

## Review article

## Endoscopic repair of post-surgical gastrointestinal complications

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## ABSTRACT

Complications following gastrointestinal surgery may require re-intervention, can lead to prolonged hospitalization, and significantly increase health costs. Some complications, such as anastomotic leakage, fistula, and stricture require a multidisciplinary approach. Therapeutic endoscopy may play a pivotal role in these conditions, allowing minimally invasive treatment. Different endoscopic approaches, including fibrin glue injection, endoclips, self-expanding stents, and endoscopic vacuum-assisted devices have been introduced for both anastomotic leakage and fistula treatment. Similarly endoscopic treatments, such as endoscopic dilation, incisional therapy, and self-expanding stents have been used for anastomotic strictures. All these techniques can be safely performed by skilled endoscopists, and may achieve a high technical success rate in both the upper and lower gastrointestinal tract. Here we will review the endoscopic management of post-surgical complications; these techniques should be considered as first-line approach in selected patients, allowing to avoid re-operation, reduce hospital stay, and decrease costs.

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## 1. Introduction

Despite continuous improvement in surgical procedures, complications following gastrointestinal surgery may represent a dreadful event. Post-surgical complications lead to prolonged hospitalization, often require one or more re-operations, and significantly increase health costs. Some complications, such as anastomotic leakage, fistula, stricture, and bleeding require a multidisciplinary approach. Therapeutic endoscopy may play a pivotal role in these conditions, allowing to resolve the complication with minimally invasive treatment.

In this article we will review the available data from the literature to identify the most appropriate endoscopic approaches for different post-surgical complications in the gastrointestinal tract.

## 2. Anastomotic leaks and fistulas

Anastomotic leakage is one of the most serious complications of gastrointestinal surgery. The reported incidence of gastrointestinal

anastomotic leaks widely ranges from 5% to 30% for oesophageal anastomoses [1–3], and from 5% to 15% for rectal resections [4–6]. Early anastomotic leaks occur in the first post-operative week, and generally require re-intervention. They are associated with a relatively high rate of both morbidity and mortality, and a further surgical procedure may be required to restore intestinal continuity [7]. Absolute indications for surgery are peritonitis or mediastinitis, persistent severe sepsis, and a large defect involving >50% of the anastomotic circumference [8].

A substantial number of leaks and fistulas occur later in the post-operative period, often with subtle clinical manifestations. In this setting, there is scarce consensus on the most appropriate treatment option.

Selected patients can be successfully treated by conservative approaches, including parenteral nutrition, intravenous broad spectrum antibiotics, and minimal surgical drainage [7]. In the last decade, different endoscopic approaches have been proposed for late gastrointestinal anastomotic leaks to obtain a less invasive, non-surgical repair of lesions. These therapeutic procedures include fibrin glue injection, positioning of endoclips, suturing devices, stent insertion and endoluminal vacuum devices. Before treatment, endoscopic debridement is generally required, with local removal of tissue remnants and elimination of pus within and around the necrotic cavity, by using grasping tools and endoluminal suction. In addition, the cavity should be rinsed with antiseptic

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fluid and hydrogen peroxide [8], and complete drainage of fluid collections in the mediastinum, pleural or peritoneal cavity is a fundamental prerequisite for a successful endoscopic procedure.

### 2.1. Fibrin glue

Fibrin glue (Tissucol, Baxter, Germany) consists of two frozen components, glue and thrombin, applied by a double injection system. The mixture of both components results in a coagulum of fibrin within a short time. In our experience, fibrin injection was able to seal only very small leaks (<5 mm diameter) not connected to cavities, and in the absence of abscesses. Although this is a relatively easy procedure for both anastomotic leak and fistula management, several reports demonstrated variable efficacy. Moreover, there are only few large patient series in this setting [9]. In a retrospective analysis of 52 patients with fistulas and anastomotic leakages in the gastrointestinal tract, endoscopic treatment was successful in 56% of cases, though in cases with fibrin glue application only, success rate was 37%. Treatment success with further endoscopic procedures was observed in 19% of cases, whilst a surgical intervention was required in 23% of patients, with persistence of lesion in the remaining 21% of cases. Eleven (21.1%) patients died during hospitalization, although only 2 deaths were potentially associated with treatment [10].

Some favourable results have also been reported with a combination of fibrin glue and Vicryl plug [11]. In a recent study [12], postoperative upper gastrointestinal fistulas or anastomotic leaks were successfully managed by endoscopic insertion of Vicryl mesh with fibrin glue, and was associated with low morbidity. Of note, this endoscopic treatment was successful in 13 (86.7%) out of 15 patients, achieving complete healing of the anastomotic leak or fistula after one to four treatment sessions.

### 2.2. Endoclips

Standard clips are widely used in endoscopy, generally for mechanical haemostasis following post-procedural bleeding. Moreover, their important role for endoscopic closure of small perforations – i.e. immediately following polypectomy or mucosectomy – is widely recognized. However, data on the efficacy of endoclips for the treatment of post-surgical leaks and fistulas are anecdotal [13,14], the low closure strength limiting their use in scarred and hardened post-surgical tissues. To overcome such a limitation, a new over-the-scope clip system, the OTSC<sup>R</sup> (Ovesco Endoscopy, Tübingen, Germany), has been recently developed [15], consisting of a large Nitinol clip, loaded at the tip of the endoscope. Such a device allows to capture a large amount of tissue and to powerfully compress and close up the margins of a lesion favouring its healing. It allows to close lesions up to 20 mm in diameter, whilst larger leaks are less amenable to treatment, although

application of two adjacent OTSCs may be attempted. Endoscopic closure of post-surgical leaks and fistulas with the OTSC application is indicated for both early and late complications (Fig. 1). A recent study [16] evaluated the efficacy of the OTSC for treatment of colorectal post-surgical leaks and fistulas, enrolling patients with an orifice <15 mm in diameter without either luminal stenosis or extraluminal abscesses. The overall success rate was 86% (87% in early and 83% in late post-surgical leaks and fistulas, respectively), and surgery was required in only 1 case. These results confirmed our previous experience [17], where endoscopic OTSC positioning was successful in 11 out of 12 (91.7%) patients with a post-surgical fistula with a diameter ranging from 6 to 25 mm. Others studies reported a lower efficacy for treatment of chronic fistulas [18]. In a recent case series including 9 patients [19], the overall success rate of OTSC application was 55%; the procedure was successful in 3 out of 5 patients with a leak, in 1 out of 3 patients with a fistula, and in the only patient with a perforation, whilst in the remaining 4 patients it was impossible to correctly deploy the OTSC due to insufficient grasping of the tissue caused by fibrosis at the edges of the lesion.

### 2.3. Self-expanding stents

Temporary placement of a fully (FSEMS) or partially (PSEMS) covered self-expanding metal stent or a self-expanding plastic stent (SEPS) is an effective treatment modality to seal anastomotic leaks after gastro-oesophageal and bariatric surgery [20–23]. The stent provides a physical barrier between the leak and the luminal contents, allowing healing of the wall lesions while providing enteral nutrition (Fig. 2). The main drawbacks of stent placement include either stent migration and tissue in- or overgrowth, particularly when the stents are positioned for a long period. Tissue overgrowth, mostly occurring on the uncovered part of PSEMS, is caused by a local fibrotic reaction and/or the proliferation of granulation tissue that can be clinically manifest as early as 2 weeks after stent placement, also causing difficulties in stent removal [24]. On the other hand, the hyperplastic tissue growing into the stent meshes may reduce the risk of stent migration, providing a better watertight barrier to saliva and fluids, favouring fistula healing [25]. The clinical efficacy and safety of temporary stent placement in oesophageal anastomotic leaks and in leaks following bariatric surgery has been evaluated in two recent reviews [24,26]. Overall, stent placement yielded clinical success in 85% out of 267 patients treated for oesophageal anastomotic leaks, with no differences among the different stents used [24]. The mean healing time was 7 weeks (range: 6–8 weeks). Stent migration occurred in 25% of patients, and it was observed most commonly with FSEMS as compared to PSEMS, whilst tissue in- or over-growth was greater for the latter, causing removal difficulties in some cases. Similar results were reported in patients with leaks following bariatric surgery

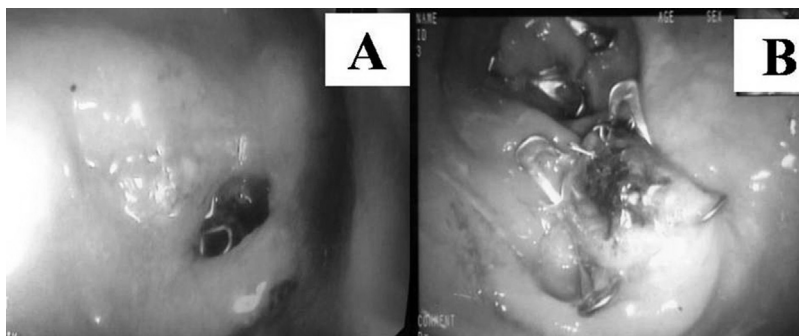
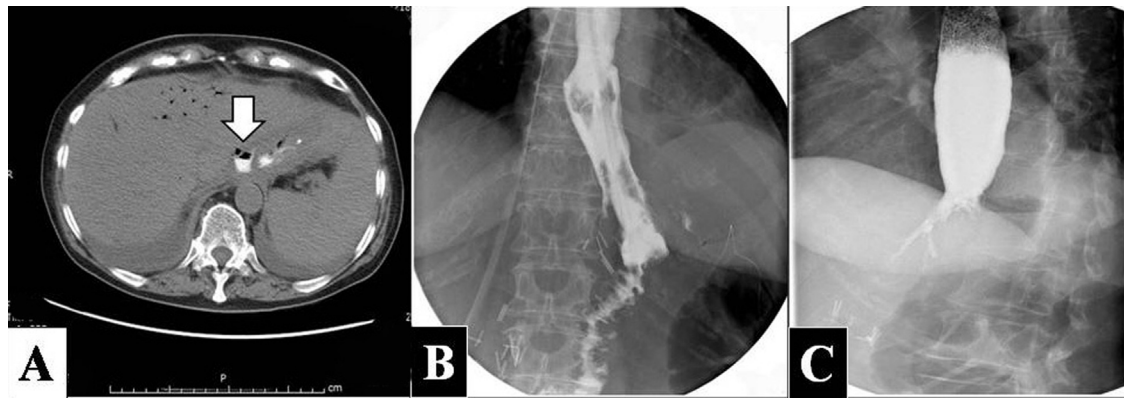


Fig. 1. Post-surgical anastomotic fistula in a patient who underwent to video-laparoscopic left-colectomy due to local advanced colonic neoplasia (A). Closure with over-the-scope clip (OTSC<sup>R</sup>) positioning (B).



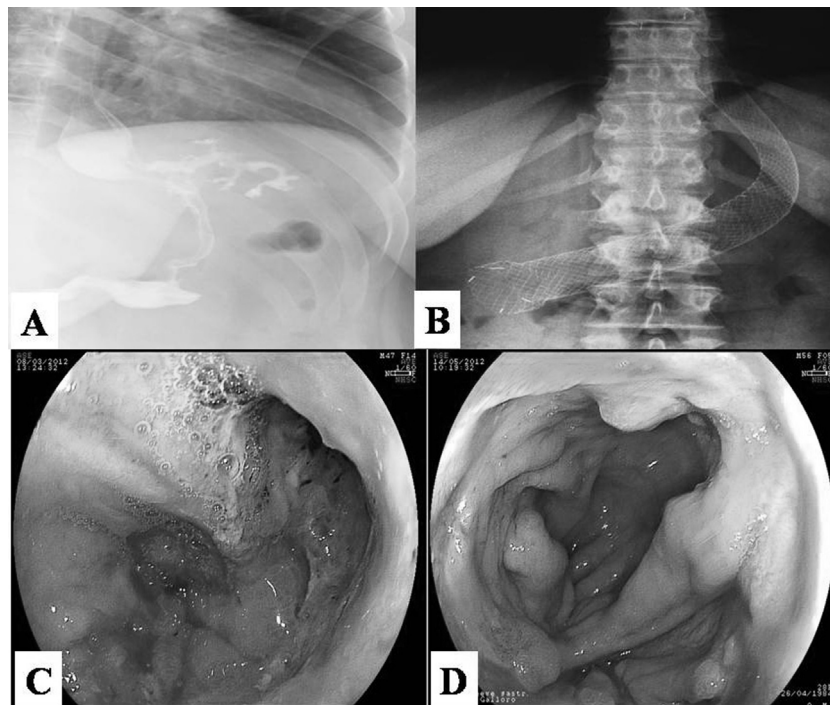
**Fig. 2.** Post-surgical anastomotic fistula in a patient who underwent to total gastrectomy due to local advanced gastric neoplasia (A). Closure with self-expanding metal stent (SEMS) positioning across the fistula tract (B). Healing of the fistula at 2 months radiological control and SEMS removal (C).

and managed with self-expandable stents [26]. Six to eight weeks has been suggested as the optimal time for stent removal (Fig. 3). Indeed, a shorter interval may lead to incomplete closure, whilst a longer interval may cause either stent migration or excessive mucosal overgrowth within the stent with subsequent dysphagia or difficulty in stent extraction. In the latter case, a useful technique to remove an embedded stent is to place a fully covered stent of the same diameter inside the first one. Such a procedure causes necrosis of the hyperplastic tissue and both stents can be more easily removed after 7–14 days [27]. Although stent placement has been proposed for leaks involving <70% of the circumference [28], complete closure has been achieved in a patient with complete dehiscence [29]. Of note, prompt stent placement for the closure of a leak or a perforation is of paramount importance, an early approach leading to a success rate of 100% as compared with 50% when stent insertion is carried out more than one month after perforation [25].

Minor complications associated with stent placement – particularly dysphagia – are reported in about 20% of patients, but these may be easily managed by either stent removal or balloon dilation [24–26]. Major complications (bleeding, perforation and tracheal compression) are rare and related to specific conditions [24–26]. In some cases, an oesophageal stricture occurs as a long-term complication following stent removal, requiring one or more balloon dilations [25]. To date, the experience with rectal stents for treatment of anastomotic leaks is limited [8].

#### 2.4. Endoscopic vacuum-assisted devices

The endoscopic vacuum-assisted closure (VAC) system device (Endo-SPONGE, B. Braun Medical Ltd) is a method first introduced in the 1990s. Basically, the system is based on negative pressure applied to the wound with a tube inserted in a polyurethane foam, resulting in arteriolar dilation, promotion of granulation tissue and



**Fig. 3.** Gastrographin® swallow shows a gastric staple-line leak with extravasation of contrast medium and a substenosis in the middle part of the sleeve (A). A stent (Megastent®, Taewoong Medical) is placed to treat both leak and stenosis (B). Endoscopic control after stent removal: whitish granulation tissue fills the leak hole (C). Endoscopic follow-up two month after stent removal shows complete healing of the leak, with a wide flat scar (D).

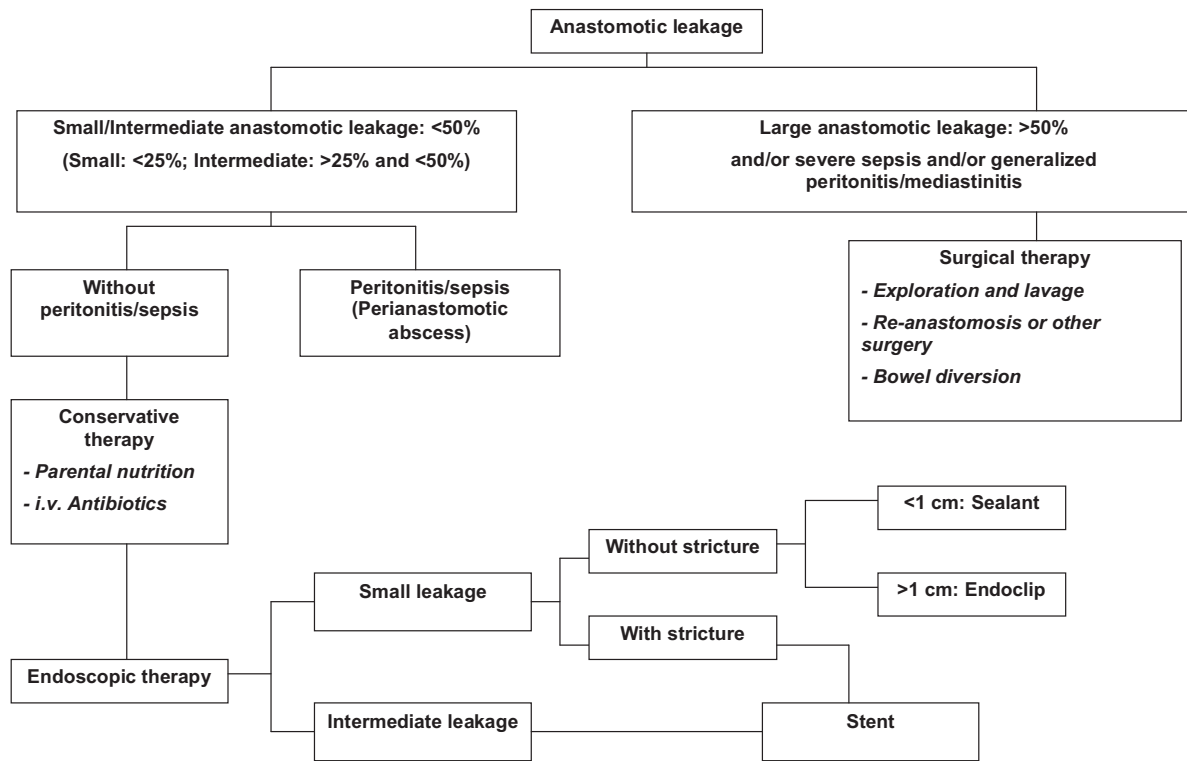


Fig. 4. Flow-chart for anastomotic leakage.

subsequent wound closure [30]. This method is generally applied to large leaks in both thoracic and rectal anastomoses that may be endoscopically explored, but few data are available in literature [31,32]. After endoscopic debridement of the wound cavity, a sponge is trimmed to the specific size as estimated by the endoscopist, fixed at the distal end of the tube and introduced into the necrotic cavity, and then continuous suction is applied. The procedure is repeated twice a week. Wedemeyer et al. [33] first reported the successful application of VAC therapy in two cases of intrathoracic anastomotic leaks. After a median of 15 days and 5 endoscopic sessions, closure of the wound cavities was achieved in both cases. In another study, complete healing of rectal anastomotic leaks was obtained in 28 (96.6%) out of 29 patients after vacuum therapy [32]. However, bowel diversion cannot be avoided by vacuum-assisted treatment of rectal leaks, because the sponge will be obstructed by stool impaction. Other limitations include the need for repeated endoscopic interventions, continuous suction, and patient discomfort. On the other hand, the endoscopic VAC system allows a regular visualization of the leak, debridement of the infected cavity, and control of septic foci [8,33]. An algorithm for post-anastomotic leak and fistula management is provided in Fig. 4.

### 3. Anastomotic strictures

The incidence of anastomotic stricture following gastrointestinal surgery is variable. Indeed, a stricture in the oesophago-gastric anastomosis occurs in 5–46% of cases after oesophageal resection, while its incidence varies from 22% to 30% following colectomy [34–36]. Postoperative complications, such as anastomotic leakage, fistulas, or ischaemic injury contribute to anastomotic stricture formation [35]. Anastomotic strictures are generally short but tenacious, sometimes angulated, irregular or have a severely narrowed diameter.

#### 3.1. Endoscopic dilation

Commonly, endoscopic dilation therapy is the first-line treatment option for anastomotic strictures. The currently used dilators can be either mechanical (Savary-Gilliard bougies) or balloon-type. Mechanical dilators exert longitudinal and radial force on the stricture, while balloon dilators only deliver radial force, however the latter can be passed through-the-scope allowing direct endoscopic control of the procedure. Endoscopic balloon dilation can be carried out by two methods: (a) out-the-scope (OTS) or over-the-wire (OTW) balloons of 35 mm diameter, and (b) through-the-scope (TTS) balloons with a smaller diameter (18 mm). No clear advantage has been demonstrated between balloon or bougie dilation [37,38]. There is only one prospective trial comparing OTW versus TTS balloon dilation in lower GI tract strictures, showing a similar efficacy. However, fewer endoscopic sessions were needed to achieve stricture resolution when OTW was used [39]. Generally, 1–3 dilations are needed in both upper and lower GI post-surgical strictures with a success rate ranging from 59% to 100% [40–46]. However, 3 or more dilation sessions are needed in up to 40% of patients to achieve an adequate result [42–46]. Furthermore, some complex strictures may require several sessions. Despite in these cases re-operation should be considered, some patients unfit for surgery may benefit from long-term continuous balloon dilations [46].

The most frequent complications include haemorrhage, bacteraemia, and perforation, the last occurring in 0.1–0.4% of cases [45,47]. To minimize the risk of perforation, the maximum dilation diameter should not be increased by more than 3 mm per session [42]. In order to prevent stricture recurrence, injection of steroids into the stricture before dilation has been tested in various studies aiming to inhibit the inflammatory response and to reduce collagen formation [48,49]. A randomized study [50] found that a combination of intra-lesional injection of 0.5 ml triamcinolone



(40 mg/ml) plus dilation associated with gastric acid suppression reduced the number of dilation sessions and increased the average time between sessions. However, this study was limited to peptic strictures.

### 3.2. Incisional therapy

Undeniably, there is a subgroup of strictures that are refractory or recurrent after dilation. A stricture is defined refractory when it is not possible to obtain a diameter of 14 mm after 5 dilation sessions carried out at 2-week intervals [51]. A recurrent stricture is diagnosed when it is impossible to maintain an adequate luminal diameter for 4 weeks after the target diameter of 14 mm has been achieved [51]. Since it is very difficult to treat refractory or recurrent strictures, an alternative approach is needed. The use of incisional therapy and temporary stent placement may represent a valid therapeutic approach in these selected cases. Incisional therapy consists in radial incisions on the stenotic ring, under direct endoscopic vision, with either sphincterotome or a needle knife catheter. The number, length and depth of the cut is gauged by the operator according to the length of the stricture and its calibre. The procedure is terminated when the endoscope can easily be passed [52–54]. Some variants are reported in literature, such as incisional therapy plus balloon dilation and incisional therapy using a polypectomy snare and additional argon plasma coagulation [55,56]. In a recent study [57], 24 patients with oesophageal anastomotic strictures were treated with endoscopic incisional therapy as first-line treatment. Notably, as many as 87.5% of patients were dysphagia-free at 24 months' follow-up after a single endoscopic session. A randomized trial found no significant difference in the success rate between incisional therapy and dilation therapy with Savary-Gilliard balloons in 62 patients with a primary anastomotic stricture after oesophagectomy [58]. Based on the available data, incisional therapy is a safe method in experienced hands, and particularly effective in 'ring type' strictures (<10 mm).

### 3.3. Self-expanding stents

In the past few years, temporary stent placement has been increasingly used for refractory or recurrent anastomotic strictures [59]. The purpose is to apply a prolonged radial force to the stenosis, which reduces the risk of recurrent stricture formation. Stent types that have been used include PSEMS, FSEMS, and, more recently, biodegradable stents [60].

The same drawbacks of stent placement for anastomotic leakage are also reported in this setting. Data on the use of SEMS in benign oesophageal anastomotic strictures are mostly available as case series and case reports. The most frequent complications include high migration rates, bleeding, fistula, perforation, and stricture recurrence. The occurrence of tissue in- and over-growth causing recurrent dysphagia was observed in >15% of patients treated with PSEMS, while early migration (<4 weeks) was found in 24% of patients treated with plastic stents for benign oesophageal strictures of variable causes [46,61]. For colonic stenting, there are few and controversial data on the use of stents in benign colorectal diseases, as the application of covered stents in benign colorectal strictures is uncommon and there are only few case series with limited number of patients or single case reports [63]. Studies have shown a technical success rate of 85–100% and a complication rate up to 30% [64]. Major complications reported in the literature include perforation, secondary fistula formation, and bleeding. The most frequent complication is stent migration, although conflicting data have been reported with migration rate in benign colorectal disease widely ranging from 5% and 24% [65,66]. Several techniques have been proposed to reduce the risk of stent migration. Recently, it has been shown that anchoring the upper flare of a fully covered

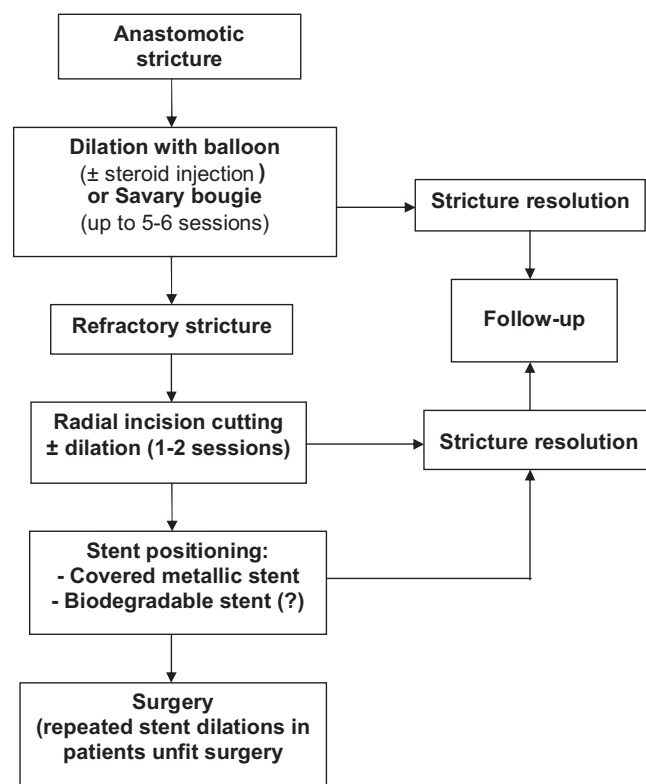


Fig. 5. Flow-chart for anastomotic stricture.

SEMS with endoscopic clips significantly reduces the risk of stent migration [62]. Very proximal or distal localization of the stricture or distal localization as well as angulated and narrowed strictures are not suitable for stent application. Only a few data are available on the use of stents in post-surgical lower GI tract strictures. In a recent study, a success rate of 50% and 36% at 12-month and 37-month follow-up respectively was reported, with a migration rate of 21%. A similar success rate (63%) was achieved in 8 patients with lower anastomotic strictures at 20-month follow-up, with a single case of stent migration [67].

Biodegradable stents represent a desirable and promising technical innovation for both anastomotic leakage and stricture management. The biodegradable stents in polydioxanone currently available are able to dissolve and be absorbed within 3 months after placement. Repici et al. reported a preliminary experience on refractory benign oesophageal strictures showing a clinical success in 45% of patients at 6-month follow-up, with stent migration occurring in 10% of cases [68]. Larger studies with longer follow-up are needed to evaluate their role in anastomotic leakage and stricture management. An algorithm for post-anastomotic stricture management is provided in Fig. 5.

## 4. Conclusions

All endoscopic techniques can be safely used with a high technical success rate for different post-surgical complications in both upper and lower gastrointestinal tract. These procedures should be performed by skilled endoscopists, generally in tertiary centres, due to the learning curve. Indeed, these endoscopic approaches usually have a high complexity, and operator expertise reduces the occurrence of complications, as well as of technical and clinical failures. Although data on OTSC and vicryl plus tissue glue combination are still scarce, the available data suggest that endoscopic OTSC closure of a post-surgical leaks and fistulas in gastrointestinal tract is safe, and achieves a high success rate in both acute

and chronic cases, including recto-vaginal and percutaneous fistulas. Moreover, OTSCs seem to be more effective than traditional endoclip, vicryl and tissucol used alone. Treatment of gastrointestinal leaks with stents has considerably increased over the last decade, largely due to the availability of easily removable SEPS and SEMS, even though high stent migration rate still limits their efficacy. Thus, more clinical experience and newer stent technologies are needed to delineate the optimal conditions for SEMS placement and to improve clinical outcomes. Endoscopic management of post-surgical complications should be considered as the first-line approach for selected patients. Indeed, such an approach may avoid a re-operation, reduce the hospital stay, and decrease costs.

#### Conflict of interest statement

None declared.

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