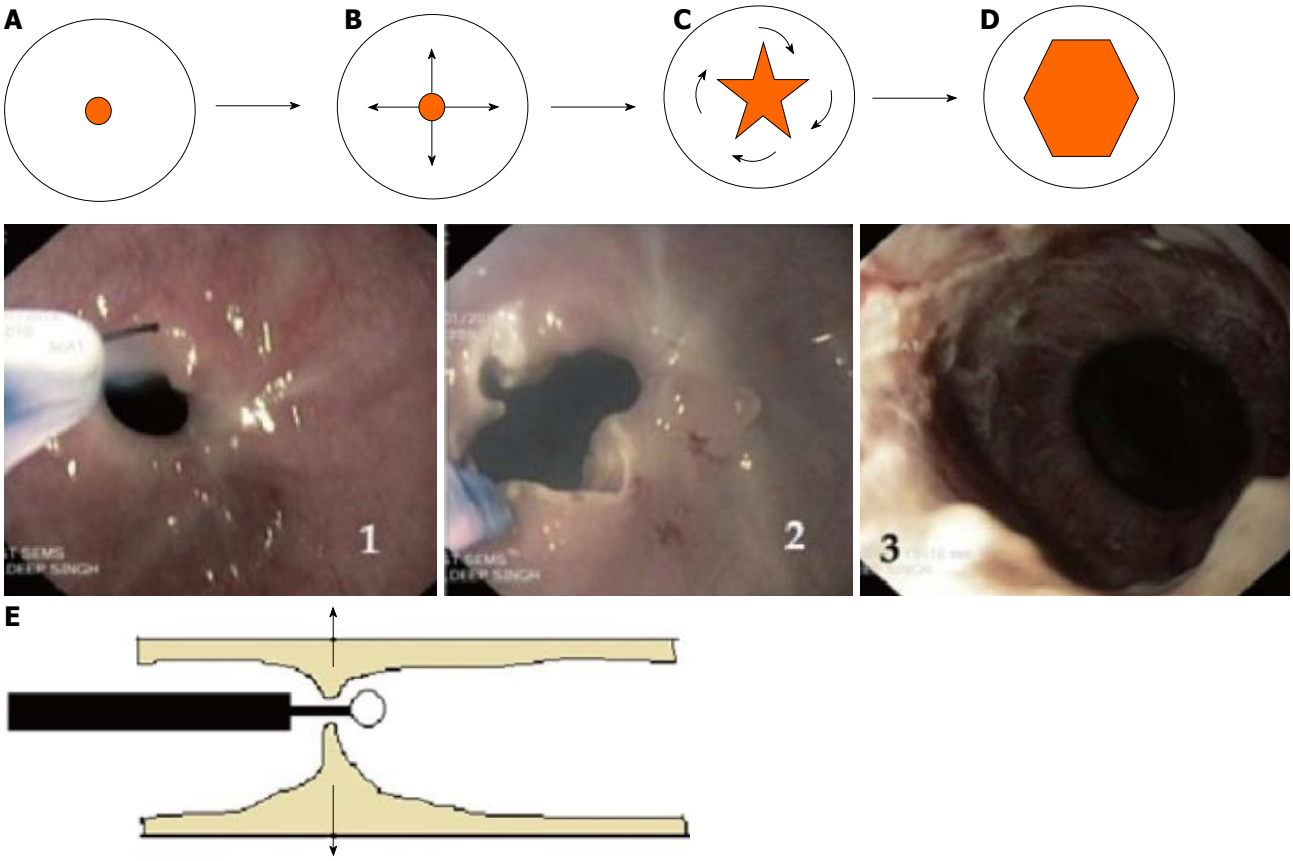

Figure 2 The technique of endoscopic incisional therapy procedure. A-D: Schematic front view of stricture site; B: Arrows depict the radial direction of incision; C: Curved arrows depict the slicing off of the intervening areas; D: Final outcome at the end of procedure; E: Lateral view of stricture site depicting the transverse working domain of the needle knife (arrows); 1: Use of needle knife for incision; 2: After radial incision; 3: At the end of EIT and balloon dilatation. EIT: Endoscopic incisional therapy.

technique is pretty straight forward, but for long segment ones, many times an opening needs to be created with multiple, short radial incisions before the scope can be negotiated for distal segments. Thus, technically difficult as it is for long segment ones, complete removal of the stenosed rim may not always be feasible; and (4) The parts of the strictured site in between the incision lines are then sliced off using the knife and the procedure is usually terminated once the scope can be easily passed across the strictured segment.

A modification to the technique proposed by Lee *et al*[24] was the use of a transparent hood attached to the scope tip for better visualization of the work field.

Post-procedure the patients are observed for immediate complications such as pain, significant bleeding or perforation. Once these have been ruled out, the patients can be discharged and assessed on a regular basis for recurrence of symptoms, grade of dysphagia or weight loss for which repeat assessment and redo of the therapy may be needed. Similar to the needle knife used for EIT various other devices such as the polypectomy snare[31] or scissors[28,33] have also been used.

Adjunctive measures

In the post-procedure phase, when the tissue has been freshly incised and chances of re-formation of stenosing fibrotic scar are high, various adjunctive measures have been described. Endoscopic balloon dilatation (EBD) with CRE balloon dilators (Boston Scientific, Natick, MA) have been done post-procedure and repeated frequently till the scarring of the cut surface[23,25,27]. Nonaka *et al*[28] have described the use of oral steroids for the prevention of re-stenosis. Yamaguchi *et al*[34] also demonstrated prevention of stricture after ESD with prednisolone. It has already been established in literature that use of intralesional steroids can prevent stricture recurrence[6-8]. The study of the efficacy of the same after EIT is currently being carried out in a large multi-center randomized control trial in Japan (UMIN Clinical Trials Registry: UMIN000014017). Argon plasma coagulation use has also been described along with incision for stepwise reduction of the scar tissue[31].

Evaluation of the treatment outcome

Recurrence of symptoms with dysphagia more than grade Ⅱ or the inability to pass a standard endoscope (9.5 mm) across the stricture site is considered as recurrent stenosis. If this condition arises even after 5 sessions of EIT, it is considered as treatment failure[30]. Post-procedure relief of symptoms, need for repeat procedure and the long term patency are factors assessed for the efficacy assessment of the procedure.

OUTCOME OF INCISIONAL THERAPY

The incisional therapy has been an alternate modality for the management of benign refractory strictures. The average time required for the procedure ranges from 6-14 min[24,25]. The majority of the published studies describe its use primarily in SR and AS. Anecdotal case reports have been found of its use in other conditions.

SR

After the first description of electrosurgical incision of SR by Raskin *et al*[22] in 1985, various studies have used it. When used as the initial intervention modality for SR (*i.e.*, without prior dilatation therapy), Guelrud *et al*[35] produced excellent results with 14 out of 17 patients (82.4%) becoming asymptomatic after a single session of EIT during a follow up of 46 mo. In the dilatation unresponsive group, Burdick *et al*[36] showed improvement in dysphagia in 6 out of 7 patients (85.7%) after a single session of EIT over a 36 mo follow-up, however later studies failed to replicate a similar outcome. DiSario *et al*[37] conducted EIT on 11 patients, who had a median of 3 dilatations prior to incision, out of whom 4 (36%) remained symptom free but 7 (64%) required further incisions or dilatations during a median follow-up of 55 mo. However, they found that there was a significant increase in the mean duration of improvement immediately after incision as compared with that of dilatation (17 mo *vs* 5 mo; $P = 0.034$).

In a prospective randomized study, comparing bougie dilatation with EIT as the initial therapy for symptomatic SR, Wills *et al*[38] demonstrated that both modalities had similar efficacy in symptom control, dysphagia and GERD, during a 12 mo follow-up period. However, the EIT group had longer symptom free survival time compared with the bougie dilatation group (7.99 mo *vs* 5.86 mo; $P = 0.03$).

AS

The most common esophageal stricture variant where EIT has been studied is the anastomotic stricture, mostly esophago-gastric anastomosis. Esophageal AS develops in 5%-46% of patients after surgical resection[2,39] and is secondary to post-operative complications such as bleeding, fistulization, leak development, anastomotic site infection and ischemia of the gastric anastomosis[2,39,40]. The success of balloon dilatation ranges from 70%-90% while 40% require more than 3 dilatations for optimal result[39-41]. A viable alternate management option has been the use of EIT as demonstrated in various studies (Table 3).

In cases of treatment naïve patients, after a single session of EIT, recurrence free course over a 6-24 mo follow up has been found to be 80.6% to 93%[24,30,31]. Thus, it is quite an effective therapy compared to dilatation without the need for repeated sessions for a considerable period of time. In fact, in a comparative trial with bougie dilatation, Hordijk *et al*[30] demonstrated that both EIT and dilatation were equally efficacious (80.6% *vs* 67.7%) at 6 mo follow-up.

In the more difficult group of refractory strictures, the symptom free rate dropped to 60% to 65%[25,42] with 44% requiring re-treatment. However, when

Table 3 Various studies of incisional therapy in esophageal anastomotic stricture

Ref.	Type of stricture	No. of patients	Length of stricture	No. of pre-procedure dilatations[1]	Follow-up duration (mo)	Outcome of single session
Schubert *et al*[31], 2003	Treatment naive	15	6.1 mm (3-10 mm)	NA	23	No recurrence - 14/15 (93%)
Simmons *et al*[23], 2006	Refractory	9	--	6	3-14	No dysphagia - 4/9 (44.4%) No response - 1/9 (11%)
Hordijk *et al*[42], 2006	Refractory	20	< 1 cm - 12 cm > 1 cm - 8 cm	8	12	No dysphagia - 12/20 (60%) Recurrence - 8/20 (40%) Treatment failure - 2/20 (10%)
[2]Hordijk *et al*[30], 2009	Treatment naive	EIT arm - 31	EIT arm - 1.35 cm	N/A	6	No difference in the success rate (80.6% *vs* 67.7%)
		SB arm - 31	SB arm - 0.55 cm (mean)			Treatment failure- EIT arm - 1; SB arm - 5
Lee *et al*[24], 2009	Treatment naive	24	< 1 cm - 21 cm > 1 cm - 3 cm	N/A	24	No recurrence - 21/24 (87.5%) Restricture - 3/24 (12.5%)
Muto *et al*[25], 2012	Refractory	EIT - 32	⩽ 5 mm - 49 mm	10	EIT - 14.8	Short term - 93.8% improvement
		EBD - 22	> 5 mm - 5 mm		EBD - 17.2	Long term - EIT better than EBD

[1]Mean number of dilatations; [2]Randomized prospective study. Treatment naïve: No previous dilatation; EIT: Endoscopic incisional therapy; SB: Savary bougienage; EBD: Endoscopic balloon dilatation; NA: Not applicable.

compared to continued dilatation therapy, EIT performed better than dilatation with significantly higher patency rates at 6 mo (65.3% *vs* 19.8%, $P < 0.005$) and 12 mo (61.5% *vs* 19.8%, $P < 0.005$) follow-up[25].

The other most important contributor of EIT response is the length of the stricture. Hordijk *et al*[42] had demonstrated that while patients with stricture length less than 1 cm had recurrence free course, all patients with stricture length greater than 1 cm had recurrence. Similar finding has been shown by Lee *et al*[24] wherein only 4.8% patients with stricture < 1 cm had re-stricture as compared to 66.7% in the group with stricture > 1 cm. This has been attributed to the increased amount of fibrosis in the longer strictures and hence decreased response.

Other strictures

In a retrospective study of 8 patients with post chemo-radiotherapy, ESD or EMR induced strictures, EIT improved dysphagia in all patients in the immediate post-procedure phase but 3 mo lumen patency was seen in only 3 (37.5%) patients[26].

Anecdotal case reports of use of endoscopic scissors have been used for management of corrosive strictures[28] and fibrous scar in proximal esophagus[33]. Stricture after surgery for esophageal atresia in a 4-year-old child has also been reported to be managed with EIT along with stenting[43].

Author's experience

A total of 14 patients with benign esophageal strictures (AS 5, corrosive strictures 4) have been subjected to incisional therapy along with balloon dilatation. Incisional therapy was done with Microknife™ XL Triple lumen knife (Boston Scientific, Natick, United States) followed by balloon dilatation with CRE™ Balloon Dilator (Boston Scientific, Natick, United States). Successful dilatation was achieved in 11 of the 14 after 3-9 sessions. No complications were noted.

COMPLICATIONS

Complications of EIT include pain, bleeding or perforation. Perforation is the most dreaded complication and can occur because of inability to gauge the depth of the esophageal wall or the length of the stricture during the incision therapy. Bleeding is usually self-limited and lesser known complication as the fibrotic strictures subjected to incisional therapy are relatively avascular. The complication rate of EIT appears to be mild comparable to dilatations with bougies or balloons, which can have perforation or significant hemorrhage at a rate of 0.1% to 0.4%[3]. For EIT, the reported perforation rate ranges from 0%-3.5%[24,25,30,37,42] with no reported evidence of significant bleeding. Perforation can be managed essentially with conservative treatment and if it fails, can be subjected to stent placement or surgery. Bleeding can be easily managed with methods such as balloon tamponade. Thus, EIT is a safe therapeutic option for stricture management.

CURRENT STATUS OF INCISIONAL THERAPY

As of the current evidence, EIT can be used as a treatment modality for refractory SR and AS with relatively short stenosis (< 1 cm). A suggested algorithm for the management of benign strictures has been shown in Figure 3.

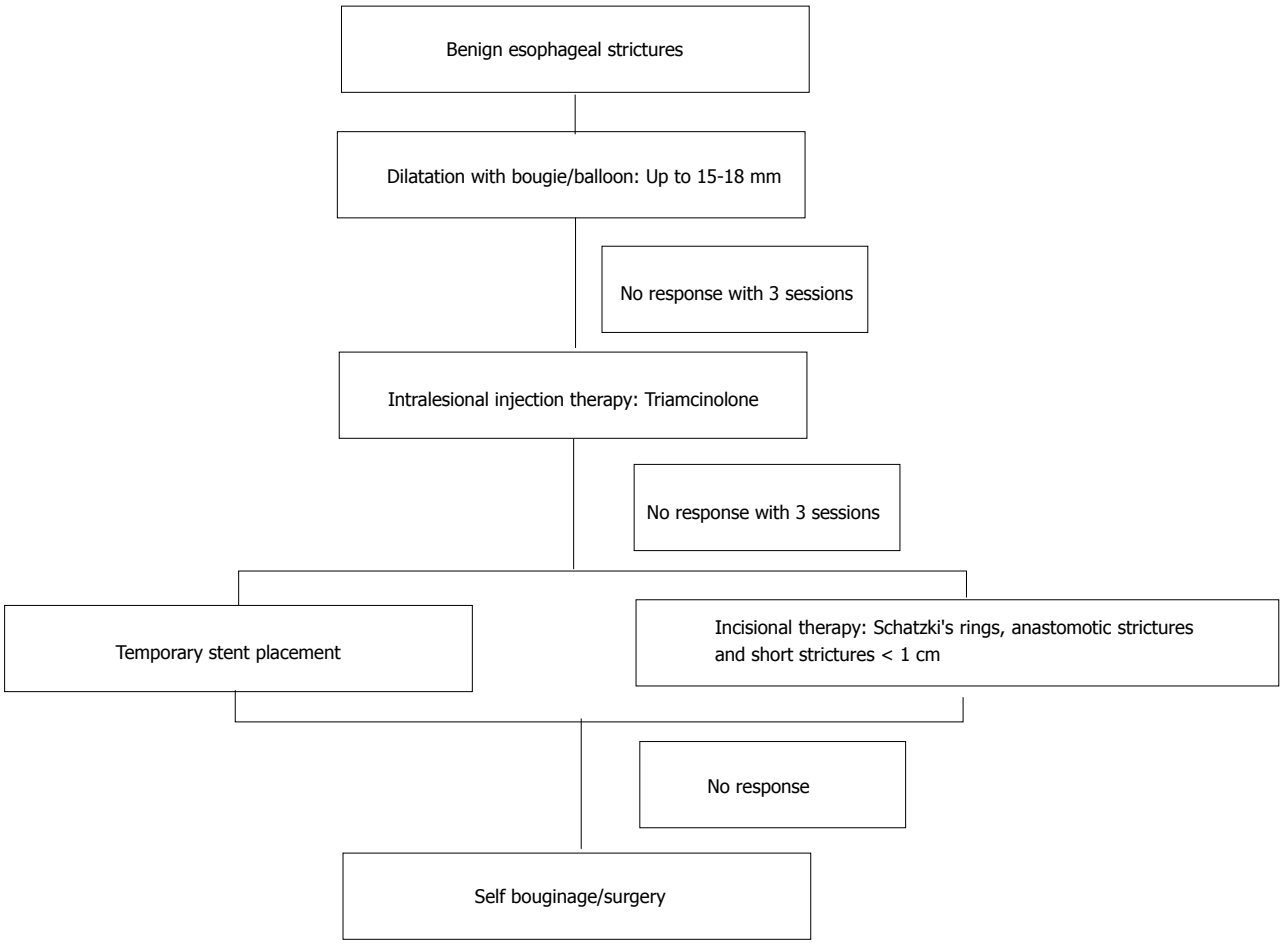

Figure 3 Algorithm for the management of benign esophageal strictures.

AREAS OF FUTURE RESEARCH

A number of questions need to be answered through larger trials before a standardized recommendation can be made regarding the use of incisional therapy in esophageal stricture management: (1) it can be used for all refractory strictures; (2) number of balloon or bougie dilatations before considering EIT; (3) cumulative risk of the procedure; (4) efficacy and applicability of instruments other than needle knife; (5) the choice of adjunctive therapy to prevent re-stenosis; (6) cost effectiveness of the therapy in the long run; and (7) technical expertise and applicability issues in day-to-day practice.

CONCLUSION

EIT is a feasible, safe and effective treatment modality for benign short refractory esophageal strictures with established evidence in SR and AS. It has good immediate symptom improvement with acceptable long-term patency.

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ORIGINAL ARTICLE

Retrospective Study

Feasibility of single-incision laparoscopic cholecystectomy for acute cholecystitis

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Author contributions: Ikumoto T collected and analyzed the data and wrote the manuscript; Ikumoto T, Iwatate M and Sano Y designed the study; Yamagishi H and Imai Y offered technical support about pathological diagnosis; Kotaka M provided administrative support; and all authors have read and approved the final version to be published.

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Abstract

AIM: To assess the safety of single-incision laparoscopic cholecystectomy (SILC) for acute cholecystitis.

METHODS: All patients who underwent SILC at Sano Hospital (Kobe, Japan) between January 2010 and December 2014 were included in this retrospective study. Clinical data related to patient characteristics and surgical outcomes were collected from medical records. The parameters for assessing the safety of the procedure included operative time, volume of blood loss, achievement of the critical view of safety, use of additional trocars, conversion to laparotomy, intraoperative and postoperative complications, and duration of postoperative hospital stay. Patient backgrounds were statistically compared between those with and without conversion to laparotomy.

RESULTS: A total of 100 patients underwent SILC for acute cholecystitis during the period. Preoperative endoscopic treatment was performed for suspected choledocholithiasis in 41 patients (41%). The mean time from onset of acute cholecystitis was 7.7 d. According to the Updated Tokyo Guidelines (TG13) for the severity of cholecystitis, 86 and 14 patients had grade Ⅰ and grade Ⅱ acute cholecystitis, respectively. The mean operative time was 87.4 min. The mean estimated blood loss was 80.6 mL. The critical view of safety was obtained in 89

patients (89%). Conversion laparotomy was performed in 12 patients (12%). Postoperative complications of Clavien-Dindo grade Ⅲ or greater were observed in 4 patients (4%). The mean duration of postoperative hospital stay was 5.7 d. Patients converted from SILC to laparotomy tended to have higher days after onset.

CONCLUSION: SILC is feasible for acute cholecystitis; in addition, early surgical intervention may reduce the risk of laparotomy conversion.

Key words: Acute cholecystitis; Single-port access surgery; Single incision laparoscopic cholecystectomy; Single incision laparoscopic surgery; Laparo-endoscopic single-site surgery

Core tip: Single-incision laparoscopic cholecystectomy (SILC) has attracted attention as a minimally invasive procedure. A scar-less operation can be achieved by making a skin incision at the umbilicus. However, the safety of this procedure for acute cholecystitis has not been established. We reported 100 consecutive cases of SILC for acute cholecystitis and their surgical outcomes. SILC was safely performed in approximately 80% of cases in this series. We believe that the results of this study indicate the feasibility of SILC for acute cholecystitis.

Ikumoto T, Yamagishi H, Iwatate M, Sano Y, Kotaka M, Imai Y. Feasibility of single-incision laparoscopic cholecystectomy for acute cholecystitis. *World J Gastrointest Endosc* 2015; 7(19): 1327-1333 Available from: URL: http://www.wjgnet.com/1948-5190/full/v7/i19/1327.htm DOI: http://dx.doi.org/10.4253/wjge.v7.i19.1327

INTRODUCTION

Cholecystectomy is widely performed as a basic treatment for acute cholecystitis. In the Updated Tokyo Guidelines issued in 2013 (TG13), early cholecystectomy is recommended as the first treatment choice, except for severe cases with organ failure[1]. Laparoscopic cholecystectomy (LC) is now a mainstream procedure. When performed by skilled surgeons, LC is considered a safe procedure even for acute cholecystitis[2].

In recent years, single-incision laparoscopic surgery (SILS) has attracted attention as a minimally invasive procedure. In SILS, multiple devices are inserted from a single skin incision into the abdominal cavity to reduce the length and number of incisions. In particular, scarless operations can be achieved by making skin incisions at the umbilicus[3]. Because cholecystectomy is performed in a nearly fixed visual field and because it does not require wide-range maneuvers, SILS is easily incorporated into cholecystectomy. SILC is becoming established as a procedural option.

However, there are limited reports on surgical outcomes of SILC for acute cholecystitis. Because maneuverability is limited in SILC compared with that in conventional LC, the safety of this procedure for acute cholecystitis has not yet been established. If SILC is as safe as conventional LC, SILC will become the procedure of choice for patients who desire better aesthetic outcomes. Although successful completion of SILC is a prerequisite for better aesthetic outcomes, data on acute cholecystitis are limited. At our hospital, we have focused on SILC and cases of acute cholecystitis. Thus, in order to address these clinical questions, we conducted a retrospective study of past cases. The objectives of this study were to assess the safety of SILC for acute cholecystitis and to investigate requirements for successful completion of SILC.

MATERIALS AND METHODS

This study included all patients who underwent SILC for acute cholecystitis at Sano Hospital (Kobe, Japan) between January 2010 and December 2014. Although SILC is, in principle, performed for all patients requiring cholecystectomy, four patients for whom laparoscopy had not been selected at the discretion of their attending physicians and one patient suspected to have concomitant gallbladder cancer were excluded. According to TG13[4], acute cholecystitis was diagnosed in patients who met all the following diagnostic criteria: (1) local inflammatory signs; (2) systemic inflammatory findings; and (3) characteristic imaging findings. Data were collected from medical records and analyzed. The parameters used to assess the safety of the surgery included operative time, volume of blood loss, achievement of the critical view of safety, use of additional trocars, conversion to laparotomy, intraoperative and postoperative complications, and duration of postoperative hospital stay.

Surgical technique

We performed SILC using a standard technique with conventional trocars and instruments. A 20-mm incision was first made at the umbilicus. An optical port, a 5-mm trocar, and 5-mm forceps were inserted in the incision. These three instruments were placed in a triangle to maximize their spacing. In addition, a 3- or 5-mm instrument was inserted beside the optical port. We did not use any devices specialized for SILS.

It is feasible to perform nearly the same surgical procedure as conventional LC because the potential interference of each device is minimized by direct insertion of two instruments without trocar. We made every effort to create the critical view of safety, as described by Strasberg. To prevent bile duct injury, we converted to open surgery when we could not create the critical view of safety or could not identify the cystic duct.

Drainage tubes were not routinely placed, even in

Table 1 Patient characteristics

	Acute cholecystitis (n = 100)
Mean age (yr ± SD)	66.8 ± 14.4
Sex	
Male	51
Female	49
Mean BMI (kg/m^2 ± SD)	23.9 ± 3.3
History of abdominal surgery	26 (26%)
Suspected choledocholithiasis	41 (41%)
Mean time from onset (d ± SD)	7.7 ± 4.1
TG13 severity grading	
Grade Ⅰ (mild)	86 (86%)
Grade Ⅱ (moderate)	14 (14%)

SD: Standard deviation; BMI: Body mass index; TG13: Updated Tokyo Guidelines.

Table 2 Surgical outcomes

	Acute cholecystitis (n = 100)
Mean operative time (min ± SD)	87.4 ± 39.3
Mean estimated blood loss (mL ± SD)	80.6 ± 162.4
Achievement of critical view of safety	89 (89%)
Additional trocar insertion	9 (9%)
Conversion to laparotomy	12 (12%)
Postoperative complication	4 (4%)
Bile leakage	(2)
Stone passage into the CBD	(2)
Mean duration of postoperative hospital stay (d ± SD)	5.7 ± 5.1

SD: Standard deviation; CBD: Common bile duct.

cases of severe inflammation. However, we placed a drainage tube from the right lateral abdomen to the liver bed in cases of suspected remnant abscess or bile leakage.

Statistical analysis

The *t* test was used to assess differences in patient age, body mass index (BMI), and days from onset. The Fisher exact test was used to assess differences in all other factors. All tests were two-sided, and *P*-values less than 0.05 were considered to indicate a statistically significant difference. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria)[5].

RESULTS

Patient characteristics

During the study period, 100 patients underwent SILC for acute cholecystitis. Their mean age was 66.8 years. The male-to-female ratio was 51:49. Their mean BMI was 23.9 kg/m^2. A history of some type of abdominal operation was found in 26 patients (26%). Choledocholithiasis was suspected in 41 patients (41%), based on imaging studies, and endoscopic lithotomy was performed before SILC. The mean time from the onset of acute cholecystitis to cholecystectomy was 7.7 d. According to TG13[4] guidelines for the severity of cholecystitis, 86 patients and 14 patients had grades I and II acute cholecystitis, respectively (Table 1).

Table 3 Histological diagnoses of resected gallbladder for acute cholecystitis

	n = 100
Edematous cholecystitis	9
Necrotizing cholecystitis	8
Suppurative cholecystitis	5
Chronic cholecystitis	74
(Acute on chronic cholecystitis)	(61)
Xanthogranulomatous cholecystitis	1
Adenocarcinoma	3

Surgical outcomes

The surgical outcomes are shown in Table 2. The mean operative time was 87.4 min, and the mean estimated blood loss volume was 80.6 mL. The critical view of safety was achieved in 89 patients (89%), although anterograde dissection of the gall bladder starting from the fundus was required for 42 of these patients. Additional trocar insertion was required in 9 patients (9%). SILC was converted to laparotomy in 12 patients (12%). A drainage tube was placed in 13 patients (13%), including 4 patients with necrotizing cholecystitis. Postoperative complications of Clavien-Dindo grade III or greater were observed in 4 patients (4%). The complications included leakage of bile from the stump of the cystic duct and passage of stones into the common bile duct in two patients each. These complications were resolved in all four patients using only endoscopic treatment. The mean postoperative hospital stay was 5.7 d.

Histological diagnosis

Histological diagnoses of the resected gallbladders included acute-on-chronic cholecystitis in 61 patients, edematous cholecystitis in 9 patients, necrotizing cholecystitis in 8 patients, suppurative cholecystitis in 5 patients, and xanthogranulomatous cholecystitis in 1 patient. Incidental adenocarcinomas were founded in 3 patients (Table 3).

Comparison of patients with and without conversion to laparotomy

The results of comparison between patients with and without conversion to laparotomy are shown in Table 4 and Figure 1. Despite the lack of statistical significance, the number of days after onset tended to be higher in patients who were converted from SILC to laparotomy.

Learning curve

The mean operative times of every five consecutive cases of SILC performed by a chief surgeon are shown

Table 4 Comparison of patients with and without conversion to laparotomy

	Without conversion (n = 88)	With conversion (n = 12)	P value
Mean age (yr ± SD)	66.1 ± 14.5	71.6 ± 13.3	NS
Sex			
Male	44	7	NS
Female	44	5	
Mean BMI (kg/m^2 ± SD)	23.9 ± 3.1	24.1 ± 4.7	NS
History of abdominal surgery	22 (25%)	4 (33.3%)	NS
TG13 severity grading			
Grade I (mild)	82 (93.2%)	4 (33.3%)	P < 0.001
Grade II (moderate)	6 (6.8%)	8 (66.7%)	
Mean time from onset (d ± SD)	7.5 ± 4.0	9.1 ± 4.4	NS

SD: Standard deviation; NS: Not significant; BMI: Body mass index; TG13: Updated Tokyo Guidelines.

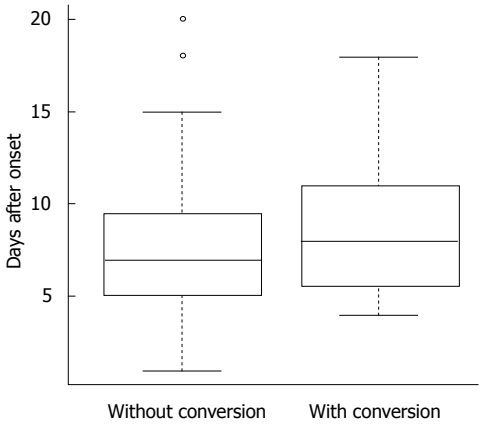

Figure 1 Time after onset of acute cholecystitis. Patients with conversion to laparotomy show a tendency toward increased preoperative days from onset.

in Figure 2. There were no obvious trends suggestive of a learning curve.

DISCUSSION

Although Navarra *et al*[6] first reported SILC in 1997, it did not initially attract much attention. However, SILC has been rapidly adopted since 2009, with improvements to platforms and devices dedicated for SILS[7-11]. Since then, SILS has been increasingly used, mainly because of its excellent aesthetic outcome; it has been widely applied not only to cholecystectomy, but also to appendectomy, colectomy, gastrectomy, urologic procedures, and gynecologic procedures[12-16]. LC in particular is relatively easy to perform with SILS, and SILC is routinely performed. The reasons for this include: (1) the surgical field is limited to the liver bed; (2) the direction of scopes and devices remains almost constant; (3) the procedure is mainly indicated for benign conditions; and (4) many patients undergoing the procedure are young. However, the drawbacks of SILS include: (1) the limited maneuverability of scopes and devices that may interfere with one another; and (2) difficulty in setting devices at different angles, as all devices are oriented in the same direction. Compared with conventional LC, SILC is technically more difficult. Because advanced endoscopic surgical techniques are required to perform SILC, it is a difficult procedure for less experienced surgeons. However, these obstacles have been gradually eliminated owing to advances such as the innovation of techniques appropriate for SILS, development of dedicated platforms, and introduction of pre-bending forceps[7,17-20].

Several randomized controlled trials (RCTs) have revealed that SILC is as safe as conventional LC[21-23]. However, to our knowledge, no RCT has assessed only patients with acute cholecystitis, for which SILC is technically more difficult, and the safety of SILC for acute cholecystitis has not been established. Thus, we reviewed 100 consecutive cases of SILC performed for acute cholecystitis and reported their surgical outcomes. The operative time tended to be longer in patients with cholecystitis; this likely reflects the difficulty of operative maneuvers. Moreover, the volume of intraoperative blood loss also tended to be higher; this may be attributable to the facts that (1) the gallbladder and its surrounding tissue affected by acute inflammation are more likely to bleed because they are congested and become edematous; and (2) the hepatic parenchyma is easily damaged because of inflammatory adherence of the gallbladder to the liver bed. These findings suggest that SILC for acute cholecystitis involves some level of difficulty. Thus, application of SILC should require careful consideration.

However, we performed SILC in all patients with acute cholecystitis who were judged to require cholecystectomy, and SILC was successfully completed without additional trocars in approximately 80% of cases. These findings indicate that SILC is applicable to many patients, even those with acute cholecystitis. Moreover, because the complication rate in this study is not higher than that reported in another study[23], we believe that SILC for acute cholecystitis is as safe as other surgical procedures under the conditions described in this study. In other words, the results of our study suggest that SILC can be performed in patients with acute cholecystitis without compromising safety. At minimum, there appears to be no need to exclude patients with acute cholecystitis from SILC.

New procedures typically have learning curves. However, there was no evidence of a learning curve for SILC

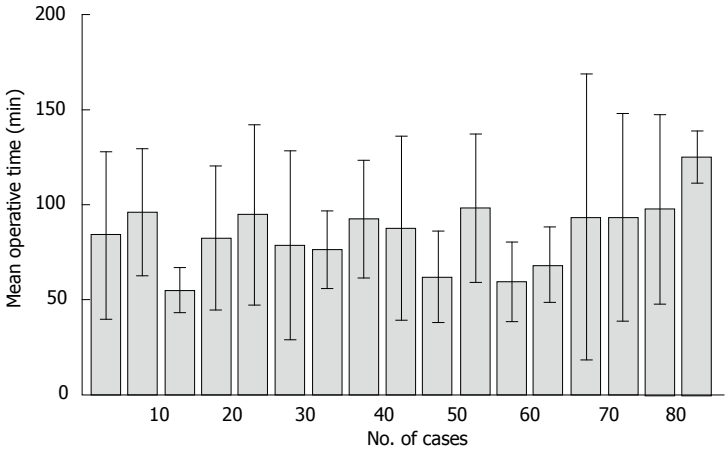

Figure 2 Mean operative time for every five consecutive cases of single-incision laparoscopic cholecystectomy for acute cholecystitis. All 85 cases performed by a chief surgeon are shown above. The standard deviation of each group is also shown. There are no obvious trends suggestive of a learning curve.

for acute cholecystitis in this study. This observation may be owing to the quality of the surgeons in our study. All surgeons who participated in this study were experienced and skilled in laparoscopic surgery and had each experienced more than 10 cases of SILC. Moreover, our SILC surgical procedure can be learned in a short time because of its similarity to conventional LC. However, the learning curve may be more obvious in less experienced surgeons.

SILC was introduced in our hospital in 2009. It was performed only in select patients during the early period after introduction while accumulating knowledge and standardizing the techniques used during the surgical procedure. Since January 2010, SILC has been applied to all patients, except those with gallbladder cancer. When the procedure is performed, we place the most emphasis on safety. Our policy is to convert SILC to laparotomy without hesitation when any difficulties present during the laparoscopic operation. The rate of conversion to laparotomy in the present study was slightly higher in patients with acute cholecystitis, likely owing to this policy. Consequently, no serious complications occurred, and excellent safety was demonstrated. Although the incidence of complications related with the bile duct was slightly high, this is likely because our institution specializes in endoscopic treatment. Many patients with suspected common bile duct problems seek treatment at our hospital. In fact, 41% of patients in this study were recommended to our facility for suspected choledocholithiasis and they underwent endoscopic treatment before cholecystectomy. This factor may have contributed to the increased incidence of these complications. Although bile leakage occurred in two patients with acute cholecystitis, it was not caused by damage during a laparoscopic operation, as neither case had been converted to laparotomy. While the common bile duct was not damaged in any of the patients, leakage was resolved by endoscopic biliary drainage after surgery. To maintain the safety of SILC, surgeons should never perform reckless operative maneuvers and convert to laparotomy before performing risky maneuvers.

However, a desire to avoid conversion to laparotomy is reasonable without compromising safety in terms of aesthetic outcome. In this study, SILC was converted to laparotomy in 12 patients (12%). The main reason for conversion was difficulties during the laparoscopic operation because of severe inflammatory fibrosis (10 patients). Operation difficulties owing to inflammation are reported related to the elapsed time between disease onset and operation[24]. The results of this study indicate that the number of preoperative days after onset tended to be higher in patients who were converted from SILC to laparotomy. Based on these findings, SILC performed as early as possible may permit resection before development of inflammatory fibrosis, and thus reduce the risk of laparotomy conversion. Avoiding laparotomy results in a less invasive procedure, less postoperative pain, and shorter postoperative hospital stay, making the merits offered by SILC more attractive. The TG13 recommends performing cholecystectomy within 72 h[25]. Unfortunately, we could not perform early surgery in many cases because of the lack of smooth cooperation with the first-contact physicians, limited availability of operation theater space, and lack of anesthetist availability. Despite our efforts to overcome these issues, some patients were unable to undergo early cholecystectomy. Conversely, in patients for whom early operation is not feasible, conservative treatment and elective SILC after complete suppression of inflammation may be preferable.

In conclusion, the results of this study suggest that SILC is feasible for acute cholecystitis and that early surgical intervention may reduce the risk of conversion to laparotomy. Although an aesthetic outcome is important, the decision to convert to laparotomy should be made based on other factors. We hope that SILC will be considered a safe procedure and be more widely used.

COMMENTS

Background

Cholecystectomy is widely performed as a basic treatment for acute cholecystitis. Laparoscopic cholecystectomy (LC) is considered a safe procedure and widely performed for acute cholecystitis.

Research frontiers

Recently, single-incision laparoscopic cholecystectomy (SILC) has been rapidly

adopted over conventional LC. SILC is considered a less invasive procedure with better aesthetic results. However, the safety of this procedure for acute cholecystitis has not yet been established.

Innovations and breakthroughs

In this study, the authors reviewed 100 consecutive cases of SILC for acute cholecystitis and reported their surgical outcomes. The authors focused on SILC as well as accumulated cases of acute cholecystitis. This study is based on single-institution and consecutive experiences.

Applications

The results of this study suggest the safety and difficulty of SILC for acute cholecystitis. SILC is feasible for acute cholecystitis. However, surgeons should not hesitate to convert to laparotomy when difficulties arise.

Terminology

SILC is also called single-port access surgery or laparo-endoscopic single-site surgery. It is a minimally invasive surgical procedure with a single skin incision. Scarless operations can be achieved by making a skin incision at the umbilicus. However, SILC is technically more difficult because of the limited maneuverability. Advanced laparoscopic surgical skills are required for SILC.

Peer-review

The authors retrospectively assessed the safety of SILC for acute cholecystitis. They concluded that SILC is feasible for acute cholecystitis and that early surgical intervention may reduce the risk of conversion to laparotomy. This article is of interest for further clinic practice.

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ORIGINAL ARTICLE

Observational Study

Cap-assisted endoscopic sclerotherapy for hemorrhoids: Methods, feasibility and efficacy

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Author contributions: Zhang T and Xu LJ contributed equally to this work; Zhang T, Xu LJ, Xiang J, He Z, Peng ZY, Huang GM, Ji GZ and Zhang FM designed the research; Xu LJ, Xiang J, Huang GM and Ji GZ performed the research; He Z and Peng ZY analyzed the data; Zhang T and Zhang FM wrote the paper.

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Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

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Abstract

AIM: To evaluate the methodology, feasibility, safety and efficacy of a novel method called cap-assisted endoscopic sclerotherapy (CAES) for internal hemorrhoids.

METHODS: A pilot study on CAES for grade Ⅰ to Ⅲ internal hemorrhoids was performed. Colon and terminal ileum examination by colonoscopy was performed for all patients before starting CAES. Polypectomy and excision of anal papilla fibroma were performed if polyps or anal papilla fibroma were found and assessed to be suitable for resection under endoscopy. CAES was performed based on the requirement of the cap, endoscope, disposable endoscopic long injection needle, enough insufflated air and sclerosing agent.

RESULTS: A total of 30 patients with grade Ⅰ to Ⅲ internal hemorrhoids was included. The follow-up was more than four weeks. No bleeding was observed after CAES. One (3.33%) patient claimed mild tenesmus within

four days after CAES in that an endoscopist performed this procedure for the first time. One hundred percent of patients were satisfied with this novel procedure, especially for those patients who underwent CAES in conjunction with polypectomy or excision of anal papilla fibroma.

CONCLUSION: CAES as a novel endoscopic sclerotherapy should be a convenient, safe and effective flexible endoscopic therapy for internal hemorrhoids.

Key words: Sclerotherapy; Hemorrhoids; Cap-assisted endoscopic sclerotherapy; Colonoscopy; Colon; Papilla fibroma; Hemorrhoidal disease

Core tip: Sclerotherapy is the most effective therapy for grade Ⅰ or Ⅱ internal hemorrhoids. Traditional sclerotherapy may cause iatrogenic risk due to misplaced injections. We designed a novel technique called cap-assisted endoscopic sclerotherapy (CAES) for hemorrhoids by flexible endoscopy. Our study demonstrated that CAES is a safe, effective and convenient endoscopic therapeutic strategy for grade Ⅰ, grade Ⅱ and partial grade Ⅲ internal hemorrhoids. The colon preparation and colonoscopy before CAES brought more benefits for patients, including possible polypectomy and excision of anal papilla fibroma under colonoscopy. This study implies the future contribution of endoscopists on hemorrhoidal disease.

Zhang T, Xu LJ, Xiang J, He Z, Peng ZY, Huang GM, Ji GZ, Zhang FM. Cap-assisted endoscopic sclerotherapy for hemorrhoids: Methods, feasibility and efficacy. *World J Gastrointest Endosc* 2015; 7(19): 1334-1340 Available from: URL: http://www.wjgnet.com/1948-5190/full/v7/i19/1334.htm DOI: http://dx.doi.org/10.4253/wjge.v7.i19.1334

INTRODUCTION

Hemorrhoidal disease is one of the most common anorectal disorders that affects mainly adults of any age and sex[1-4]. The etiology of hemorrhoids remains controversial. Nowadays, the most widely accepted theory is that hemorrhoidal disease is the abnormal dilatation and distortion of the vascular channel, together with destructive changes in the supporting connective tissue of the anal cushion[5]. The submucosal vascular cushions are a normal anatomical structure of the anal canal and their existence with symptoms such as bleeding, prolapse, pain, thrombosis, mucus discharge and pruritus indicates hemorrhoidal disease[6]. The true incidence of hemorrhoids is difficult to estimate as many patients are reluctant to seek medical suggestions for various personal, cultural and socioeconomic reasons[7]. Approximately 50% of individuals require treatment for hemorrhoids in their 50s or older, and 10%-20% of patients need surgical therapies[8].

Hemorrhoids have been well described for thousands of years. However, the treatment of hemorrhoids has only substantially evolved during the past few decades[1]. The current therapies for hemorrhoids can be grouped into conservative management, office-based procedures and surgical treatment[8-10]. Increased fiber intake, medical therapies and lifestyle changes are included in the conservative treatment options for non-thrombosed hemorrhoids[10]. If conservative management is unsuccessful, several office-based modalities could be options, including rubber-band ligation, injection sclerotherapy, laser photocoagulation, bipolar diathermy, cryotherapy, Dopplerguided hemorrhoidal artery ligation and infrared coagulation[8,9,11]. When an office-based therapy is still ineffective, patients may consider further intervention, such as hemorrhoidectomy, thrombectomy of external hemorrhoids and stapled hemorrhoidectomy[7,9].

As an crucial component of many non-surgical practices, sclerotherapy is most effective for grade I and Ⅱ internal hemorrhoids, especially for patients who have an increased risk of bleeding[2]. However, traditional sclerotherapy is performed by physicians through an anoscope. This method may cause iatrogenic risk and complications due to misplaced injections[2]. Therefore, there is scope for improvement in the field of sclerotherapy for hemorrhoids.

With the development of interventional flexible endoscopy and in order to solve the problems above, we designed a novel method called cap-assisted endoscopic sclerotherapy (CAES) for internal hemorrhoids. This article presents our pilot study on the methodology, feasibility, safety and clinical findings using CAES for internal hemorrhoids.

MATERIALS AND METHODS

Patient inclusion and exclusion criteria

This observational study was carried out in the Second Affiliated Hospital of Nanjing Medical University. All eligible patients with symptoms and signs of grade Ⅰ, grade Ⅱ or grade Ⅲ internal hemorrhoids requiring further interventional procedures after failure of conservative treatment were included in the study. Internal hemorrhoids are graded based on protrusion and reducibility (grade Ⅰ, hemorrhoids characterized by prominent vasculature with engorgement but no prolapse; grade Ⅱ, hemorrhoids prolapse only with straining but spontaneously reduce; grade Ⅲ, hemorrhoids prolapse beyond the dentate line with straining and require manual reduction; grade Ⅳ, hemorrhoids prolapse beyond the dentate line with straining but cannot be reduced manually)[12,13]. All included cases for analysis were followed up for at least four weeks.

Acute thrombosed hemorrhoids with anal pain, stricture, fissure, fistula, fecal incontinence, ulcerative colitis, Crohn's disease and any bleeding risk condition were excluded. Patients with acute diarrhea in the last

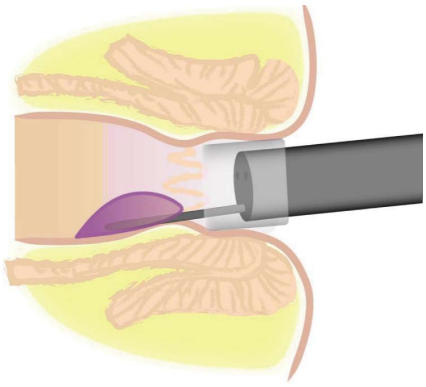

Illustration: Jacob Peichuan Ji

Figure 1 Illustration of cap-assisted endoscopic sclerotherapy.

12 h, severe complications, cancer, stroke, pregnancy, puerperium, mental disorders and portal hypertension were also excluded. Colon and terminal ileum examination by colonoscopy was performed for all patients before starting CAES. Polypectomy was performed if polyps were found and assessed to be suitable to be resected under endoscope. Informed consent was obtained from all participants.

Concept and methods of CAES

As shown in Figure 1, the regular cap used in endoscopic submucosal dissection was fixed on the top of the colonoscope. This cap is used to maximize visibility of the endoscopic view with enough insufflated air through the channel within the endoscope. A disposable endoscopic long injection needle (*e.g.,* the specially designed long needle: DT-EN-W322, 10/15/20 mm length, 22 g, Detian Medical, Changzhou, China) through the operating channel is used for the injection of the sclerosing agent. The needle is advanced into the submucosa of the targeted area of the hemorrhoids. The injecting points are above the dentate line. The sclerosing agent (Lauromacrogol injection, Tianyu Pharmaceutical, Xi'an, China), 1-2 mL for each injecting point, is injected while retracting the needle slowly. During the procedure, enough air is given for exposure of the endoscopic view. Before the complete retrieval of the needle from the tissue, as a suggestion, it is found to be helpful if you do not withdraw and stop the needle from moving for 5 s to prevent bleeding. The same procedure is performed for each targeted site under endoscopic view. Before taking out the endoscope, enough suction of air in the colon and visible rectal contents should be carried out to avoid or relieve abdominal distention and the feeling of defecation after the procedure.

Preparation and education

Although antibiotic prophylaxis was suggested for predisposing valvular heart disease because of the possibility of bacteremia after sclerotherapy[14], antibiotics were not used before and after CAES in this study. Besides, for safety considerations and observational requirements in this study, patients were required to rest in bed on the first night after the procedure. All individuals were required to follow medical instructions for avoiding constipation and diarrhea. Medicines were prescribed to soften the stools after the procedure if the patient had constipation.

Safety and satisfaction survey

Complications were recorded during and four weeks after CAES. The intensity of CAES and the relationship between the complications and CAES were described using the Common Terminology Criteria for Adverse Events (version 3.0). Intensity of complications was classified as mild, moderate, severe and disabling. The relationship between the complications and CAES was categorized as unrelated, possible, probable and definitely related to CAES. All patients were required to have a face to face communication at the doctor's office for the assessment of safety, efficacy and degree of satisfaction of the CAES. The level of satisfaction was classified into two degrees: positive, satisfied and pleased to introduce the CAES to other patients; negative, not satisfied and did not like this procedure. The second colonoscopy would be performed if the patient had bleeding or any other anorectal symptoms.

RESULTS

Patient characteristics

Table 1 shows the characteristics of the patients, including gender, age, classification of the internal hemorrhoids, grade of prolapse, previous hemorrhoidectomy history and other related information. A total of 30 patients with grade Ⅰ, grade Ⅱ or grade Ⅲ internal hemorrhoids was included for analysis in this study.

Clinical findings

Colon and terminal ileum examination by colonoscopy before CAES was performed in all patients for differential diagnosis of other possible diseases related to intestinal bleeding. No complications were observed during the procedure. However, we have to highlight that the needle could not be retrieved immediately when the injection was finished. It is suggested to keep the needle stable within the tissue for 5 s. If the needle was taken out from the tissue too quickly, bleeding would occur and the endoscopic view was affected by the blood. Figure 2 shows the procedures of CAES for internal hemorrhoids and the excision for anal papilla fibroma.

The patients were required to stay in hospital for 12 h after the procedure for safety considerations in this pilot observational study. No complications were observed during and after the procedure of polypectomy, CAES, excision of anal papilla fibroma and biopsy of polyps on the hemorrhoid lesion. All patients could return to normal activities after they were discharged from hospital. One (3.33%) patient claimed mild tenesmus within four days after CAES. This adverse event was finally confirmed as the result of one injection site that was chosen below the dentate line by an endoscopist who performed this procedure for the first time. One hundred percent

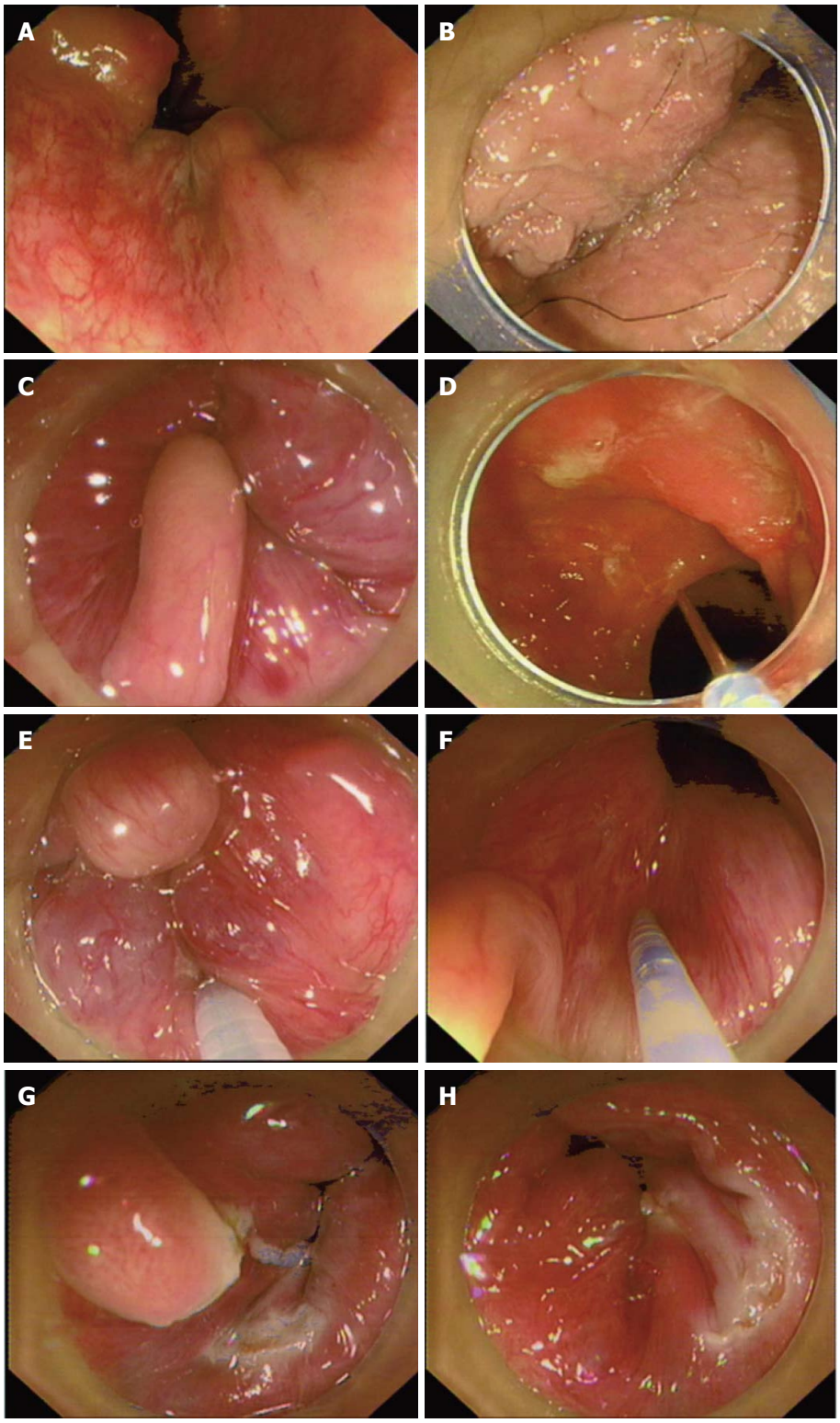

Figure 2 Procedures of cap-assisted endoscopic sclerotherapy for internal hemorrhoids and the excision for anal papilla fibroma. A: Internal hemorrhoids with retroflection of the endoscope; B: The anal region under cap-assisted endoscopic view; C: Internal hemorrhoids and anal papilla fibroma under cap-assisted endoscopic view with enough insufflated air; D: The disposable endoscopic long injection needle through operating channel; E: Injection of lauromacrogol into submucosa of internal hemorrhoids with the cap-assisted endoscopic view; F: Injecting of lauromacrogol into submucosa of internal hemorrhoids close to papilla fibroma before dissection; G: Dissection of anal papilla fibroma (confirmed by the followed pathology) after cap-assisted endoscopic sclerotherapy (CAES); H: No bleeding after CAES and dissection of anal papilla lesion before ending all procedures.

of patients were satisfied with this novel procedure. Those patients who underwent CAES in junction with polypectomy or excision of anal papilla fibroma expressed strong feeling of satisfaction for the therapeutic strategy.

DISCUSSION

Sclerotherapy dates back at least one century[15] and has been regarded as traditional therapy for grade Ⅰ and Ⅱ internal hemorrhoids. A variety of sclerosing agents, including ethanolamine, quinine, hypertonic saline solution, 5% phenol in oil, aluminum potassium sulfate and tannic acid, have been used in injection sclerotherapy for treating hemorrhoids[16-19]. Traditionally doctors had to use an anoscope during the sclerotherapy procedure. Misplacement of the sclerosing injection may result in potential complications, including pain, impotence, prostatitis, mucosal ulceration or necrosis

Table 1 Patient demographics and clinical results

Patient demographics	*n* (%)
Total included cases	30
Classification of internal hemorrhoids	
Grade Ⅰ	7 (23.33)
Grade Ⅱ	21 (70.0)
Grade Ⅲ	2 (6.67)
Grade Ⅳ	0
Male	22 (73.33)
Age (mean ± SD)	45.5 ± 4.2
With hemorrhoidectomy history	6 (20.0)
With rectal mucosal prolapse	4 (13.33)
With polyps on hemorrhoid lesions	1 (3.33)
With external hemorrhoids	0
Colon and terminal ileum examination before CAES	30 (100)
Polypectomy during colonoscopy before CAES	7 (23.33)
Excision of anal papilla fibroma after CAES	1 (3.33)
Biopsy for the polyps on hemorrhoids before CAES	1 (3.33)
Complications during and post-CAES	0
Post-CAES rectal bleeding	0
Post-CAES rectal mild pain or tenesmus	1 (3.33)
Positive satisfaction on CAES	30 (100)

Data are frequency counts (percentage of total) or the mean ± SD. CAES: Cap-assisted endoscopic sclerotherapy.

and prostatic abscess[10]. These complications emphasize the importance of precise placement of the injection with the sclerosing agent. In order to avoid the above complications, this prospective study was designed to evaluate the feasibility and efficacy of CAES for internal hemorrhoids under colonoscopy.

The preliminary results based on 30 cases demonstrated that CAES should be an effective interventional flexible endoscopic therapy for selected candidates with grade Ⅰ to grade Ⅲ internal hemorrhoids. After CAES, 100% of patients achieved the expected clinical response. The follow-up within 4 wk showed sustained clinical efficacy. No severe or obvious complications were observed and none of the suffered complications were definitely related to CAES in the study. These results indicated that CAES was safe and helpful to prevent iatrogenic risk from misplaced injections. The length of a common commercial endoscopic injection needle was not suggested in CAES because of its short length (*e.g.,* 4 or 5 mm), which seems to require more sites for injection and induce more mucosal injury and potential inflammation. Our specially designed needle, with a 15-20 mm length, is an important tool for enough submucosal injection with the sclerosing agent. Based on our experience, this CAES technique with the transparent cap is able to treat all hemorrhoids in a forward view fashion. There might be no need to have retroflection for the CAES procedure. Importantly, it is impossible for endoscopist to have retroflection in all cases.

In the present study, a high level of patient satisfaction (100%) and the convenience from adequate medical health or psychophysical protection for doctors also provide evidence to support CAES to be promising for the future. Actually, CAES brought additional benefits for patients, such as colonoscopy, possible polypectomy, excision of anal papilla fibroma and biopsy of polyps on hemorrhoid lesions under endoscopy.

Another advantage of doing an endoscopic procedure before CAES to that of using a plain disposable anoscope is that bleeding and other anorectal symptoms related to different colorectal diseases could be better differentiated[20]. A population-based study in the United States[21] reported in the hematochezia cohort showed significantly higher rates of diverticulosis, polyp or multiple polyps, mucosal abnormality/colitis, tumor and solitary ulcers on colonoscopy findings. Anorectal diseases, including hemorrhoids, are frequent in patients with intestinal disease. Hemorrhoids have been reported to occur in 20% of patients with UC[22] and approximately 7% of patients with CD[23]. In these selected cases, lesions in the colon and terminal ileum were observed during the examination by colonoscopy before CAES, which should be an effective way to have an early diagnosis of CD and UC with hemorrhoids. Therefore, colon preparation and colonoscopy is important when dealing with hemorrhoids as it would save the related medical cost and colon preparation for patients.

The cap, endoscope, air, long needle, sclerosing agent and endoscopic view should be the key points for the endoscopist to perform the CAES. This CAES technique is simple but the possible risk should be considered for physicians. One patient claimed mild tenesmus within four days after CAES. This complication was finally confirmed as the result of one injection site chosen below the dentate line by an endoscopist who performed this procedure for the first time. This lesson highlighted the importance of training for CAES. With the necessary training, the angle, direction and depth of injection under endoscopic view could be controlled very well and it would be easy to avoid the risk of injuring deeper tissues or injecting outside of the hemorrhoid.

All cases were required to be hospitalized for bed rest on the first night after the procedure, according to the design of this observational study. However, this hospitalization would not be required if the patient has no other condition except hemorrhoids. For prevention of recurrence of hemorrhoids, medicines and health education are important to maintain soft defecation within the first week after CAES if necessary.

There are some limitations in the present study. The sample size of this pilot study was small but a larger prospective study based on these preliminary results is ongoing. This was not a controlled study with the comparison of other traditional interventional therapies. Therefore, a rigorous randomized clinical trial should be designed to provide more evidence for the practice of CAES. Although CAES and the required preparation of colon and colonoscopy showed advantages and low medical costs for the diagnosis and therapy of anorectal diseases related to hemorrhoidal disease, a cost-effective analysis is needed for further study.

In conclusion, CAES is an innovation of endoscopic

sclerotherapy. It should be a convenient, safe and effective flexible endoscopic therapy for internal hemorrhoids. Traditionally, hemorrhoids are commonly treated by surgeons. However, the present study implies the future contribution of endoscopists for hemorrhoidal disease.

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COMMENTS

Background

The current therapies for hemorrhoids can be grouped into conservative management, office-based procedures and surgical treatment. As a crucial component of many non-surgical practices, sclerotherapy is most effective for grade I and II internal hemorrhoids. However, traditional sclerotherapy is performed by physicians using an anoscope. This method may cause iatrogenic risk and complications due to misplaced injections. Additionally, an anoscope has the limitation of only being used within the anus. Therefore, there is scope for improvement in the field of sclerotherapy for hemorrhoids.

Research frontiers

With the development of interventional flexible endoscopy, the authors designed a novel method called cap-assisted endoscopic sclerotherapy (CAES) for internal hemorrhoids. This article presents the authors' pilot study with the methodology, feasibility, safety, clinical findings and their experience using CAES for internal hemorrhoids.

Innovations and breakthroughs

This study demonstrated CAES is a safe, effective and convenient endoscopic therapeutic strategy for grade Ⅰ, grade Ⅱ and partial grade Ⅲ internal hemorrhoids. The colon preparation and colonoscopy are the steps before the final sclerotherapy. The colon preparation and colonoscopy before CAES brought more benefits for patients, including possible polypectomy and excision of anal papilla fibroma under endoscopy. Besides, in these selected cases, lesions in the colon and terminal ileum were observed before CAES during the colonoscopy itself, which should be an effective way to have an early diagnosis of Crohn's disease and Ulcerative colitis with hemorrhoids. Therefore, it would save the related medical cost and colon preparation for patients. This study implies the future contribution of endoscopists on hemorrhoidal disease.

Applications

This pilot study based on 30 cases demonstrated that CAES should be an effective interventional flexible endoscopic therapy for selected candidates with grade Ⅰ to grade Ⅲ internal hemorrhoids. After CAES, 100% of patients achieved the expected clinical response. The follow-up within 4 wk further showed the sustained clinical efficacy. No severe or obvious complications were observed and none of the suffered complications were definitely related to CAES in the study. These results indicated that CAES was safe and helpful in preventing iatrogenic risk from misplaced injections. The authors' specially designed needle, 10/15/20 mm in length, is an important tool to ensure enough submucosal injection with the sclerosing agent. Based on the authors' experience, this CAES technique with the transparent cap is able to treat all hemorrhoids in a forward view fashion. There may be no need for retroflection for the CAES procedure. Importantly, it is impossible for endoscopist to have retroflection in all cases. In the present study, a high level of patient satisfaction (100%) and the convenience of adequate medical health or psychophysical protection for doctors also provide evidence for supporting CAES to be promising for the future. Actually, CAES brought additional benefits for patients, such as colonoscopy, possible polypectomy, excision of anal papilla fibroma and biopsy of polyps on hemorrhoid lesions under endoscopy.

Terminology

The concept and methods of CAES: The regular cap used in endoscopic submucosal dissection was fixed on the top of the colonoscope. This cap is used to maximize visibility of the endoscopic view with enough insufflated air through the channel within the endoscope. A disposable endoscopic long injection needle through the operating channel is advanced into the submucosa of the targeted area of the hemorrhoids. The injecting points are above the dentate line. The sclerosing agent for each injecting point is injected slowly while retracting the needle slowly. During the procedure, enough air was given for exposure of the endoscopic view. Before the complete retrieval of the needle from the tissue, as a suggestion, it is helpful if you do not withdraw and stop the needle from moving for 5 s to prevent bleeding. The same procedure is performed for each targeted site under endoscopic view.

Peer-review

The authors describe a modification of the band ligation technique of hemorrhoid therapy by using ESD caps with sclerotherapy. The use of a cap mounted on the tip of an endoscope was useful to stabilize its position for precise injection of a sclerosing agent through a long needle. Overall, the model is elegant and the results seem to be promising. In addition to a novel technique, their analysis is rigorous, including the use of a post-procedure questionnaire. The images and diagram are also excellent.

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SYSTEMATIC REVIEWS

Systematic review and meta-analysis on the prophylactic role of non-steroidal anti-inflammatory drugs to prevent post-endoscopic retrograde cholangiopancreatography pancreatitis

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Abstract

AIM: To critically appraise the published randomized, controlled trials on the prophylactic effectiveness of the non-steroidal anti-inflammatory drugs (NSAIDs), in reducing the risk of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis.

METHODS: A systematic literature search (MEDLINE, Embase and the Cochrane Library, from inception of the databases until May 2015) was conducted to identify randomized, clinical trials investigating the role of NSAIDs in reducing the risk of post-ERCP pancreatitis. Random effects model of the meta-analysis was carried out, and results were presented as odds ratios (OR) with corresponding 95%CI.

RESULTS: Thirteen randomized controlled trials on 3378 patients were included in the final meta-analysis. There were 1718 patients in the NSAIDs group and 1660 patients in non-NSAIDs group undergoing ERCP. The use of NSAIDs (through rectal route or intramuscular route) was associated with the reduced risk of post-ERCP pancreatitis [OR, 0.52 (0.38-0.72), P = 0.0001]. The use of pre-procedure NSAIDs was effective in reducing approximately 48% incidence of post-ERCP pancreatitis, number needed to treat were 16 with absolute risk reduction of 0.05. But the risk of post-ERCP pancreattis was reduced by 55% if NSAIDs were administered after procedure. Similarly, diclofenac was more effective (55%) prophylactic agent compared to indomethacin (41%).

CONCLUSION: NSAIDs seem to have clinically proven advantage of reducing the risk of post-ERCP pancreatitis.

Key words: Non-steroidal drugs; Pancreatitis; Diclofenac; Indomethacin; Endoscopic retrograde cholangiopancreatography

Core tip: Current meta-analysis of 13 randomized controlled trials on 3378 patients successfully demonstrates the usefulness of non-steroidal anti-inflammatory drugs (NSAIDs) in the prevention of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis. Post-procedure use of NSAIDs by any route has clinically proven advantage of reducing 55% risk of post-ERCP pancreatitis. Diclofenac (55%) compared to indomethacin (41%) was more effective prophylactic agent.

Sajid MS, Khawaja AH, Sayegh M, Singh KK, Philipose Z. Systematic review and meta-analysis on the prophylactic role of non-steroidal anti-inflammatory drugs to prevent post-endoscopic retrograde cholangiopancreatography pancreatitis. *World J Gastrointest Endosc* 2015; 7(19): 1341-1349 Available from: URL: http://www.wjgnet.com/1948-5190/full/v7/i19/1341.htm DOI: http://dx.doi.org/10.4253/wjge.v7.i19.1341

INTRODUCTION

Since its introduction into the field of gastroenterology, hepatology and hepato-pancreatico-biliary surgery, the endoscopic retrograde cholangiopancreatography (ERCP) has advanced to be an important and essential diagnostic and therapeutic tool. The introduction of magnetic resonance cholangiopancreatography and endoscopic ultrasound with several technological developments has sidelined ERCP into a largely a therapeutic tool in the management of sphincter of Oddi disorders, choledocholithiasis, pancreatic duct pathologies, and benign or malignant strictures of the common bile duct. However, ERCP carries significant risk, with post-ERCP pancreatitis being the most frequent and dreaded of these. The reported prevalence of post-ERCP pancreatitis is as high as 10%[1-4] in the medical literature. Nevertheless, it may exceed up to 30% in certain high-risk cluster of female patients with sphincter of Oddi dysfunction[5]. Post-ERCP pancreatitis may result in prolonged hospital stay, pancreatic oedema, pancreatic necrosis, pancreatic pseudocyst, systemic inflammatory response syndrome and mortality up to 1% in addition to adding a significant financial burden on health-care resources[6].

Considering the morbidity, mortality and financial burden related to post-ERCP pancreatitis, it is vital to consider every preventive strategy to reduce its incidence. Risk-benefit analysis and then right patient selection may be the best way to avoid un-necessary ERCP and its subsequent complications. Several studies have reported promising modalities of prophylaxis including pancreatic duct stenting of patients with sphincter of Oddi dysfunction, administration of NSAIDs of various types by various routes and other diverse measures. The evidence of these prophylactic measures is conflicting and so far has failed to demonstrate the accurate effectiveness[7-11]. Based upon the available evidence, NSAIDs are the most commonly used modality for post-ERCP pancreatitis prevention. The possible advantages of NSAIDs use are cost-effectiveness, easily accessible and effortlessly administrable. The aim of this systematic review is to critically appraise the published randomized, controlled trials in the clinical effectiveness of the NSAIDs in reducing the risk of post-ERCP pancreatitis.

MATERIALS AND METHODS

Electronic medical databases such as the Medline, EMBASE, Cochrane Colorectal Cancer Group Controlled Trial Register, the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library and Science Citation Index Expanded were explored until May 2015 to find published randomized, controlled trials. The MeSH terms related to the NSAIDs and post-ERCP pancreatitis were retrieved from the search engine of PubMed and were used to search electronic databases. Attempts to include additional studies were also made by the hand searching of the citations of published studies. The statistical analysis of the extracted data was conducted according to the guidelines provided by the Cochrane Collaboration including the use of RevMan 5.3® statistical software, random-effects model analysis, heterogeneity testing by χ^2 test, heterogeneity quantification by I-squared test and the use of forest plots for the graphical display of the combined outcomes[12-18]. The critical appraisal tool to score the quality of included trials was adopted from the published guidelines of Jadad *et al*[19] and Chalmers *et al*[20]. The short summary of the resulting evidence was presented in a tabulated form by using tool GradePro®[21], provided by the Cochrane Collaboration.

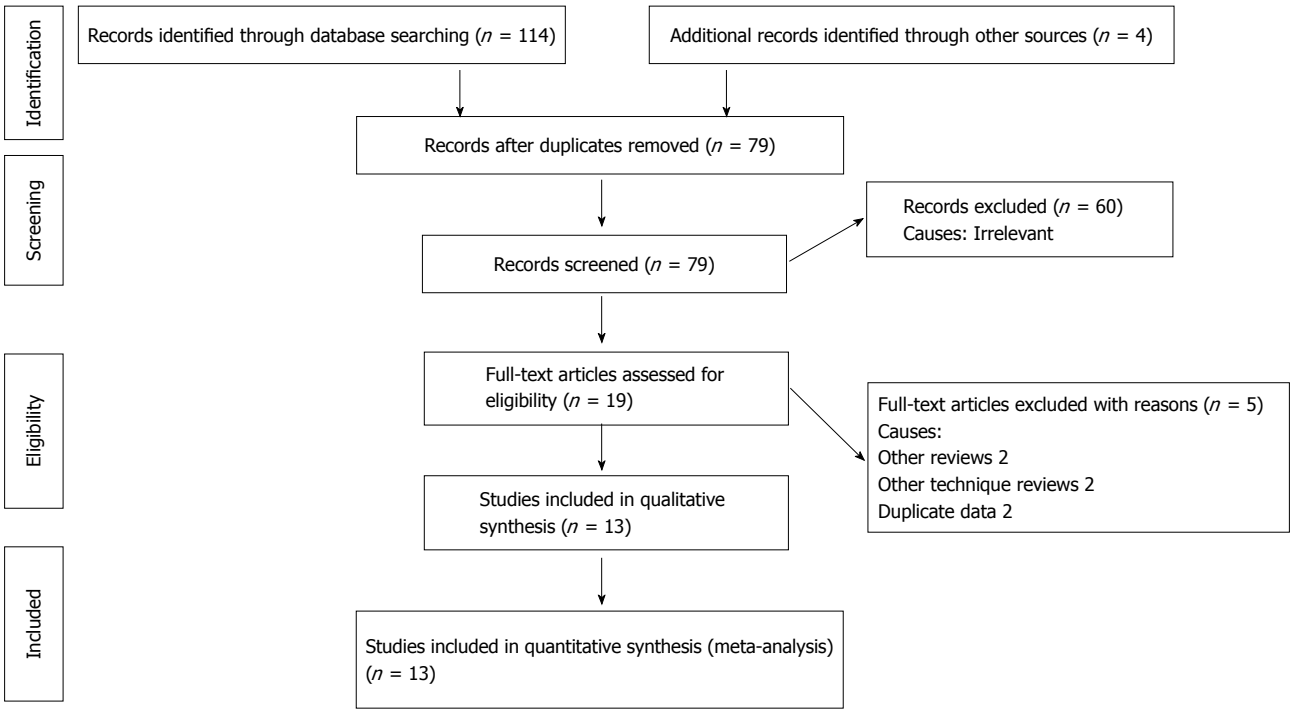


Figure 1 PRISMA flow chart.

RESULTS

Number of studies on first hit in search engines and their subsequent shortlisting is given in the PRISMA flow chart (Figure 1). Thirteen randomized, controlled trials[22-34] on 3378 patients undergoing ERCP were analysed in this study. Some 1718 patients were assigned in NSAIDs group whereas 1660 patients were in no-NSAIDs group. The characteristics of included studies are given in Table 1. The short summary on the quality of evidence generated from the combined analysis of trials used in this meta-analysis is given in Table 2. The study quality based scores of included trials were graded adequate based upon the reporting of four quality indicator variables, *i.e.*, optimum randomization technique, power calculations, concealment and intention-to-treat analysis.

Incidence of post-ERCP pancreatitis in NSAIDs vs placebo trials

As shown in Figure 2A, there was minimal and non-significant heterogeneity [Tau^2 = 0.11, χ^2 = 18.60, df = 12, (P = 0.10); I^2 = 35%] among trials. In the random effects model (OR, 0.52; 95%CI: 0.38, 0.72; Z = 4.02; P < 0.0001) analysis, the risk of post-ERCP pancreatitis was significantly lower (48% lower) following the use of NSAIDs. The NNT was 16 with absolute risk reduction of 0.05.

Incidence of post-ERCP pancreatitis in per rectal NSAIDs vs placebo trials

As shown in Figure 2B, there was no heterogeneity [Tau^2 = 0.11, χ^2 = 9.86, df = 7, (P = 0.20); I^2 = 29%] among trials. In the random effects model (OR, 0.43; 95%CI: 0.28, 0.67; Z = 3.77; P = 0.0002) analysis, the risk of post-ERCP pancreatitis was significantly lower (57% lower) following rectal administration of NSAIDs.

Incidence of post-ERCP pancreatitis in diclofenac vs placebo trials

As shown in Figure 2C, there was significant heterogeneity [Tau^2 = 0.38, χ^2 = 14.49, df = 6, (P = 0.02); I^2 = 59%] among trials. In the random effects model (OR, 0.45; 95%CI: 0.24, 0.83; Z = 2.55; P = 0.01) analysis, the risk of post-ERCP pancreatitis was significantly lower (55% lower) following the use of diclofenac.

Incidence of post-ERCP pancreatitis in indomethacin vs placebo trials

As shown in Figure 2D, there was no heterogeneity [Tau^2 = 0.00, χ^2 = 3.81, df = 4, (P = 0.43); I^2 = 0%] among trials. In the random effects model (OR, 0.59; 95%CI: 0.39, 0.88; Z = 2.61; P = 0.009) analysis, the risk of post-ERCP pancreatitis was significantly lower (41% lower) following the use of indomethacin. Based upon this finding it seems like diclofenac is more effective NSAIDs compared to indomethacin for the prevention of post-ERCP pancreatitis.

Incidence of post-ERCP pancreatitis if NSAIDs are administered before procedure

As shown in Figure 2E, there was no heterogeneity [Tau^2 = 0.05, χ^2 = 5.96, df = 5, (P = 0.31); I^2 = 16%] among trials. In the random effects model (OR, 0.52; 95%CI: 0.34, 0.80; Z = 2.93; P = 0.003) analysis, the risk of post-ERCP pancreatitis was significantly lower (48% lower) if NSAIDs are administered before the

Table 1 Characteristics of included trials

Ref.	Year	Country	Time of administration	Route	Dose	Type of NSAIDs used
Cheon *et al*[22]	2007	United States	Before ERCP	Oral	50 mg	Diclofenac
Döbrönte *et al*[23]	2012	Hungary	Before ERCP	Rectal	100 mg	Indomethacin
Döbrönte *et al*[24]	2014	Hungary	Before ERCP	Rectal	100 mg	Indomethacin
Elmunzer *et al*[25]	2012	United States	After ERCP	Rectal	100 mg	Indomethacin
Khoshbaten *et al*[26]	2008	Iran	After ERCP	Rectal	100 mg	Diclofenac
Montaño Loza *et al*[27]	2006	Mexico	Before ERCP	Rectal	100 mg	Indomethacin
Montaño Loza *et al*[28]	2007	Mexico	Before ERCP	Rectal	100 mg	Indomethacin
Murray *et al*[29]	2003	United Kingdom	After ERCP	Rectal	100 mg	Diclofenac
Otsuka *et al*[30]	2012	Japan	Before ERCP	Rectal	50 mg	Diclofenac
Park *et al*[31]	2014	United States South Korea	After ERCP	Intramuscular	90 mg	Diclofenac
Senol *et al*[32]	2009	Turkey	After ERCP	Intravenous infusion	75 mg	Diclofenac
Sotoudehmanesh *et al*[33]	2007	Iran	Before ERCP	Rectal	100 mg	Indomethacin
Zhao *et al*[34]	2014	China	After ERCP	Intramuscular	75 mg	Diclofenac

NSAIDs: Non-steroidal anti-inflammatory drugs; ERCP: Endoscopic retrograde cholangio-pancreaticography.

Table 2 Summary and strength of the evidence from trials analysed on GradePro®

Author(s): Sajid *et al*

Date: 20/10/2015

Question: NSAID's are an effective modality to reduce the incidence of post-ERCP pancreatitis?

Settings: All patients undergoing booth elective or emergency ERCP in endoscopy department for any indication by an experienced gastroenterologist/ endoscopists

Bibliography: Adapted from the Cochrane Database of Systematic Reviews [2015, Issue (Is)]

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID's *vs* placebo	Control	Relative (95%CI)	Absolute		
Incidence of overall pancreatitis (follow-up mean 3 mo; assessed with: Odds ratio)												
14	Randomised trials	Serious	No serious inconsistency	No serious indirectness	No serious imprecision	Strong association	138/1900 (7.3%)	248/1878 (13.2%)	OR 0.49 (0.36 to 0.67)	63 fewer per 1000 (from 40 fewer to 80 fewer)	High	Critical
								15.7%		73 fewer per 1000 (from 46 fewer to 94 fewer)		

NSAIDs: Non-steroidal anti-inflammatory drugs; ERCP: Endoscopic retrograde cholangio-pancreaticography.

procedure of ERCP compared to placebo.

Incidence of post-ERCP pancreatitis if NSAIDs are administered after procedure

As shown in Figure 2F, there was minimal heterogeneity [Tau^2 = 0.21, χ^2 = 10.30, df = 5, (P = 0.07); I^2 = 51%) among trials. In the random effects model (OR, 0.45; 95%CI: 0.27, 0.77; Z = 2.90; P = 0.004) analysis, the risk of post-ERCP pancreatitis was significantly lower (55% lower) if NSAIDs are administered after the procedure of ERCP compared to placebo.

DISCUSSION

Summary of main results

Results of this meta-analysis demonstrate that the use of NSAIDs (by any route of administration) meaningfully reduces the incidence of post-ERCP pancreatitis; rectal administration is slightly more effective; diclofenac seems to be clinically better than indomethacin and post-ERCP administration has shown superior results. The use of pre-procedure NSAIDs was effective in reducing approximately 48% but the risk of post-ERCP pancreatitis was reduced by 55% if NSAIDs were administered after the procedure.

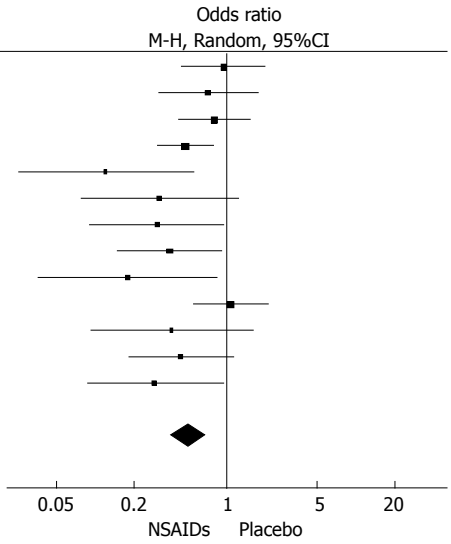
Overall completeness and applicability of evidence

The findings of current study are pertinent to only those groups of patients which may require either therapeutic or diagnostic ERCP and fit enough to undergo the procedure. Despite the reporting of several systematic reviews and meta-analysis[35-46] evaluating the role of NSAIDs in reducing

A

Study or subgroup	NSAID'S Event	Total	Placebo Event	Total	Weight	Odds ratio M-H, Random, 95%CI
Cheon *et al*[22]	17	105	17	102	10.4%	0.97 [0.46, 2.02]
Döbrönte *et al*[23]	11	130	11	98	8.4%	0.73 [0.30, 1.76]
Döbrönte *et al*[24]	20	347	22	318	12.3%	0.82 [0.44, 1.54]
Elmunzer *et al*[25]	27	295	52	307	15.0%	0.49 [0.30, 0.81]
Khoshbaten *et al*[26]	2	50	13	50	3.5%	0.12 [0.03, 0.56]
Montaño Loza *et al*[27]	3	61	8	56	4.3%	0.31 [0.08, 1.23]
Montaño Loza *et al*[28]	4	75	12	75	5.5%	0.30 [0.09, 0.96]
Murray *et al*[29]	7	110	17	110	7.8%	0.37 [0.15, 0.94]
Otsuka *et al*[30]	2	51	10	53	3.5%	0.18 [0.04, 0.85]
Park *et al*[31]	22	173	20	170	11.9%	1.09 [0.57, 2.09]
Senol *et al*[32]	3	40	7	40	4.1%	0.38 [0.09, 1.60]
Sotoudehmanesh *et al*[33]	7	221	15	221	7.9%	0.45 [0.18, 1.12]
Zhao *et al*[34]	4	60	12	60	5.4%	0.29 [0.09, 0.94]
Total (95%CI)		1718		1660	100.0%	0.52 [0.38, 0.72]
Total events	129		216			

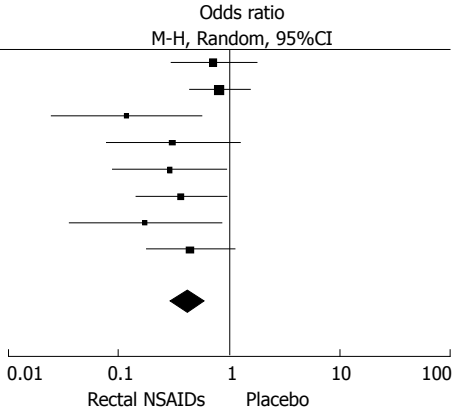
Heterogeneity: Tau^2 = 0.11; χ^2 = 18.60, df = 12 (P = 0.10); I^2 = 35%
Test for overall effect: Z = 4.02 (P < 0.0001)



B

Study or subgroup	Rectal NSAID'S Event	Total	Placebo Event	Total	Weight	Odds ratio M-H, Random, 95%CI
Döbrönte *et al*[23]	11	130	11	98	15.7%	0.73 [0.30, 1.76]
Döbrönte *et al*[24]	20	347	22	318	23.1%	0.82 [0.44, 1.54]
Khoshbaten *et al*[26]	2	50	13	50	6.7%	0.12 [0.03, 0.56]
Montaño Loza *et al*[27]	3	61	8	56	8.1%	0.31 [0.08, 1.23]
Montaño Loza *et al*[28]	4	75	12	75	10.3%	0.30 [0.09, 0.96]
Murray *et al*[29]	7	110	17	110	14.7%	0.37 [0.15, 0.94]
Otsuka *et al*[30]	2	51	10	53	6.5%	0.18 [0.04, 0.85]
Sotoudehmanesh *et al*[33]	7	221	15	221	14.9%	0.45 [0.18, 1.12]
Total (95%CI)		1045		981	100.0%	0.43 [0.28, 0.67]
Total events	56		108			

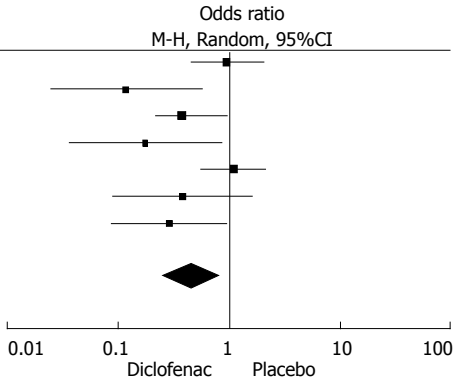
Heterogeneity: Tau^2 = 0.11; χ^2 = 9.86, df = 7 (P = 0.20); I^2 = 29%
Test for overall effect: Z = 3.77 (P = 0.0002)



C

Study or subgroup	Diclofenac Event	Total	Placebo Event	Total	Weight	Odds ratio M-H, Random, 95%CI
Cheon *et al*[22]	17	105	17	102	19.2%	0.97 [0.46, 2.02]
Khoshbaten *et al*[26]	2	50	13	50	9.9%	0.12 [0.03, 0.56]
Murray *et al*[29]	7	110	17	110	16.6%	0.37 [0.15, 0.94]
Otsuka *et al*[30]	2	51	10	53	9.7%	0.18 [0.04, 0.85]
Park *et al*[31]	22	173	20	170	20.4%	1.09 [0.57, 2.09]
Senol *et al*[32]	3	40	7	40	10.9%	0.38 [0.09, 1.60]
Zhao *et al*[34]	4	60	12	60	13.3%	0.29 [0.09, 0.94]
Total (95%CI)		589		585	100.0%	0.45 [0.24, 0.83]
Total events	57		96			

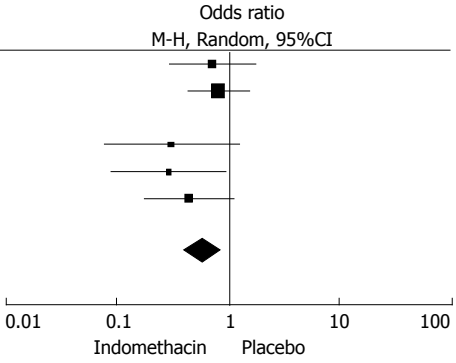
Heterogeneity: Tau^2 = 0.38; χ^2 = 14.49, df = 6 (P = 0.02); I^2 = 59%
Test for overall effect: Z = 2.55 (P = 0.01)



D

Study or subgroup	Indomethacin Event	Total	Placebo Event	Total	Weight	Odds ratio M-H, Random, 95%CI
Döbrönte *et al*[23]	11	130	11	98	20.6%	0.73 [0.30, 1.76]
Döbrönte *et al*[24]	20	347	22	318	40.7%	0.82 [0.44, 1.54]
Elmunzer *et al*[25]	27	295	523	307		Not estimable
Montaño Loza *et al*[27]	3	61	8	56	8.4%	0.31 [0.08, 1.23]
Montaño Loza *et al*[28]	4	75	12	75	11.4%	0.30 [0.09, 0.96]
Sotoudehmanesh *et al*[33]	7	221	15	221	18.9%	0.45 [0.18, 1.12]
Total (95%CI)		1129		1075	100.0%	0.59 [0.39, 0.88]
Total events	72		591			

Heterogeneity: Tau^2 = 0.00; χ^2 = 3.81, df = 4 (P = 0.43); I^2 = 0%
Test for overall effect: Z = 2.61 (P = 0.009)



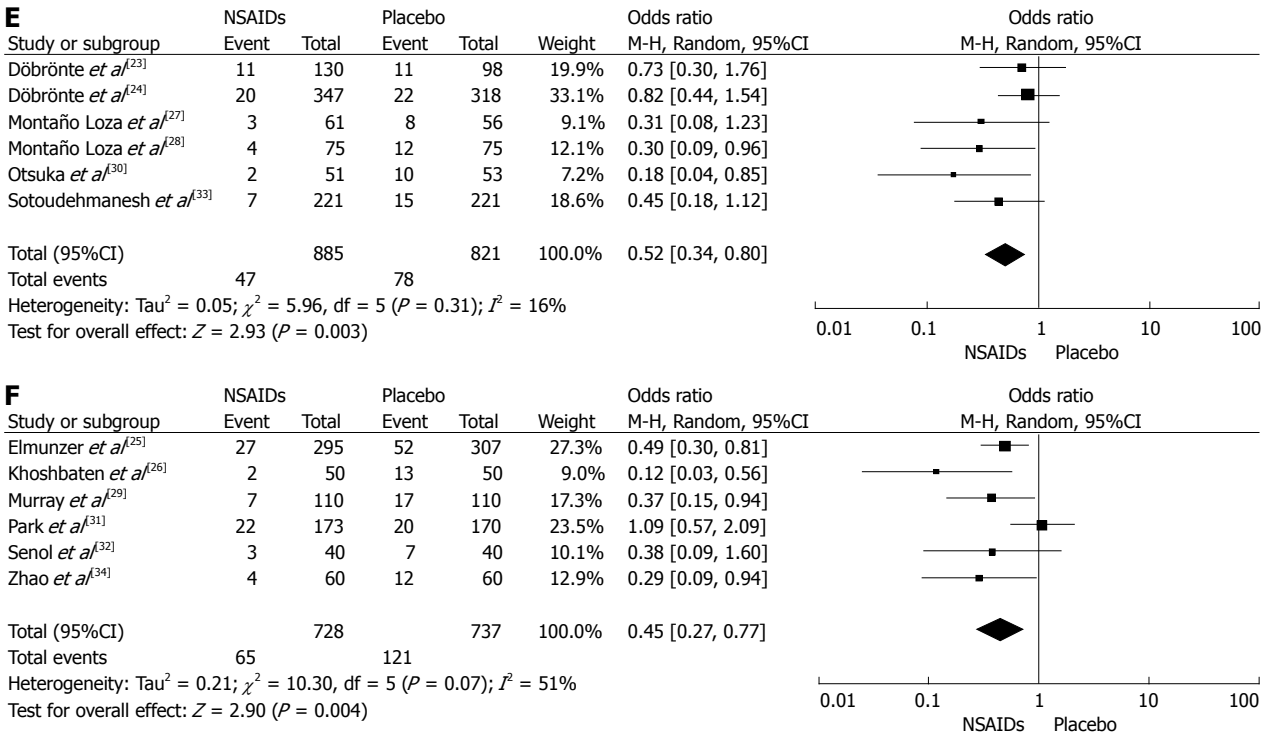


Figure 2 Forest plot for incidence of post-endoscopic retrograde cholangiopancreatography pancreatitis. A: In non-steroidal anti-inflammatory drugs *vs* placebo groups; B: In rectal non-steroidal anti-inflammatory drugs *vs* placebo groups; C: In diclofenac *vs* placebo groups; D: In indomethacin *vs* placebo groups; E: In pre-endoscopic retrograde cholangiopancreatography non-steroidal anti-inflammatory drugs *vs* placebo groups; F: In post-endoscopic retrograde cholangiopancreatography non-steroidal anti-inflammatory drugs *vs* placebo groups. Odds ratios are shown with 95%CIs.

the risk of consequent pancreatitis resulting from ERCP, this is the only study providing evidence on the role of NSAIDs, route of NSAIDs administration, type of NSAIDs being more effective and the timing of the NSAIDs administration to reduce the incidence of post-ERCP pancreatitis.

Quality of evidence

This study reports a total of 3378 participants from 13 randomized, controlled trials undergoing ERCP reporting post-ERCP pancreatitis as primary outcome preferentially. The risk of bias in the included trials was low to moderate when scores against the standard quality guidelines and therefore, the quality of resulting evidence may be considered adequate (Table 2). The variable experience of endoscopists might have influenced the outcomes. Other confounding factors which might have influenced the final outcome of the ERCP include the use of different endoscopes, type and dosage of sedation, variable use of scope-guide technique, indications of ERCP, sundry patient selection and diverse biochemical measuring tools for the diagnosis of post-ERCP pancreatitis.

Potential biases in the review process

Authors adopted the standard Cochrane Collaboration methodology to perform the statistical analysis, interpretation as well as to present the quality of evidence. The quality of included (Table 3) randomized, controlled trials was assessed for risk of bias in one of the six domains (blinding) and at unclear risk of bias in another domain (allocation concealment). The low risk of bias was mainly attributable to the presence of blinding in all the trials and presence of allocation concealment in the majority of the studies. Presence of adequate randomization technique and optimum utilization of the power calculations in all included trials provided adequate strength to generate higher level of evidence to support the conclusion. There are no trials comparing pre-procedure *vs* post-procedure prophylactic use of NSAIDS. This inference was made based upon their comparisons against placebo. Same limitation also applies on the effectiveness of diclofenac *vs* indomethacin. However, the conclusion in terms of an individual agent *vs* other agent effectiveness and timing of NSAIDS administration may reluctantly be drawn from the available studies comparing effectiveness against placebo.

Agreement and disagreement with other published evidence

The findings of current meta-analysis are in accordance with the conclusions of the previously published reviews[35-46]. However, this study provides up to date, comprehensive and cumulative evidence on the use of NSAIDs (by any route of administration) meaningfully reducing the incidence of post-ERCP pancreatitis, suggesting the rectal administration of NSAIDs being more effective, indomethacin proven to be clinically better than diclofenac and pre-ERCP administration of NSAIDs showing superior results.

Implications for practice and research

This study quite successfully validates that NSAIDs may

Table 3 Reported quality variables in included studies

Ref.	Randomization	Power calculations	ITT	Blinding	Concealment
Cheon *et al*[22]	Yes	Yes	Yes	Yes	Yes
Döbrönte *et al*[23]	Yes	Yes	No	Yes	Yes
Döbrönte *et al*[24]	Yes	Yes	No	Yes	Yes
Elmunzer *et al*[25]	Yes	Yes	Yes	Yes	Yes
Khoshbaten *et al*[26]	Yes	Yes	No	Yes	Yes
Montaño Loza *et al*[27]	Yes	Yes	No	Yes	Yes
Montaño Loza *et al*[28]	Yes	Yes	No	Yes	Not reported
Murray *et al*[29]	Yes	Yes	No	Yes	Yes
Otsuka *et al*[30]	Yes	Yes	No	Yes	Yes
Park *et al*[31]	Yes	Yes	No	Yes	Yes
Senol *et al*[32]	Yes	Yes	No	Not reported	Not reported
Sotoudehmanesh *et al*[33]	Yes	Yes	No	Yes	Yes
Zhao *et al*[34]	Yes	Yes	No	No	Not reported

routinely be used to prevent the post-ERCP pancreatitis. However, the aforementioned confounding factors influencing the final outcomes must be acknowledged and attempts must be made to generate less biased evidence by removing these limitations. This study categorically reports the superiority of rectal administration of NSAIDs, diclofenac over indomethacin and post-ERCP administration of NSAIDs to reduce post-ERCP pancreatitis. However, these results cannot be generalized because the preventative strategy for post-ERCP pancreatitis in group of patients with known peptic ulcer disease, asthma, and allergy to NSAIDS needs also to be formulated. In addition, NSAIDs cannot be used in patients with chronic kidney disease. Other measures to prevent post-ERCP pancreatitis must not be completely abandoned and may be applicable in these situations. In addition, there are no reported trials comparing pre-procedure *vs* post-procedure prophylactic use of NSAIDS. This inference was made based upon their comparisons against placebo. Same limitation also applies on the effectiveness of diclofenac *vs* indomethacin. Trials targeting these questions must be considered for a validated conclusion from direct evidence instead of the presented indirect inference. Current review is unable to quantify the potential complication of bleeding following the prophylactic use of NSAIDs in ERCP patients, especially in patients undergoing sphincterotomy simultaneously. Although this is beyond the scope of this study but reported incidence of bleeding is almost negligible. Neither the length of incision nor the pre-procedure use of aspirin or other NSAIDs appear to be important predictors of ERCP-sphincterotomy linked bleeding[47].

COMMENTS

Background

Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis can be a serious complication resulting in increased mortality and morbidity in already sick patients. Therefore, the preventative strategies for post-ERCP are vital to reduce its consequences. The use of non-steroidal anti-inflammatory drugs (NSAIDs) is simple, economical and reported to be effective to reduce the incidence of post-ERCP pancreatitis. This article highlights the evidence in the form of meta-analysis to define the role of NSAIDs.

Research frontiers

Other preventive measures to reduce the incidence of post-ERCP pancreatitis include sphincterotomy of the sphincter of Oddi and pancreatic duct stenting. However, the use of NSAIDs seems to be less invasive and most economical. Several studies have reported its effectiveness and current study is an attempt to advance this evidence further.

Innovations and breakthroughs

Current meta-analysis of 13 randomized controlled trials on 3378 patients successfully demonstrates the usefulness of NSAIDs in the prevention of post-ERCP pancreatitis. Post-procedure use of NSAIDs by any route has clinically proven advantage of reducing 55% risk of post-ERCP pancreatitis. Diclofenac (55%) compared to indomethacin (41%) was more effective prophylactic agent.

Applications

Based upon the findings of this study the use of NSAIDs has clinical advantage in the reduction of post-ERCP pancreatitis and may routinely be used.

Terminology

ERCP: Endoscopic retrograde cholangiopancreaticography; NSAIDs: Non-steroidal anti-inflammatory drugs; MRCP: Magnetic resonance cholangio-pancreaticography.

Peer-review

The manuscript is overall well written.

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CASE REPORT

Challenges of banding jejunal varices in an 8-year-old child

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Abstract

Endoscoic variceal ligation (EVL) by the application of bands on small bowel varices is a relatively rare procedure in gastroenterology and hepatology. There are no previously reported paediatric cases of EVL for jejunal varices. We report a case of an eight-year-old male patient with a complex surgical background leading to jejunal varices and short bowel syndrome, presenting with obscure but profound acute gastrointestinal bleeding. Wireless capsule endoscopy and double balloon enteroscopy (DBE) confirmed jejunal varices as the source of bleeding. The commercially available variceal banding devices are not long enough to be used either with DBE or with push enteroscopes. With the use of an operating gastroscope, four bands were placed successfully on the afferent and efferent ends of the leads of the 2 of the varices. Initial hemostasis was achieved with obliteration of the varices after three separate applications. This case illustrates the feasibility of achieving initial hemostasis in the pediatric population.

Key words: Endoscopic variceal ligation; Endoscopic hemostasis; Pediatrics; Gastrointestinal hemorrhage; Varices; Variceal banding

Core tip: Banding jejunal varices in the pediatric population is feasible, safe and can achieve initial hemostasis in complex surgical patients.

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INTRODUCTION

Ectopic varices are defined as large porto-systemic venous collaterals occurring anywhere in the abdomen except in the cardio-esophageal region[1].

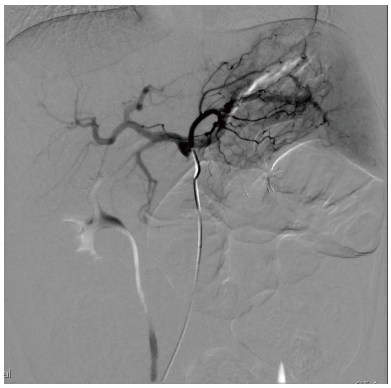

Figure 1 Computed tomography angiography with multiple serpiginous vessels in the left side of the bowel mesentery.

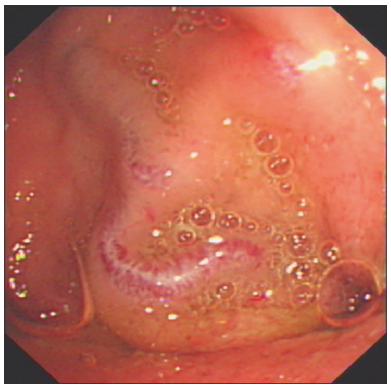

Figure 2 Suspicion of varices.

They account for up to 5% of all variceal bleeding[2]. Ectopic varices have been reported to occur at numerous sites, including 18% in the jejunum or ileum, 17% in the duodenum, 14% in the colon, 8% in the rectum, and 9% in the peritoneum[3]. Jejunal variceal bleeding, although rare, can be life threatening. There are only a few reports on the managements of jejunal varices in the paediatric population[4]. We present a rare case of severe and recurrent gastrointestinal bleeding secondary to jejunal varices in an 8-year-old patient. The management strategies including the use of endoscopic variceal ligation (EVL) are discussed.

CASE REPORT

An 8-year-old male patient was transferred from another tertiary hospital for assessment for obscure but profound acute gastrointestinal bleeding (AGIB).

He had a complex background of gastroschisis at birth associated with duodenal and colonic atresia. He had a repair of gastroschisis on day 1 of life and subsequently underwent a duodenojejunal anastamosis with right hemicolectomy and ileostomy formation, followed by ileo-colonic anastamosis and closure of the stoma. He had short gut syndrome and received nutritional supplementation *via* a balloon gastrostomy.

He had had multiple episodes of GI bleeding since he was 18 mo of age, which were thought to be associated with a superior mesenteric vein thrombosis. These were intermittent in nature and managed conservatively. The patient had a period of two years without a GI bleed prior to this presentation.

In 2014 however, the patient had 17 episodes of AGIB. Seven episodes were significant, mainly of hematochezia with clots or large melena. His lowest recorded hemoglobin was 22 g/L. The patient had multiple blood transfusions and was given 4 weekly iron infusions. He underwent computed tomography (CT) angiography which revealed distorted adjacent vascular structures around the pancreas with the splenic vein looping over the superior edge of the pancreas.

Normal enhancement was noticed in the portal vein, its left and right branches, the splenic vein (SV) and the superior mesenteric vein (SMV). However; there is unusual prominent venous structure draining in to the right side of the confluence of the SMV and the SV. There were multiple serpiginous vessels in the left side of the bowel mesentery with in particular a clump of varices/collaterals in the small bowels mesentery (Figure 1). All connections from these apparent varices couldn't be established, however; there was at least a connection to a looping vessel which extends into the left side of the SMV. Further looping vessels were seen in the anterior aspect of the mesentery from a proximal loop of the jejunum. Theses dilated blood vessels and collaterals around the mesentery of the small bowel raised the suspicion of mesenteric varices in the upper abdomen, but no active bleeding source was recognised. The patient was put intermittently on octreotide infusion but wasn't given primary or secondary prophylaxis as it was felt that the varices were more confined to some areas and secondary to mesenteric venous obstruction/abnormalities rather than strong evidence of generalised portal hypertension.

On arrival to our hospital in the same year, upper GI endoscopy revealed no esophago-gastric varices but identified portal gastropathy. Ileo-colonoscopy was normal apart from an erythematous ileo-colonic anastamotic rim. WCE identified a suspicious area (around 50 cm from the pylorus) of nodular shaped lesions with bluish discoloration, suspicious of varices. Two days later, further profound hematochezia occurred and therefore octreotide infusion (5 mcg/kg per hour) was commenced. Trans-oral double balloon enteroscopy (DBE) confirmed a normal esophagus, mild evidence of portal gastropathy, a normal duodenum, and jejunal examination revealed 4 moderately large isolated jejunal varices around 40-50 cm post-pylorus (Figures 2 and 3). Four bands were placed successfully on the afferent and efferent ends of the leads of the 2 of the varices using an operating gastroscope (Figure 4). The commercially available variceal banding devices are not long enough to be used either with DBE which was initially used diagnostically. Trans-anal DBE was performed and showed a small potential varix

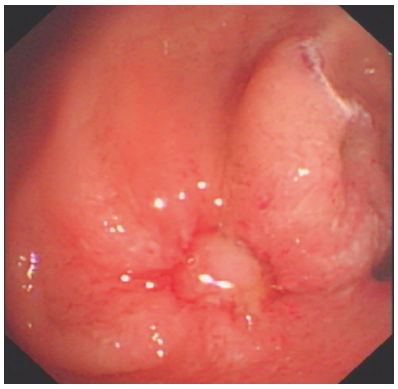

Figure 3 Appearance of jejunal varices using the double balloon enterosocpy.

approximately 120 cm proximal to the ileo-colonic anastamosis and this was not considered a risk and was not bleeding therefore was not banded. This area was marked for future reference with methylene blue tattoo injection. One week later a further endoscopy revealed the 2 banded varices to be thrombosed and now absent and sloughing within the bands was noted which were beginning to fall off the mucosa. The remaining 2 variceal vessels were then also banded. Two weeks subsequently the patient was well with no further bleed and a further endoscopy revealed friable variceal beds but no active bleeding. One further varix was banded at that time with hemostasis identified.

However the patient developed recurrence of bleed two weeks later possibly from an ileo-colonic source. The patient had shunting procedure few weeks later (mesenterico-caval shunt).

DISCUSSION

Our patient presented with the classical clinical signs reported previously in the literature for jejunal varices, evidence of abnormal vasculature in the mesentery with or without portal hypertention, a history of abdominal surgery, and hematochezia with or without hematemesis[5].

The exact pathology for developing jejunal varices in our case is not fully understood. It is likely to be a combination of superior mesenteric vein thrombosis (subsequently re-canalised however) and adhesions. A history of abdominal surgery appears to predispose to the development of ectopic varices around adhesions[6]. It seems that small-bowel anastomotic and adhesion-related varices can form within adhesions in the setting of mesenteric venous obstruction with or without portal hypertension[5].

Collateral formation within adhesions from previous surgery is the usual mechanism for the development of ectopic varices[3], with a likely mechanism that adhesions bring the parietal surface of the viscera in contact with the abdominal wall and portal hypertension results in the formation of varices below the intestinal mucosa[7].

The mainstay for the diagnosis of jejunal varices in our case was a combination of CT angiography and

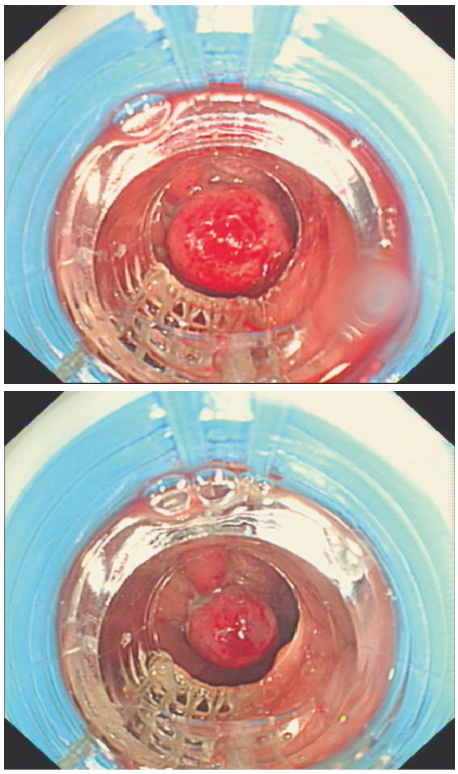

Figure 4 Banding of the jejunal varices using the operative gastroscope.

wireless capsule endoscopy.

Jejunal varices in wireless capsule endoscopy appear as serpiginous or nodular shapes, with or without a bluish discoloration. The variceal mucosa appears mosaic-like, shining, or normal compared with surrounding mucosa[8].

Capsule endoscopy is invaluable for the diagnosis of small-bowel varices. It is highly sensitive for detecting fresh blood in the small bowel. Clinical suspicion, capsule endoscopy image recognition, and alertness during capsule endoscopy interpretation are keys to diagnosis[8].

Several approaches for the treatment of jejunal varices have been described including surgery[9], portal venous stenting[10-12], percutaneous embolisation[13,14] and thne endoscopic options[5,15-18].

Surgical treatment options for small bowel variceal bleeds include resection of the afferent area of bowel and re-anastomosis[13]. However this can be challenging in patients with short gut and multiple adhesion as in our case.

Transjugular intrahepatic portal-systemic shunt or a decompressive shunting procedure is recommended in patients with overt systemic portal hypertension[13,19,20]. With the addition of coil or embolization has been reported to be particularly useful for ectopic varices, as these can continue to bleed despite successful portal pressure reduction[21].

The effectiveness of beta-blockers for primary prophylaxis and octreotide treatment for acute hemorrhage of anastomotic and segmental varices is uncertain[5].

It has been reported that endoscopic treatment including sclerosing agents can be used for treatment

of actively bleeding duodenal or jejunal varices or to prevent re-bleeding from focal varices with hemorrhage. However, while hemostasis is feasible, ulceration and re-bleeding rates can be high[5]. The use of N-butyl-2-cyanoacrylate (Histoacryl®) injection has been described in several case reports, for hemostasis of actively bleeding duodenal varices[15,22,23]. In one series all the varices had developed around the anastamotic sites and only two had elevated systemic portal pressure[18]. Another case report describes successful treatment of bleeding jejunal varices using cyanoacrylate sclero-therapy *via* enteroscopy in an adult patient[16].

EVL has a theoretical increased risk of complications in the small bowel because of its thin wall, *e.g.*, perforation. However, there are several reports of successfully treated duodenal varices by EVL in adults without complications. In a review of 19 cases (all adults) with duodenal EVL only 3 (15.8%) rebled after treatment with no deaths reported due to complications or rebleeding[16]. In a report of 4 patients with duodenal EVL, 2 achieved complete resolution of varices after one treatment session, one had remaining varices on surveillance endoscopy but no bleeding in a 9 mo period and one case required surgical resection after several banding sessions[17].

The standard ligation balloon devices available are too short to be adapted for an enteroscope or a colonoscope but are applicable to standard upper GI endsocopes. The operating gastroscope (GIF-2TQ260M) allowed 3 way tip deviation and is stiffer than conventional upper GI endsocopes allowing successful banding to occur.

In this case, EVL was used successfully to achieve initial hemostasis with obliteration of the varices after three separate applications, however bleeding subsequently occurred from an ileo-colonic source.

Frequently ectopic variceal bleeding is difficult to manage and traditionally surgery or shunting is required depending on the underlying disease and the patency of the portal vein.

Endoscopic treatment as a minimally invasive approach is feasible and safe in this case and represents a viable alternative.

To the best of our knowledge, this is the first reported case in the literature describing EVL in the management of jejunal variceal bleeding in the pediatric population.

This case illustrates the technical feasibility and apparent safety of EVL in the management of jejunal variceal bleeding in children.

COMMENTS

Case characteristics
Recurrent severe gastrointestinal bleeding.

Clinical diagnosis
Jejunal varices.

Differential diagnosis
Upper gastrointestinal endoscopy ruled out esophageal and gastric variceal bleeding. Ilio-colonosconoscopy and wireless capsule ruled out other diagnosis like polyps or other vascular malformation. Wireless capsule showed features suggestive of ectopic varices.

Laboratory diagnosis
Extensive investigations including complete blood count, Lipase, liver enzymes, kidney function, radiological images with computed tomography (CT) angiography. The diagnosis was confirmed with wireless capsule endoscopy and endoscopy of the affected small bowel.

Imaging diagnosis
Imaging study using CT scan demonstrated thickening and irregularity of the mesentery surrounding in keeping with the diagnosis of mesenteric panniculitis.

Pathological diagnosis
Variceal bleeding was the diagnosis as per the wireless capsule endoscopy and the endoscopic finding.

Treatment
The patient was treated with pharmacological agents including octreotide. Blood transfusion was needed frequently to stabilise the patient. Endoscopic variceal ligation was successfully applied to achieve initial hemostasis.

Related reports
Clark *et al* reported successful endoscopic ectopic variceal ligation: A series of 4 cases and review of the literature in adult population.

Experiences and lessons
Jejunal varices is a rare disorder that can present with recurrent severe gastrointestinal bleeding in complex surgical paediatric patient, the authors describe a novel intervention in paediatric using endoscopic variceal ligation to achieve initial hemostasis.

Peer-review
In this case report the authors present the case of an 8-year-old child treated with endoscopic band ligation for jejunal varices. This kind of pathology is rare and the therapeutic options could be challenging.

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