World Journal of Gastroenterology

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DOI: 10.3748/wjg.v21.i37.10542

*World J Gastroenterol* 2015 October 7; 21(37): 10542-10552
ISSN 1007-9327 (print) ISSN 2219-2840 (online)
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TOPIC HIGHLIGHT

2015 Advances in Gastrointestinal Endoscopy

# Endoscopic management of gastrointestinal perforations, leaks and fistulas

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**Conflict-of-interest statement:** The authors declare no conflicts of interest.

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**Received:** April 28, 2015
**Peer-review started:** May 6, 2015
**First decision:** June 2, 2015
**Revised:** July 1, 2015
**Accepted:** August 31, 2015
**Article in press:** August 31, 2015
**Published online:** October 7, 2015

## Abstract

Gastrointestinal perforations, leaks and fistulas may be serious and life-threatening. The increasing number of endoscopic procedures with a high risk of perforation and the increasing incidence of leakage associated with bariatric operations call for a minimally invasive treatment for these complications. The therapeutic approach can vary greatly depending on the size, location, and timing of gastrointestinal wall defect recognition. Some asymptomatic patients can be treated conservatively, while patients with septic symptoms or cardio-pulmonary insufficiency may require intensive care and urgent surgical treatment. However, most gastrointestinal wall defects can be satisfactorily treated by endoscopy. Although the initial endoscopic closure rates of chronic fistulas is very high, the long-term results of these treatments remain a clinical problem. The efficacy of endoscopic therapy depends on several factors and the best mode of treatment will depend on a precise localization of the site, the extent of the leak and the endoscopic appearance of the lesion. Many endoscopic tools for effective closure of gastrointestinal wall defects are currently available. In this review, we summarized the basic principles of the management of acute iatrogenic perforations, as well as of postoperative leaks and chronic fistulas of the gastrointestinal tract. We also described the effectiveness of various endoscopic methods based on current research and our experience.

**Key words:** Endoscopic; Management; Perforation; Leak; Fistula; Stent; Clips

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**Core tip:** Most gastrointestinal perforations, leaks and fistulas can be satisfactorily treated by endoscopy. The efficacy of endoscopic therapy depends on several factors. Many endoscopic tools for effective closure of gastrointestinal wall defects are currently available. In this review, we summarize the basic principles of

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Rogalski P, Daniluk J, Baniukiewicz A, Wroblewski E, Dabrowski A. Endoscopic management of gastrointestinal perforations, leaks and fistulas. *World J Gastroenterol* 2015; 21(37): 10542-10552 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i37/10542.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i37.10542

## INTRODUCTION

Gastrointestinal perforations may result from endoscopic or laparoscopic procedures, or they can be spontaneous (*e.g.*, Boerhaave syndrome). Although the majority of perforations during endoscopic procedures are adverse events, the increasing use of advanced endoscopic techniques, including natural orifice transluminal endoscopic surgery (NOTES), or the transgastric drainage of fluid collections, is increasing the incidence of intentional perforations. The risk of gastrointestinal perforation during a diagnostic procedure is extremely low, while interventional endoscopy is associated with significantly higher risk[1]. Endoscopic procedures with the highest risk of iatrogenic perforations include: endoscopic submucosal dissection (ESD), stricture dilation, foreign body removal, endoscopic mucosal resection (EMR), tumor ablation and peroral endoscopic myotomy (POEM). A difficult esophageal intubation is a risk factor of perforation even during diagnostic endoscopy. The delayed perforations which can result from thermal injury are a significant clinical problem.

Anastomotic leaks usually result from technical difficulties during a surgical procedure. After esophageal resections this complication occurs in 10%-20% of cervical anastomoses, 5%-10% of thoracic anastomoses, and after 3%-22% of colorectal resections[2,3]. The increasing frequency of bariatric procedures contributes to a higher incidence of postoperative leaks and other unusual complications[4]. Gastrointestinal fistulas are also chronic complications of inflammatory diseases or malignancy[5].

## GASTROINTESTINAL PERFORATIONS

Most perforations that occur during endoscopic procedures can be treated endoscopically, with no need for surgery. On the other hand, gastrointestinal perforation is a medical emergency and, even after successful endoscopic closure of the gastrointestinal wall, the patients require close monitoring. The key to successful treatment is early recognition of the perforation, correctly assigning the patient to endoscopic or surgical management and adequate treatment of life-threatening complications.

The initial steps after diagnosis of a gastrointestinal perforation should include proper positioning of the patient to reduce the risk of intraluminal content leakage, parenteral antibiotics and cardiopulmonary monitoring. Patients with upper gastrointestinal tract perforations should receive proton pump inhibitors.

Most of the data regarding endoscopic treatment of gastrointestinal perforations are based on small studies including case reports, case series, and animal studies. However, when the perforation is detected during an endoscopic procedure, and is amenable to endoscopic closure, it should be closed immediately, in the same procedure. Endoscopic assessment of the defect is crucial, before attempting closure. Insufflation of carbon dioxide instead of room air may be helpful at this point. The endoscopist should assess the size, and the edge of the defect in the gastrointestinal wall and any potential bleeding. Endoscopic closure can be achieved by a variety of methods and devices and the corresponding endoscopic techniques vary depending on the location, size of the defect and timing of recognition (see Table 1). In most cases a failed endoscopic closure of a perforation requires surgical intervention. Asymptomatic perforations that are recognized 24 h or more after the procedure may be managed conservatively[1].

The mainstays of postoperative care after successful endoscopic closure are antibiotics, avoidance of oral intake, nasogastric suctioning, intravenous fluids, and analgesia. Some patients may also require surgical drainage of fluid collections. Parenteral or enteral nutrition should also be considered in selected patients. If the postoperative course is uncomplicated, oral food can be resumed four days after successful closure of a perforation[6,7].

The most serious complications of gastrointestinal tract perforations are the abdominal compartment syndrome, tension pneumothorax, tension pneumoperitoneum, subcutaneous emphysema and peritonitis. Tension pneumothorax and tension pneumoperitoneum are medical emergencies requiring immediate needle decompression. It should be emphasized that extraluminal air does not mean that surgery is needed, and the volume of extraluminal air is generally not proportional to size of the gastrointestinal wall defect[8]. Subcutaneous emphysema can be life-threatening and may require endotracheal intubation, due to the risk of airway obstruction by air dissecting through the soft tissues of the neck. A surgical evaluation for possible lavage or perforation closure should be considered in patients with peritonitis.

Radiologic examinations may also be appropriate after the endoscopic closure of perforations. Contrast studies using water-soluble agents can demonstrate persistent leaks and computed tomography (CT) can detect extraluminal air, fluid collections, and other complications.

**Table 1 Clinical presentation and preferred endoscopic management according to site of perforation[1,7,8,54]**

| Location of perforation | Clinical presentation | Preferred endoscopic closure techniques | Comments |
|---|---|---|---|
| Esophagus | Subcutaneous emphysema, neck pain, chest pain, emesis | Small perforations (< 2 cm) can be closed with clips (TTSC or OTSC) | The use of endoscopic techniques may be challenging in the proximal esophagus, due to space constraints and patient intolerance - consider conservative treatment in stable patients |
| | Tachycardia with chills and fever suggest mediastinitis and sepsis development | Perforations < 2 cm size with everted edges may be treated with OTSC clips | Stent fixation with clip application or suturing techniques may be useful to prevent migration of the stent |
| | | Large perforations (> 2 cm) or defects associated with esophageal stenosis may be managed with fully covered and partially covered SEMS or endoscopic suturing techniques | Fibrin glue application and EVAC use has been reported for closure of esophageal perforations but experiences are limited |
| Stomach | Abdominal pain, abdominal fullness | Endoscopic clipping techniques (TTSC, OTSC) are the mainstay of gastric perforation closure | Most perforations of the stomach are small defects that occur during EMR, ESD procedures and can be successfully closed with TTSC. |
| | Breathing deterioration and shock symptoms suggest development of tension pneumoperitoneum | Omental patch closure technique, clipping plus endoloop or OTSC may be an option in closing large defects (> 1 cm) | Closing perforations in proximal stomach may be challenging |
| | Peritonitis and abscess formation result from leakage of gastric contents | Endoscopic suturing is an optional method especially in closing post-ESD defects | Endoscopic band ligation for gastric perforation closure has been reported but experiences are limited |
| | Pneumomediastinum and pneumothorax are relatively rare complications of perforations in cardiac region | Endoscopic stents may be useful to treat perforations following pyloric or gastroenteric anastomosis dilation | |
| Duodenum and biliary tract | Retroperitoneal nature of the injuries may mask the severity | Peri-ampullary or biliary tract perforations may be treated with biliary stent placement or TTSC | The use of transparent cap may be helpful in difficult locations |
| | The severity of perforations varies from asymptomatic retroperitoneal air alone (which is not true perforation), to life-threatening perforations with | Large perforations most often require immediate surgery. However, when the defect size < 15 mm consider perforation closure with TTSC, OTSC | Closure of medial duodenal wall defects with clips may be challenging due to risk of clipping the ampulla and anatomic location |
| | persistent pancreatic and biliary leaks into retroperitoneal or intraperitoneal space | Fully covered duodenal SEMS are also the therapeutic option in nonperiampullary perforations | Nasoduodenal drain to divert pancreatic and biliary secretions may be beneficial |
| | Peritonitis is a late finding associated with poor outcome | | Asymptomatic patients with retroperitoneal air alone need no additional treatment |
| Colon, Rectum | Abdominal pain, abdominal fullness, subcutaneous emphysema | Small perforations (< 2 cm) can be closed with clips (TTSC or OTSC) | The success rate of endoscopic closure is higher when the perforation is recognized and closed during the same procedure, the quality of bowel preparation is good, and there is no leakage of intraluminal contents |
| | Breathing deterioration and shock symptoms suggest development of tension pneumoperitoneum | Clipping plus endoloop is an option to close large colonic defects | Large vertical perforations should be closed from top to bottom, and horizontal perforations should be clipped from left to right |
| | Peritonitis and abscess formation are the consequence of intraluminal fecal leakage | Endoscopic band ligation can also be useful to treat colonic perforations | |

SEMS: Self-expanding metal stent; OTSC: Over-the-scope clip; TTSC: Through-the-scope clip; EVAC: Endoscopic vacuum- assisted closure; EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosal dissection; ERCP: Endoscopic retrograde cholangio-pancreatography.

## GASTROINTESTINAL LEAKS AND FISTULAS

Both acute and chronic leakage may be caused by inflammatory or malignant processes, but one of the commonest causes is an anastomotic leak after gastrointestinal surgery. Postoperative leaks remain a major clinical problem, responsible for significant morbidity and a very high mortality, which may exceed 60% when treatment is delayed[9]. Early diagnosis and appropriate treatment are crucial to reduce this mortality. Typical symptoms of leakage of gastrointestinal contents into body cavities (mediastinum, pleura, peritoneum) are: fever, a systemic inflammatory response syndrome, septic shock, increased levels of C-reactive protein and a raised white blood cell count[10]. Upper gastrointestinal radiography with water-soluble contrast (*e.g.*, Gastrografin) confirms the leakage. Endoscopy allows direct visualization of the lumen defect, its extension and the concomitant inflammation of surrounding tissues. Direct visualization of the fistula orifice can be facilitated by injecting methylene blue through an external catheter.

The most efficient treatment for gastrointestinal leaks remains controversial. Some authors suggest aggressive therapy with surgical re-operation, while others recommend conservative treatment with broad-spectrum antibiotics, nasogastric tubes, parenteral nutrition and adequate drainage. However, conventional therapy is associated with a prolonged hospital stay, increased costs and a mortality rate of up to 60%[11]. In the past decade, an increasing number of publications has described endoscopic therapy for gastrointestinal (GI) disruptions of different etiologies. The current endoscopic management of leaks and fistulas includes stent placement, endoclipping, application of tissue sealants and suturing devices[12,13]. There are certain requirements for the proper use of these techniques. Tissue sealants and clip application are considered the best therapeutic options for small defects, while endoscopic stent placement should be used for dehiscences ranging between 30% and 70% of the lumen circumference. Larger disruptions should be treated surgically[10]. During the endoscopic procedure, carbon dioxide insufflation is preferred because of possible gas leaks into body cavities. To reduce septic and respiratory complications, some cases will need adequate mediastinal or pleural drainage[2]. The effectiveness of closure after endoscopic treatment should be confirmed by imagining studies, including a contrast study with Gastrografin.

## CLIPPING TECHNIQUES

### *Through-the scope clips*

Hayashi *et al*[14] reported the first use of clips in gastrointestinal endoscopy in 1975. Endoscopic clips were initially used primarily to treat gastrointestinal bleeding. They are now used in many other situations, to both treat and diagnose gastrointestinal tract diseases. Non-hemostatic applications of endoscopic clips include-the closing of perforations, fistulas and postoperative gastrointestinal leaks; preventing post-polypectomy bleeding; marking lesions for further surgical or fluoroscopic-guided therapy; attaching feeding tubes; and fixing stents to prevent migration. The various endoscopic clips and their delivery systems differ in many properties relating to the size and shape of the arms, the width of the opening span, the possibility for rotation and clip reopening and the pressure force of the closed arms. The clips are available in preloaded and reloadable forms, and their properties determine both the application time and time of clip retention in the tissue. In general, through-the scope clips (TTSC) can close luminal defects < 2 cm in size. However, for defects > 1 cm, a combined technique using an endoloop and TTSC, or omental patching, are recommended[1]. Applying of the clip can be difficult when the tissue surrounding the defect is inflamed or indurated. To enhance successful clip application, gentle suction should be applied before clip closing so that the edges of the defect are reversed and approximated and more tissue is captured by the clip arms[8].

A pooled analysis of 17 patients with acute, intermediate and chronic esophageal wall defects showed that endoclips closed esophageal perforations ranging from 3 to 25 mm effectively[15]. Gastric perforation during endoscopic resection procedures (EMR, ESD) can also be treated by endoclipping as reported by Minami *et al*[16]. In a retrospective analysis, endoscopic closure was successful in 115/117 (98.3%) patients, and only 2 patients (whose endoclip closure was unsuccessful) underwent emergency surgery. Endoclipping of iatrogenic colonic perforations has also been also investigated: in a series of 7598 colonoscopies, defects were effectively closed in 25/27 patients[17].

### *Over the scope clips*

A single application of over the scope clips (OTSC) can provide full thickness closure of open defects up to 2-3 cm. The design of the device, commonly known as the "bear claw" is fundamentally different from that of TTS clips. The advantage of OTS over TTS clips is their ability to close long-lasting leaks and fistulas even when the tissue surrounding the defect is inflamed or indurated. This is possible due to the greater compressive force and tissue capture of the OTS devices. Defects with everted edges can also be effectively closed with OTSC. Two commercially available and currently popular OTS clip systems are the OTSC (OTSC, Ovesco Endoscopy AG, Tübingen, Germany) and the Padlock clip (Aponos Medical Corp., Kingston, New Hampshire).

### *OTSC (Ovesco Endoscopy AG, Tübingen, Germany)*

The OTSC System Set comprises an applicator cap with a mounted OTSC clip, a thread, thread retriever and a hand wheel for clip release[18]. The transparent applicator cap is mounted on the tip of the endoscope. A thread is introduced into the working channel and is fixed onto a hand wheel at the working channel access port of the endoscope[19]. The clip is made of a biocompatible material, Nitinol®, and can remain in the body for a long time. Caps are available in three different sizes suitable for almost all commercially available endoscopes: 11 mm, 12 mm, and 14 mm. There are two different depths of caps for grasping more or less tissue during approximation. The clips are available in three sizes adapted to the cap sizes. There are also three different clip tooth shapes suitable for different indications and tissues: (t) traumatic, (a) atraumatic, and (gc) gastrostomy closure. The traumatic (t) clip is more commonly used to close

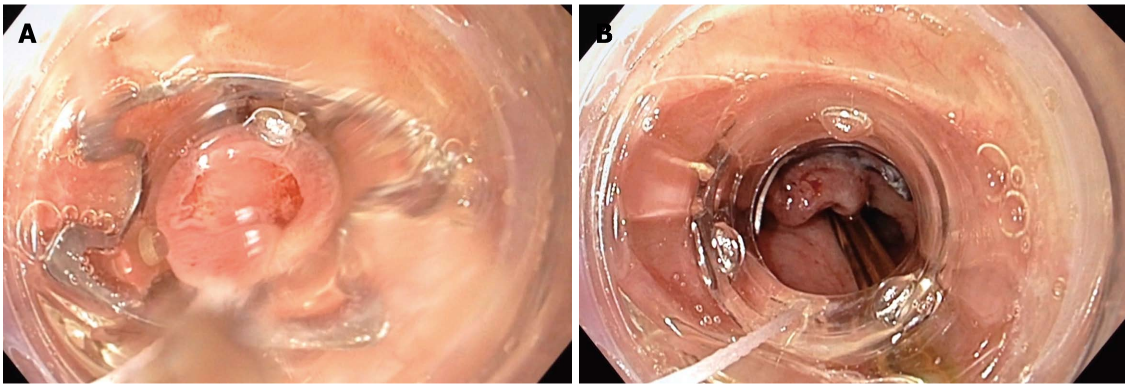


**Figure 1 Over the scope clip closure of an esophageal perforation.** A: Over the scope clip closure of the defect caused by thermal damage during cardiac surgery; B: Endoscopy showing complete closure of the defect. Taken from Department of Gastroenterology and Internal Medicine, Medical University of Bialystok, Poland.

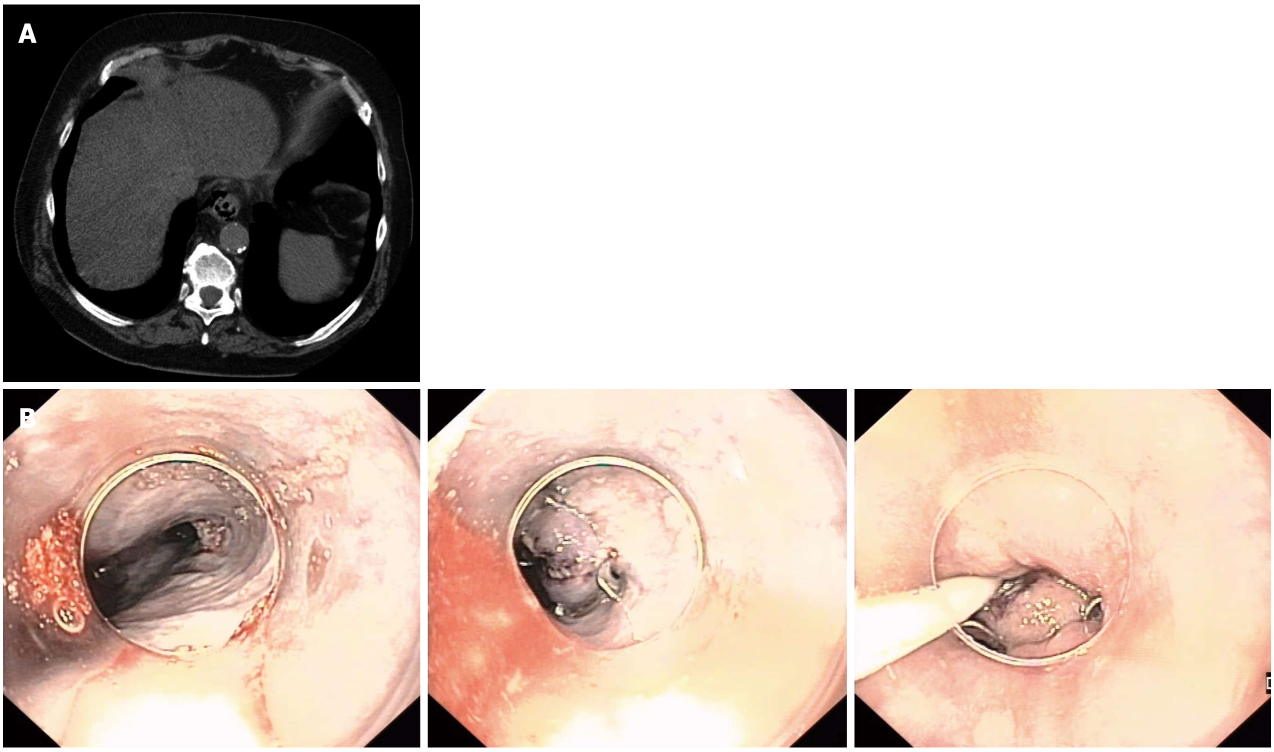


**Figure 2 Boerhaave syndrome.** A: Computed tomography scan showing the presence of air in the mediastinum; B: Over the scope clip closure of the perforation and feeding tube placement. Taken from Department of Gastroenterology and Internal Medicine, Medical University of Bialystok, Poland.

fistulas and perforations, while the atraumatic (a) clip is preferred to control bleeding. The approximation of the gaping edges of a lesion, especially when the tissue is indurated, can be facilitated by two dedicated accessories, the OTSC Twin Grasper and the OTSC Anchor. It is also possible to reload a second clip onto an already mounted OTSC system using OTSC Reloader. Note that the insertion of an endoscope with preloaded clips may be difficult because the mounted OTSC system increases the diameter of the endoscope.

After targeting the lesion, the tissue is aspirated or pulled into the cap. By tightening the thread with the hand wheel the OTSC is released and closes itself to anchor firmly to the tissue (Figure 1). Before attempting to close the defect, we suggest performing an endoscopy with a transparent distal attachment (Figure 2) without the clip and attempting to aspirate or grasp the edges of the defect to the cap with or without any additional accessories. If the tissue cannot be aspirated or grasped into the cap, there is a little chance of the defect being effectively closed by the OTS clip. Some authors have suggested that ablating the tissue edges and areas surrounding the fistula orifice with argon plasma coagulation, or abrading them with the cytology brush, before closing the fistula may help the defect to heal[20].

In a recent European multicenter prospective cohort study of 36 consecutive patients with iatrogenic perforations (5 esophageal, 6 gastric, 12 duodenal, and 13 colonic), 89% of patients had successful closures without adverse events after OTSC application. The primary end point, successful closure, was defined as endoscopic closure without leakage and the absence of adverse events within 30 d of the procedure[21].

Although previous studies have demonstrated a high rate of early fistula closure using OTSC, data on long-term fistula closure are scant. A retrospective review of all patients who underwent OTSC placement at the Mayo Clinic Rochester and Virginia Mason Medical Center to close chronic fistulas demonstrated a high initial technical success rate (42/47 patients, 89%), which was defined by a lack of contrast extravasation immediately after OTSC placement[22]. Nonetheless, a recurrent fistula, defined by the recurrence of symptoms and/or re-demonstration of fistula after initial success occurred in 19/41 (46%) patients at a median of 39 d (IQR: 26-86 d). Only 25/47 (53%) patients followed for a median duration of 178 d (IQR: 63-326) demonstrated delayed clinical success, despite frequent clip retention.

### *Padlock-G clip (Aponos Medical Corp., Kingston, New Hampshire)*

Padlock clip is another commercially available system, and consists of a clear plastic cap with a preloaded clip mounted at the tip of the endoscope, a trigger wire that runs alongside the endoscope and a control handle. The feasibility, reproducibility, and efficacy of this system has been investigated in animal studies with promising results; however, data regarding its clinical efficacy are scant[23].

## ENDOSCOPIC SUTURING

### *Overstitch endoscopic suturing system (Apollo Endosurgery, Austin, Tex)*

Endoscopic suturing techniques allow for the closing of larger defects; however, it is technically much more difficult than clip application. The OverStitch Endoscopic Suturing System is currently approved for clinical use. The system provides for the approximation of tissues by full-thickness stitches. The device requires a double channel therapeutic endoscope (GIF 2T160, Olympus Corp. Tokyo, Japan). The main parts of the system are: the end cap, the needle driver handle, and an anchor exchange catheter. The end cap is mounted on the distal tip of the endoscope. The tissue approximation and suture placement may be facilitated by a tissue-retracting helix device or grasping forceps. During the procedure, additional assist components can be inserted through the working channel of the endoscope. The OverStitch Endoscopic Suturing System allows interrupted or continuous stitches without needing to remove the device. Both absorbable and non-absorbable sutures are available.

Endoscopic suturing has been used to close both acute perforations and chronic fistulas. Two studies demonstrated a high rate of complete primary closure of gastro-gastric fistulas after bariatric surgery[24,25]. However, the long-term results of large (> 2 cm) chronic fistula closure with this technique are disappointing. Kantsevoy *et al*[26] reported that closing large post-ESD defects, to prevent delayed complications, is technically feasible and cost effective with the OverStitch endoscopic suturing device. A case series reports the use of endoscopic suturing to fix esophageal stents and prevent migration[27].

## SELF-EXPANDING METAL AND PLASTIC STENTS

Stents are commonly used as a palliative treatment for malignant esophageal or colonic strictures. However, recent data suggest that the application of endoscopic stents - either fully (FSEMS) or partially covered (PSEMS) self-expanding metal stents, or self-expanding plastic stents (SEPS) - is effective, minimally invasive therapy for GI disruptions, including post-surgical leaks, fistulas and perforations. Though not approved by the FDA for these benign disorders, many studies confirm that stents are effective[3,28-30]. Partially or fully covered SEMS and SEPS effectively seal of GI disruptions, while the stent radial force prevents their migration. It allows outflow of the fluid from the defect to be temporarily blocked. The major advantage of stent placement is the immediate control of leaks, protection of the esophageal wall during mucosal healing, possibility of early oral feeding and prevention of stricture formation[31]. Uncovered and partially covered stents have a lower tendency to migrate. On the other hand tissue in- and overgrowth through the stent hampers removal of the device. Fully covered stents are ideal for controlling leakage but are more prone to dislodge spontaneously. It is extremely important to assure proper drainage of a leakage site, and especially a perforation, because the implantation of a fully covered stent may prevent adequate drainage of a cavity, leading to sepsis, as well as preventing the GI wall leak. A recent analysis of unsuccessful esophageal stent placement in the treatment of gastrointestinal leaks identified four factors that significantly reduce the effectiveness of therapy: (1) leak located in the proximal cervical esophagus; (2) stent traversing gastroesophageal junction; (3) esophageal injury longer than 6 cm; and (4) anastomotic leak associated with a more distal conduit leak[32]. Despite all the known limitations, stent placement appears to be a promising treatment for GI wall disruptions.

SEPSs are an effective, safe and relatively noninvasive treatment for esophageal leaks and perforations[30]. Polyflex (Boston Scientific, United States) is the most commonly used SEPS for this purpose. It is made of polyester, fully covered with silicone, and with a flared proximal end to prevent migration. It has some advantages over a SEMS for treating of GI disruptions: the soft material provides secure and efficient force to close the leakage, and the silicone membrane prevents tissue ingrowth. This facilitates easy repositioning and removal of the stent. The disadvantages of SEPS placement area complicated loading and delivery device, the large diameter of the provider and a high stent migration rate[30]. Polyflex stents have been used for 15 years to manage esophageal disruptions. The high effectiveness of SEPS for treating esophageal leaks and perforations is well documented[2,30,33-35]. The rate of successful stent placement in a correct position varies between 90% and 100%, and the healing rate is also very high (80%-100%)[30]. Moreover, compared with conservative treatment, stent placement resulted in earlier oral intake, a shorter hospital stay and lower in-hospital mortality[2]. The optimal timing of stent placement is not well established, but most of the studies suggest insertion of the stent immediately after the diagnosis of a GI disruption. The diameter of the stent depends on the localization of GI disruption. Generally, stents for cervical leaks should have a smaller diameter (18-23 mm) than those for post-gastrectomy leaks (21-25 mm), to avoid excessive tracheal compression and foreign body sensation[33]. Stents should be removed when healing of the disruption is confirmed by water-soluble contrast examination, endoscopy, and resolution of clinical symptoms. In most studies, SEPSs were removed within 28 d. The most common complication, stent migration, was observed in 8%-23% of cases in the short -term and in almost 40% of cases after long-term follow-up[30,33-35]. The high frequency of stent migration results from the smooth outer surface of Polyflex and a lack of concomitant stenosis at the site of the leak. This complication may be avoided by placing large-diameter stents, or by using endoscopic clips at the stent margin to anchor the prosthesis to the gastrointestinal wall.

Previously, self-expanding metal stents were not considered first-line therapy for benign gastrointestinal disorders because of their relatively high migration rate in the absence of stenosis and possibility of tissue in- and overgrowth in uncovered parts of the prosthesis[36,37]. The stent material influences the extent of tissue hyperplasia, with metal or Nitinol® stents causing more hypertrophy than plastic stents. Recent reports showed that SEMSs are promising tool for the management of GI disruptions, with a high rate of healing and relief of symptoms[28,31,38]. Moreover, this prosthesis is relatively easy and safe to use. In one of the largest studies, which included 88 patients with upper GI leaks, fistulas, and perforations, Swinnen *et al*[38] demonstrated the effectiveness of partially covered SEMS. The stents were properly placed in all patients (average 1.74 PSEMSs per patient) for an average of 128.6 d, with the lekage resolved in 78% of patients after primary and 84% after repeated endoscopic treatment. Spontaneous migration occurred in 11% of stentings. Minor (dysphagia, hyperplasia, rupture of stent coating) and major complications (bleeding, perforation, tracheal compression) occurred in 21% and 6% of patients, respectively. PSEMSs were successfully removed from 96% of patients. To facilitate stent removal, the authors suggested rat-tooth forceps, provided that there was only mild tissue hyperplasia at the end of prosthesis. In the case of moderate to severe hyperplasia, inserting a SEPS (Polyflex) inside the SEMS for 1-3 wk can induce necrosis of the hypertrophic tissue and facilitate removal of the stent. Alternatively, ingrown tissue can be treated with argon plasma coagulation to expose the metal mesh of the stent. To prevent excessive tissue in- and overgrowth most experts recommend stent removal 6 to 10 wk after treatment[31,38,39].

Two relatively large retrospective studies assessed the usefulness of different types of stents (FSEMS, PSEMS, SEPS) in the treatment of GI disruptions[29,31]. A total of 52 and 54 patients received 83 and 132 stents, respectively, to treat anastomotic leaks, fistulas and perforations. Successful stent placement was observed in 99%-100% of cases. Clinical success, defined as closing the leakage, was achieved in 76%-83% of patients, with no differences between partially and fully covered metal or plastic stents. Stent migration occurred more frequently with FSEMS (20%), than with SEPS (14%) or PSEMS (10%), while tissue in- and/or overgrowth occurred only with PSEMS (11%)[31]. The authors identified two factors associated with the successful primary closure of a GI disruption: a shorter time between diagnosis of esophageal leakage and stent insertion and a smaller luminal opening diameter[29]. This is in agreement with a previous study that showed a 100% success rate after immediate closure of a perforation, compared with 50% when the SEMS was inserted after one month[38]. In summary, both plastic and metal SEMS offer a favorable alternative to surgery or conservative management for the treatment of benign upper GI leaks, fistulas and perforations.

Lower GI fistulas and anastomotic leaks after colorectal resection are a serious clinical problem. SEMSs are less often used to treat lower GI leakage because the more vigorous motility of the colon increases the probability of proximal or distal stent migration. This prevents closure of the leakage and increases the risk of procedure-related complications such as obstruction, perforation, and bleeding. Recently, Lamazza *et al*[3] presented the results of placing mostly full-covered SEMS in patients with symptoms of lower GI leakage after colorectal surgery. The area of leakage included at least 30% of the anastomotic circumference. Stents were successfully placed in all patients. During the observation period (mean 2 years) the leakage resolved in 84% of patients treated with FSEMS. Based on limited data, SEMS placement seems to be an attractive alternative for some patients with symptomatic leakage after colorectal resection.

## TISSUE SEALANTS

Tissue sealants have been used for more than 20 years with a good results for GI disruptions[40]. The most common tissue sealants in clinical use are biologic (fibrin) glue and cyanoacrylate[12,41,42]. The two main components of fibrin glue are human fibrinogen reconstituted with aprotinin and thrombin reconstituted with calcium chloride. They are applied *via* a double lumen catheter to form a fibrin cloth (in a process mimicking blood coagulation) in the area of the leak. Fibrin glue requires endoscopic removal of tissue remnants and pus because it is most effective when applied to a dry area. *N*-butyl-2-cyanoacrylate (Histoacryl, B. Braun, Germany) is the most popular cyanoacrylate used to treat leakage. Once applied, cyanoacrylate polymerizes after contact with moisture, causing tissue necrosis and an inflammatory response. It is not affected by gastric or pancreatic enzymes. Moreover, it has antibacterial properties and can be applied to an infected site[12,42]. Usually, before applying a sealant, the mucosa around the opening is de-epithelialized (with a cytology brush or argon plasma coagulation) to promote inflammation and to facilitate healing of the fistula[13].

Tissue sealants are applied as monotherapy or in combination with other endoscopic techniques (*i.e.*, clips, Vicryl mesh). In one of the most recent studies, endoscopic application of tissue sealants successfully closed anastomotic leaks in 61 of 63 patients[12]. The median total volume of fibrin glue applied was 12 mL (average of four sessions required) and 1.5 mL for cyanoacrylate (average of two sessions). Similar favorable results were obtained in other studies, with successful fistula sealing rates ranging between 37% and 87% after fibrin glue was applied over 2.5 to 4 sessions[43,44]. High-output GI fistulas require multimodal therapy that combines sealants with other methods. For large diameter upper gastrointestinal fistulas, Böhm *et al*[41] reported promising results by combining Vicryl mesh and fibrin glue. Successful fistula healing was obtained in 87% of patients, with re-epithelialization of the lesion within a mean of 44 d. Another therapeutic approach for large diameter fistulas is a combination of fibrin glue and stent placement[45]. A recent study compared the safety and efficacy of endoscopic therapy (including the use of tissue sealants in 14 of the 20 patients) with surgical methods[46]. Endoscopic therapy resulted in a very high technical success rate (95%) and lower frequency of leakage at the end of the study, compared to surgical treatment (17.5% *vs* 58.3%). In conclusion, tissue sealants are a valuable tool for the successful treatment of postoperative gastrointestinal leaks and fistulas.

## OTHER TECHNIQUES

### *EBL*

Two case series investigate endoscopic band ligation of iatrogenic gastric and colonic perforations following failed endoclip closure, with promising results[47,48]. This technique should be taken into account as a salvage therapy when clip application is technically difficult.

### *Cardiac septal defect occluder*

The Amplatzer Septal Occluder (AGA Medical Group, Plymouth, MN) is a device developed for the occlusion of atrial septal defects but has also been used off-label to close GI fistulae[19]. The device consists of two self-expandable disks made of Nitinol® mesh covered by polyester fabric, connected by a short waist that has various diameters. Before implanting the occluder, the size of the defect should be measured *e.g.*, by inflating a balloon under fluoroscopic guidance. The 70-cm delivery system is too short to deploy the device through the scope, but the occluder can be implanted under direct visualization, by passing it alongside the endoscope over an endoscopically placed guidewire.

Gastric leaks and esophagotracheal fistulae have been successfully closed with the cardiac septal defect occluder[49,50]. Melmed *et al*[51] reported successful endoscopic management of refractory gastrocolonic fistula in a two-step endoscopic approach using the cardiac septal defect occluder with cyanoacrylate glue and a CardioSEAL septal repair implant with cyanoacrylate glue and hemoclips.

### *Endoscopic vacuum assisted closure*

**Endo-SPONGE:** Endoluminal vacuum therapy is a minimally invasive method to treat anastomotic leakage, especially following rectal surgery. Endo-SPONGE consists of an open-pored polyurethane sponge and a suction tube connected to a wound drainage system. The sponge can be cut to the size of the wound cavity. After a diagnostic endoscopy, an endoscope and overtube are inserted into the wound cavity. The sponge is placed into position and released using the pusher. Several sponges can be used during one session, depending on the size of the wound cavity. The sponge allows a gentle, continuous suction to be transferred evenly over all tissues in contact with the sponge surface and provides appropriate drainage with a gradual reduction in the size of the wound cavity. One disadvantage is the need to change the sponge every 48-72 h, until the wound cavity has healed.

Arezzo *et al*[52] evaluated the long-term efficacy of endoscopic vacuum therapy for the treatment of anastomotic leaks after colorectal surgery. In this retrospective review, endoscopic vacuum assisted closure (EVAC) was applied in 14 patients with an overall success rate of 79%. The treatment had a median duration of 12.5 sessions (range: 4-40 sessions) and a median time to complete healing was of 40.5 d. Another retrospective analysis of 71 patients compared stent placement (SEMS or SEPS) with EVAC for the nonsurgical closure of intrathoracic leakage[53]. The overall closure rate was significantly higher in the EVAC group (84.4%) compared with the SEMS/SEPS group (53.8%). Based on the available studies, EVAC seems to be an effective and interesting alternative to other methods for the treatment of anastomotic leaks.

## CONCLUSION

The appropriate management of patients with gastrointestinal leaks, fistulas and perforations requires cooperation between the gastroenterologist, surgeon and radiologist. The increasing number of endoscopic procedures with a high risk of perforation and the increasing incidence of leakage associated with bariatric operations necessitate minimally invasive treatment of these complications. Endoscopic closure techniques are a promising alternative to surgical treatment. Nevertheless, there is a need for further, large, randomized, controlled trials comparing the clinical efficacy of the different endoscopic techniques, as well as the outcomes of endoscopic and surgical management of gastrointestinal wall defects. With the introduction of new endoscopic devices, we expect the results of endoscopic treatment of gastrointestinal perforations, leaks and fistulas improve significantly.

## REFERENCES


1 **Paspatis GA**, Dumonceau JM, Barthet M, Meisner S, Repici A, Saunders BP, Vezakis A, Gonzalez JM, Turino SY, Tsiamoulos ZP, Fockens P, Hassan C. Diagnosis and management of iatrogenic endoscopic perforations: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. *Endoscopy* 2014; **46**: 693-711 [PMID: 25046348 DOI: 10.1055/s-0034-1377531]

2 **Hünerbein M**, Stroszczynski C, Moesta KT, Schlag PM. Treatment of thoracic anastomotic leaks after esophagectomy with self-expanding plastic stents. *Ann Surg* 2004; **240**: 801-807 [PMID: 15492561]

3 **Lamazza A**, Sterpetti AV, De Cesare A, Schillaci A, Antoniozzi A, Fiori E. Endoscopic placement of self-expanding stents in patients with symptomatic anastomotic leakage after colorectal resection for cancer: long-term results. *Endoscopy* 2015; **47**: 270-272 [PMID: 25668426 DOI: 10.1055/s-0034-1391403]

4 **Rogalski P**, Hady HR, Baniukiewicz A, Dąbrowski A, Kaminski F, Dadan J. Gastric band migration following laparoscopic adjustable gastric banding (LAGB): two cases of endoscopic management using a gastric band cutter. *Wideochir Inne Tech Maloinwazyjne* 2012; **7**: 114-117 [PMID: 23256012 DOI: 10.5114/wiitm.2011.25983]

5 **Hady HR**, Baniukiewicz A, Luba M, Rogalski P, Dabrowski A, Dadan J. Bronchobiliary fistula as a complication after long-term stenting of hepatic ducts, applied by ERCP after hepatobiliary surgery due to hydatid cyst. *Endoscopy* 2011; **43** Suppl 2 UCTN: E178-E179 [PMID: 21557156 DOI: 10.1055/s-0030-1256295]

6 **Katsinelos P**, Kountouras J, Chatzimavroudis G, Zavos C, Pilpilidis I, Tzilves D, Paroutoglou G. Endoscopic closure of a large iatrogenic rectal perforation using endoloop/clips technique. *Acta Gastroenterol Belg* 2009; **72**: 357-359 [PMID: 19902872]

7 **Boumitri C**, Kumta NA, Patel M, Kahaleh M. Closing perforations and postperforation management in endoscopy: duodenal, biliary, and colorectal. *Gastrointest Endosc Clin N Am* 2015; **25**: 47-54 [PMID: 25442957 DOI: 10.1016/j.giec.2014.09.010]

8 **Baron TH**, Wong Kee Song LM, Zielinski MD, Emura F, Fotoohi M, Kozarek RA. A comprehensive approach to the management of acute endoscopic perforations (with videos). *Gastrointest Endosc* 2012; **76**: 838-859 [PMID: 22831858 DOI: 10.1016/j.gie.2012.04.476]

9 **Urschel JD**. Esophagogastrostomy anastomotic leaks complicating esophagectomy: a review. *Am J Surg* 1995; **169**: 634-640 [PMID: 7771633]

10 **Kumar N**, Thompson CC. Endoscopic therapy for postoperative leaks and fistulae. *Gastrointest Endosc Clin N Am* 2013; **23**: 123-136 [PMID: 23168123 DOI: 10.1016/j.giec.2012.10.002]

11 **Karl RC**, Schreiber R, Boulware D, Baker S, Coppola D. Factors affecting morbidity, mortality, and survival in patients undergoing Ivor Lewis esophagogastrectomy. *Ann Surg* 2000; **231**: 635-643 [PMID: 10767784]

12 **Kotzampassi K**, Eleftheriadis E. Tissue sealants in endoscopic applications for anastomotic leakage during a 25-year period. *Surgery* 2015; **157**: 79-86 [PMID: 25444220 DOI: 10.1016/j.surg.2014.06.002]

13 **Willingham FF**, Buscaglia JM. Endoscopic Management of Gastrointestinal Leaks and Fistulae. *Clin Gastroenterol Hepatol* 2015; Epub ahead of print [PMID: 25697628 DOI: 10.1016/j.cgh.2015.02.010]

14 **Hayashi I**, Yonezawa TM, Kuwabara T, Kudoh I. The study on staunch clip for the treatment by endoscopy. *Gastrointest Endosc* 1975; **17**: 92-101

15 **Qadeer MA**, Dumot JA, Vargo JJ, Lopez AR, Rice TW. Endoscopic clips for closing esophageal perforations: case report and pooled analysis. *Gastrointest Endosc* 2007; **66**: 605-611 [PMID: 17725956 DOI: 10.1016/j.gie.2007.03.1028]

16 **Minami S**, Gotoda T, Ono H, Oda I, Hamanaka H. Complete endoscopic closure of gastric perforation induced by endoscopic resection of early gastric cancer using endoclips can prevent surgery (with video). *Gastrointest Endosc* 2006; **63**: 596-601 [PMID: 16564858 DOI: 10.1016/j.gie.2005.07.029]

17 **Magdeburg R**, Collet P, Post S, Kaehler G. Endoclipping of iatrogenic colonic perforation to avoid surgery. *Surg Endosc* 2008; **22**: 1500-1504 [PMID: 18071812 DOI: 10.1007/s00464-007-9682-1]

18 **Singhal S**, Changela K, Papafragkakis H, Anand S, Krishnaiah M, Duddempudi S. Over the scope clip: technique and expanding clinical applications. *J Clin Gastroenterol* 2013; **47**: 749-756 [PMID: 23751852 DOI: 10.1097/MCG.0b013e318296ecb9]

19 **Banerjee S**, Barth BA, Bhat YM, Desilets DJ, Gottlieb KT, Maple JT, Pfau PR, Pleskow DK, Siddiqui UD, Tokar JL, Wang A, Song LM, Rodriguez SA. Endoscopic closure devices. *Gastrointest Endosc* 2012; **76**: 244-251 [PMID: 22658920 DOI: 10.1016/j.gie.2012.02.028]

20 **Felsher J**, Farres H, Chand B, Farver C, Ponsky J. Mucosal apposition in endoscopic suturing. *Gastrointest Endosc* 2003; **58**: 867-870 [PMID: 14652554]

21 **Voermans RP**, Le Moine O, von Renteln D, Ponchon T, Giovannini M, Bruno M, Weusten B, Seewald S, Costamagna G, Deprez P, Fockens P; CLIPPER Study. Efficacy of endoscopic closure of acute perforations of the gastrointestinal tract. *Clin Gastroenterol Hepatol* 2012; **10**: 603-608 [PMID: 22361277 DOI: 10.1016/j.cgh.2012.02.005]

22 **Law R**, Wong Kee Song LM, Irani S, Baron TH. Immediate technical and delayed clinical outcome of fistula closure using an over-the-scope clip device. *Surg Endosc* 2015; **29**: 1781-1786 [PMID: 25277480 DOI: 10.1007/s00464-014-3860-8]

23 **Guarner-Argente C**, Córdova H, Martínez-Pallí G, Navarro R, Cuatrecasas M, Rodríguez de Miguel C, Beltrán M, Lacy AM, Ginès A, Pellisé M, Llach J, Fernández-Esparrach G. Yes, we can: reliable colonic closure with the Padlock-G clip in a survival

porcine study (with video). *Gastrointest Endosc* 2010; **72**: 841-844 [PMID: 20883864 DOI: 10.1016/j.gie.2010.06.054]
24 **Spaun GO**, Martinec DV, Kennedy TJ, Swanström LL. Endoscopic closure of gastrogastric fistulas by using a tissue apposition system (with videos). *Gastrointest Endosc* 2010; **71**: 606-611 [PMID: 20018279 DOI: 10.1016/j.gie.2009.09.044]
25 **Fernandez-Esparrach G**, Lautz DB, Thompson CC. Endoscopic repair of gastrogastric fistula after Roux-en-Y gastric bypass: a less-invasive approach. *Surg Obes Relat Dis* 2010; **6**: 282-288 [PMID: 20510291 DOI: 10.1016/j.soard.2010.02.036]
26 **Kantsevoy SV**, Bitner M, Mitrakov AA, Thuluvath PJ. Endoscopic suturing closure of large mucosal defects after endoscopic submucosal dissection is technically feasible, fast, and eliminates the need for hospitalization (with videos). *Gastrointest Endosc* 2014; **79**: 503-507 [PMID: 24332082 DOI: 10.1016/j.gie.2013.10.051]
27 **Fujii LL**, Bonin EA, Baron TH, Gostout CJ, Wong Kee Song LM. Utility of an endoscopic suturing system for prevention of covered luminal stent migration in the upper GI tract. *Gastrointest Endosc* 2013; **78**: 787-793 [PMID: 23871095 DOI: 10.1016/j.gie.2013.06.014]
28 **Wilson JL**, Louie BE, Farivar AS, Vallières E, Aye RW. Fully covered self-expanding metal stents are effective for benign esophagogastric disruptions and strictures. *J Gastrointest Surg* 2013; **17**: 2045-2050 [PMID: 24065368 DOI: 10.1007/s11605-013-2357-4]
29 **El Hajj II**, Imperiale TF, Rex DK, Ballard D, Kesler KA, Birdas TJ, Fatima H, Kessler WR, DeWitt JM. Treatment of esophageal leaks, fistulae, and perforations with temporary stents: evaluation of efficacy, adverse events, and factors associated with successful outcomes. *Gastrointest Endosc* 2014; **79**: 589-598 [PMID: 24125513 DOI: 10.1016/j.gie.2013.08.039]
30 **Moyes LH**, Mackay CK, Forshaw MJ. The use of self-expanding plastic stents in the management of oesophageal leaks and spontaneous oesophageal perforations. *Diagn Ther Endosc* 2011; **2011**: 418103 [PMID: 21785560 DOI: 10.1155/2011/418103]
31 **van Boeckel PG**, Dua KS, Weusten BL, Schmits RJ, Surapaneni N, Timmer R, Vleggaar FP, Siersema PD. Fully covered self-expandable metal stents (SEMS), partially covered SEMS and self-expandable plastic stents for the treatment of benign esophageal ruptures and anastomotic leaks. *BMC Gastroenterol* 2012; **12**: 19 [PMID: 22375711 DOI: 10.1186/1471-230X-12-19]
32 **Freeman RK**, Ascioti AJ, Giannini T, Mahidhara RJ. Analysis of unsuccessful esophageal stent placements for esophageal perforation, fistula, or anastomotic leak. *Ann Thorac Surg* 2012; **94**: 959-964; discussion 964-965 [PMID: 22795060 DOI: 10.1016/j.athoracsur.2012.05.047]
33 **Langer FB**, Wenzl E, Prager G, Salat A, Miholic J, Mang T, Zacherl J. Management of postoperative esophageal leaks with the Polyflex self-expanding covered plastic stent. *Ann Thorac Surg* 2005; **79**: 398-403; discussion 404 [PMID: 15680802 DOI: 10.1016/j.athoracsur.2004.07.006]
34 **Schubert D**, Scheidbach H, Kuhn R, Wex C, Weiss G, Eder F, Lippert H, Pross M. Endoscopic treatment of thoracic esophageal anastomotic leaks by using silicone-covered, self-expanding polyester stents. *Gastrointest Endosc* 2005; **61**: 891-896 [PMID: 15933696]
35 **Dai YY**, Gretschel S, Dudeck O, Rau B, Schlag PM, Hünerbein M. Treatment of oesophageal anastomotic leaks by temporary stenting with self-expanding plastic stents. *Br J Surg* 2009; **96**: 887-891 [PMID: 19591167 DOI: 10.1002/bjs.6648]
36 **Watson A**. Self-expanding metal oesophageal endoprostheses: which is best? *Eur J Gastroenterol Hepatol* 1998; **10**: 363-365 [PMID: 9619379]
37 **Dumonceau JM**, Cremer M, Lalmand B, Devière J. Esophageal fistula sealing: choice of stent, practical management, and cost. *Gastrointest Endosc* 1999; **49**: 70-78 [PMID: 9869726]
38 **Swinnen J**, Eisendrath P, Rigaux J, Kahegeshe L, Lemmers A, Le Moine O, Devière J. Self-expandable metal stents for the treatment of benign upper GI leaks and perforations. *Gastrointest Endosc* 2011; **73**: 890-899 [PMID: 21521563 DOI: 10.1016/j.gie.2010.12.019]
39 **van Heel NC**, Haringsma J, Spaander MC, Bruno MJ, Kuipers EJ. Short-term esophageal stenting in the management of benign perforations. *Am J Gastroenterol* 2010; **105**: 1515-1520 [PMID: 20234349 DOI: 10.1038/ajg.2010.104]
40 **Eleftheriadis E**, Tzartinoglou E, Kotzampassi K, Aletras H. Early endoscopic fibrin sealing of high-output postoperative enterocutaneous fistulas. *Acta Chir Scand* 1990; **156**: 625-628 [PMID: 2264442]
41 **Böhm G**, Mossdorf A, Klink C, Klinge U, Jansen M, Schumpelick V, Truong S. Treatment algorithm for postoperative upper gastrointestinal fistulas and leaks using combined vicryl plug and fibrin glue. *Endoscopy* 2010; **42**: 599-602 [PMID: 20432210 DOI: 10.1055/s-0029-1244165]
42 **Pramateftakis MG**, Vrakas G, Kanellos I, Mantzoros I, Angelopoulos S, Eleftheriades E, Lazarides C. Endoscopic application of n-butyl-2-cyanoacrylate on esophagojejunal anastomotic leak: a case report. *J Med Case Rep* 2011; **5**: 96 [PMID: 21392389 DOI: 10.1186/1752-1947-5-96]
43 **Lippert E**, Klebl FH, Schweller F, Ott C, Gelbmann CM, Schölmerich J, Endlicher E, Kullmann F. Fibrin glue in the endoscopic treatment of fistulae and anastomotic leakages of the gastrointestinal tract. *Int J Colorectal Dis* 2011; **26**: 303-311 [PMID: 21190028 DOI: 10.1007/s00384-010-1104-5]
44 **Rábago LR**, Ventosa N, Castro JL, Marco J, Herrera N, Gea F. Endoscopic treatment of postoperative fistulas resistant to conservative management using biological fibrin glue. *Endoscopy* 2002; **34**: 632-638 [PMID: 12173084 DOI: 10.1055/s-2002-33237]
45 **Victorzon M**, Victorzon S, Peromaa-Haavisto P. Fibrin glue and stents in the treatment of gastrojejunal leaks after laparoscopic gastric bypass: a case series and review of the literature. *Obes Surg* 2013; **23**: 1692-1697 [PMID: 23912265 DOI: 10.1007/s11695-013-1048-2]
46 **Lee S**, Ahn JY, Jung HY, Lee JH, Choi KS, Kim do H, Choi KD, Song HJ, Lee GH, Kim JH, Kim BS, Yook JH, Oh ST, Kim BS, Han S. Clinical outcomes of endoscopic and surgical management for postoperative upper gastrointestinal leakage. *Surg Endosc* 2013; **27**: 4232-4240 [PMID: 23783553 DOI: 10.1007/s00464-013-3028-y]
47 **Han JH**, Lee TH, Jung Y, Lee SH, Kim H, Han HS, Chae H, Park SM, Youn S. Rescue endoscopic band ligation of iatrogenic gastric perforations following failed endoclip closure. *World J Gastroenterol* 2013; **19**: 955-959 [PMID: 23429885 DOI: 10.3748/wjg.v19.i6.955]
48 **Han JH**, Park S, Youn S. Endoscopic closure of colon perforation with band ligation; salvage technique after endoclip failure. *Clin Gastroenterol Hepatol* 2011; **9**: e54-e55 [PMID: 21195795 DOI: 10.1016/j.cgh.2010.12.026]
49 **Kumbhari V**, Azola A, Okolo PI, Hughes A, Saxena P, Bapat V, Storm AC, Yung R, Khashab MA. Closure of a chronic tracheoesophageal fistula by use of a cardiac septal occluder. *Gastrointest Endosc* 2014; **80**: 332 [PMID: 25034840 DOI: 10.1016/j.gie.2014.05.335]
50 **Kumbhari V**, Storm AC, Saxena P, Okolo PI. Closure of a persistent gastric leak using a cardiac septal occluder. *Endoscopy* 2014; **46** Suppl 1 UCTN: E147-E148 [PMID: 24756267 DOI: 10.1055/s-0034-1364948]
51 **Melmed GY**, Kar S, Geft I, Lo SK. A new method for endoscopic closure of gastrocolonic fistula: novel application of a cardiac septal defect closure device (with video). *Gastrointest Endosc* 2009; **70**: 542-545 [PMID: 19699982 DOI: 10.1016/j.gie.2009.03.027]
52 **Arezzo A**, Verra M, Passera R, Bullano A, Rapetti L, Morino M. Long-term efficacy of endoscopic vacuum therapy for the treatment of colorectal anastomotic leaks. *Dig Liver Dis* 2015; **47**: 342-345 [PMID: 25563812 DOI: 10.1016/j.dld.2014.12.003]
53 **Brangewitz M**, Voigtländer T, Helfritz FA, Lankisch TO, Winkler M, Klempnauer J, Manns MP, Schneider AS, Wedemeyer J.

Endoscopic closure of esophageal intrathoracic leaks: stent versus endoscopic vacuum-assisted closure, a retrospective analysis. *Endoscopy* 2013; **45**: 433-438 [PMID: 23733727 DOI: 10.1055/s-0032-1326435]

54 **Stavropoulos SN**, Modayil R, Friedel D. Closing perforations and postperforation management in endoscopy: esophagus and stomach. *Gastrointest Endosc Clin N Am* 2015; **25**: 29-45 [PMID: 25442956 DOI: 10.1016/j.giec.2014.09.008]

**P- Reviewer:** Tan HJ **S- Editor**: Ma YJ **L- Editor**: A
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ISSN 1007-9327

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