Chapter

Endoscopic Management of Leaks and Fistula in Gastrointestinal Tract

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Abstract

Leak, perforation, and fistula are the three main types of transmural defects in the gastrointestinal (GI) tract. Evolution of interventional endoscopic\ techniques as well as widespread use of laparoscopic and bariatric surgical procedures has contributed to the rising incidence of GI defects. The basic principle for management of leaks and fistula is to provide a barricade to the flow of luminal contents across the defect. This can be achieved either by a surgical or endoscopic method. Minimally invasive closure techniques such as clipping, stenting, suturing, and endoscopic vacuum therapy have revolutionized the management of GI defects. This chapter deals with endoscopic techniques and their present status in the management of luminal GI leaks and fistula.

Keywords: leaks, fistula, endoscopic management, through-the-scope clip, over-the-scope clip, suture, sealants, stents

1. Introduction

Leak, perforation, and fistula are the three main types of transmural defects in the gastrointestinal (GI) tract. Evolution of interventional endoscopic techniques as well as widespread use of laparoscopic and bariatric surgical procedures has contributed to the rising incidence of GI defects [1–3]. Some of these defects may be serious and life-threatening and require emergency interventions. Successful endoscopic closure of gastrointestinal (GI) leaks and fistulae has shifted the management from surgery to a more conservative endoscopic approach.

Minimally invasive closure techniques such as clipping, stenting, suturing, and endoscopic vacuum therapy have revolutionized the management of GI defects [4–6]. These techniques provide a more affordable alternative to surgery with less morbidity and hospital stay. Innovations in interventional endoscopy like over-the-scope clips (OTSCs) have shown promising results in closing GI defects with good safety and efficacy [7]. This chapter deals with endoscopic techniques and their present status in the management of luminal GI leaks and fistula. Pancreatic and biliary leaks, which have somewhat different approaches, are not covered in this review.

- Iatrogenic:
  - Diagnostic endoscopy
  - EVL
  - Dilatation
  - ESD/EMR
  - POEM
  - Trauma
  - PEG and feeding tubes
  - Post-stenting
  - Postsurgical anastomotic dehiscence
- Spontaneous
  - Boerhaave's
- Foreign body
- Tuberculosis
- Crohn's
- Malignancy

EVL: endoscopic variceal ligation; ESD: endoscopic submucosal dissection; EMR: endoscopic mucosal resection; POEM: peroral endoscopic myotomy; PEG: percutaneous endoscopic gastrostomy.

Table 1.
Etiology of GI leaks and fistula.

2. Definitions and etiology

While the terms perforation, leak, and fistula are often used interchangeably, they in strict terms can be defined as follows:

Perforation—Acute full thickness defect in GI tract [8].
Leak—Disruption at a surgical anastomosis resulting in a fluid collection [9].
Fistula—Abnormal communication between two epithelialized surfaces [9].

Perforation occurs spontaneously or more commonly after an injury, iatrogenic or traumatic [8]. GI leaks are most commonly seen at the site of surgical anastomosis and depending on the site of anastomosis can be either intra-peritoneal or extra-peritoneal. GI fistula can be internal (between GI organs) or external (between GI tract and body surface). **Table 1** enumerates the various etiologies of GI leaks and fistula [10–18].

3. Approach to management

The basic principle for management of leaks and fistula is to provide a barricade to the flow of luminal contents across the defect. This can be achieved either by a surgical or endoscopic method. Regardless of the chosen technique, the management requires a multi-disciplinary approach. The general measures which must be involved include: bowel rest, intravenous fluid as clinically indicated, appropriate antibiotic coverage, maintenance of nutrition, drainage of associated collection, and close hemodynamic monitoring. Proton pump inhibitors should be added in upper GI tract leaks. Contrast radiological studies help in defining and delineating the site of leak. European Society of Gastrointestinal Endoscopy (ESGE) position statement [19] recommends that endoscopic closure should be considered depending on the type of perforation, its size, and the endoscopist expertise available at the center.

Different techniques are combined together for successful closure of leaks and fistulae in many cases. For example, an esophagogastric fistula may be initially

Diversion	Closure
• Luminal stents - Covered self-expandable stents - Plastic stents	• Endoclips - Through-the-scope clips - Over-the-scope clips
	• Injection of fibrin glue/cyanoacrylate
	• Suture devices

Table 2.
Endoscopic modalities for management of leaks/fistula.

managed with fibrin glue injection and endoscopic clip closure. An esophageal stent should be placed across the fistula site following the closure for diversion of the luminal stream. **Table 2** (adapted [20]) lists the different modalities which can be used for endoscopic management of GI leaks and fistula.

3.1 Luminal stenting

Stent placement for managing leaks and fistulae has been commonly used in the upper GI tract. The basic purpose of stenting is to cover the luminal disruption and divert the GI secretions/GI content away from the point of defect. This provides a temporary barricade to the region and prevents influx of enzymatic fluid through the opening. Therefore, preferred stents are the covered one's (at least partially covered) which can be removed once the defect is sealed. **Figure 1** (adapted [20]) shows the different stents available to close GI defects.

All of these stents are self-expanding metallic stent except for a single design of plastic stent (Polyflex, Boston, MA, USA). Fully covered stents are generally preferred in benign conditions as they can be removed easily later on. **Figure 2** (adapted [20]) shows a patient with leak following gastrojejunostomy managed successfully with a covered stent placed across the leak [20].

Table 3 compares the different studies on esophageal stent placement for management of leaks/fistulae [21–23]. The overall stent migration rate was between 28 and 33% and is one of the major issues with use of covered stent for closing of the GI defects. Large diameter stents (Mega stents by Niti or Danis stents by Ella;

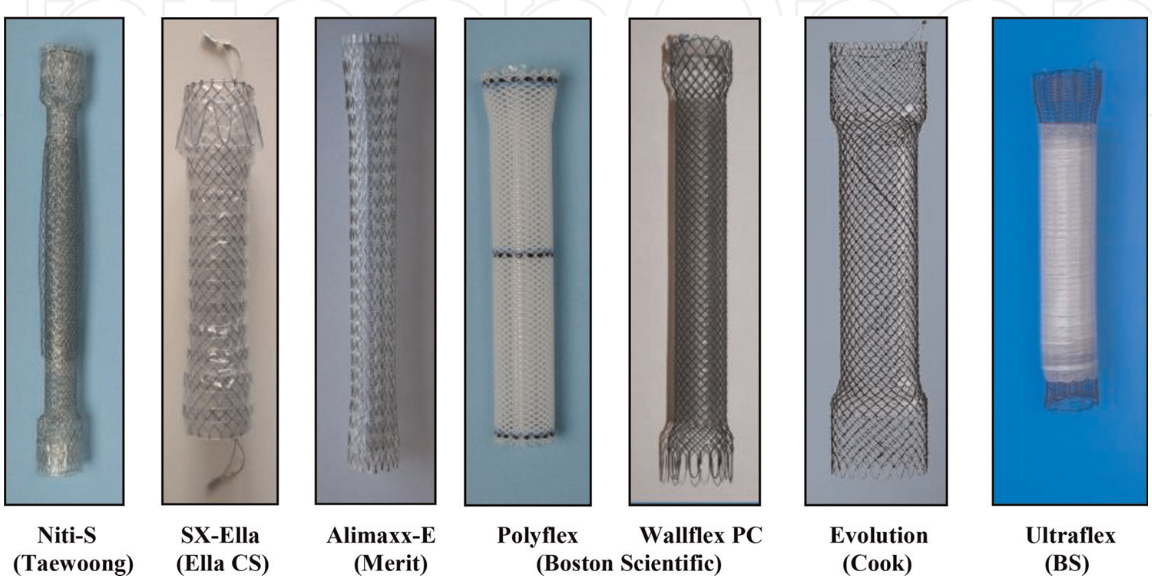

Figure 1.
Stents for GI leaks and fistula.

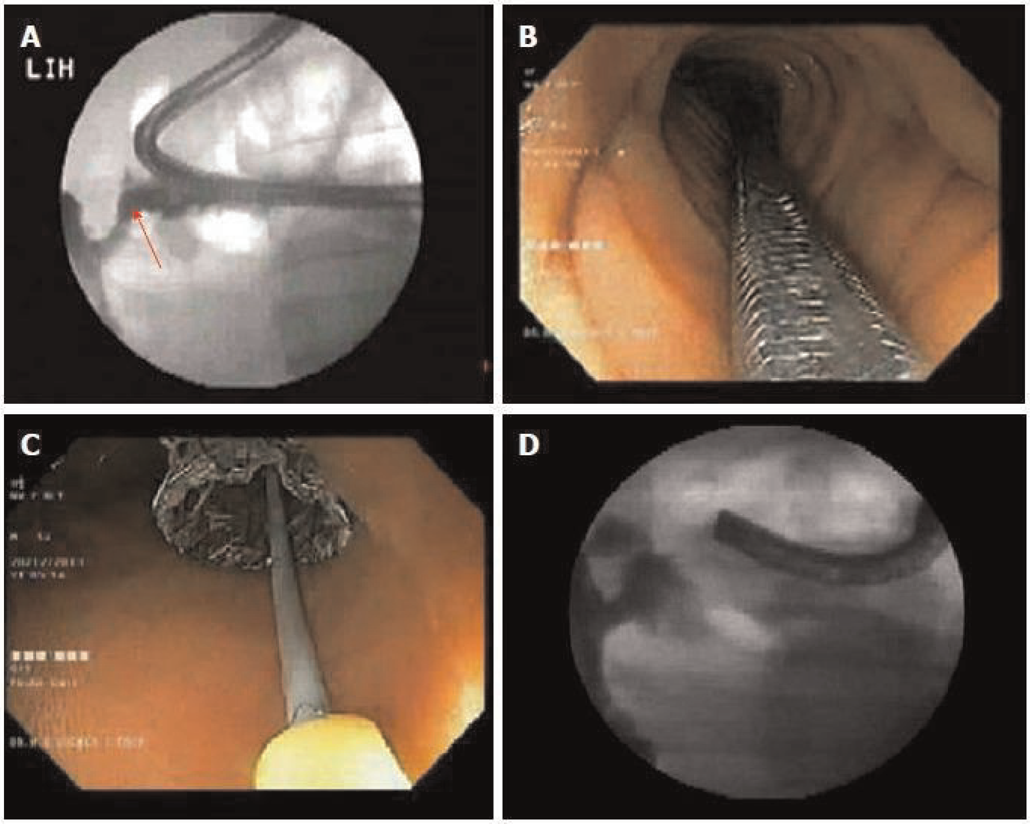

Figure 2.
(A) Contrast introduced through the surgical drain site shows site of the leak (arrow); (B and C) fully covered stent being deployed; (D) post-stenting contrast showing closure of the leak.

	Eloubeidi et al. [21]	Buscaglia et al. [22]	El Hajj et al. [23]
Total patients included	35	31	54
Patients with leaks/fistulae	12	15	44
Stent type(s) used	AliMaxx-E FCSEMS	Wallflex FCSEMS	SEPS, PCSEMS, FCSEMS
Overall technical success rate (%)	100	100	100
Closure of leak/fistula (%)	44	80 (short-term closure)	83
Overall stent migration rate (%)	33	33	28

FCSEMS: fully covered self-expandable metal stents; SEPS: self-expandable plastic stents; PCSEMS: partially covered self-expandable metal stents.

Table 3.
Comparison of studies on esophageal stent placement for management of leaks/fistulae.

Figure 3) and the modified stent designs (**Figure 4**) (adapted [20]) reduce the chances of stent migration [20].

3.2 Endoclip closure

Endoclips, which are more commonly used for controlling GI bleed, can also be used for closing the GI wall disruptions [24]. For the first time in 1993, endoclips were used successfully for closure of a GI perforation after endoscopic removal of gastric leiomyoma [25]. Endoclips are of two types, through-the-scope clips (TTSCs) and over-the-scope clips (OTSCs). In TTSCs, the clip is loaded on the clip applicator which is introduced through the biopsy channel of the endoscope. TTSCs have been

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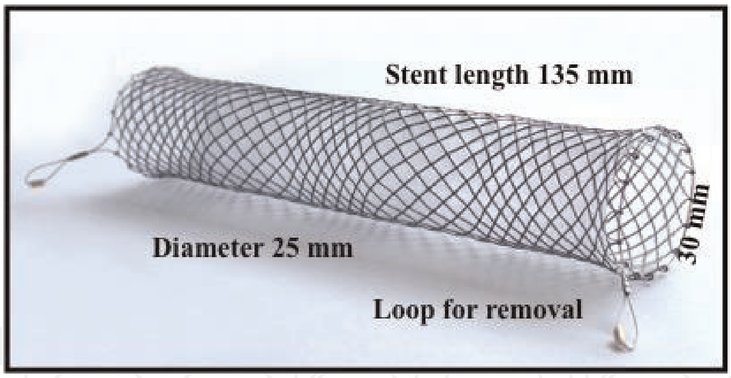

Figure 3.
Danis stent; length—135 mm; end diameter—30 mm; mid diameter—25 mm; provided with a loop at the end for removal.

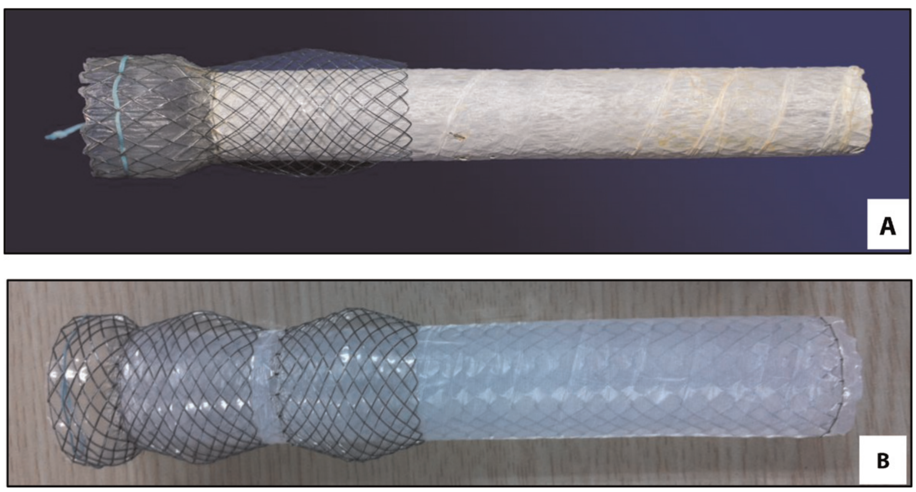

Figure 4.
Modified stent design with extra covering or dumb-bell shape.

used successfully to close leaks following endoscopic mucosal resection (EMR) [26] and endoscopic submucosal dissection (ESD) [27]. TTSCs are usually less effective for defects of >1 cm, where another technique should be combined with TTSC. The TTSCs available from different manufacturers differ in size and mechanical properties. The most commonly used TTSCs (**Figure 5**) (adapted [20]) are the Quick clip (Olympus, America Inc., Center Valley, PA, USA), Instinct clip (Cook Medical Inc., Bloomington, IN, USA), and Resolution clip (Boston Scientific Inc., Natick, MA, USA). Most of the recent versions of TTSC are re-operable and rotatable; these properties allow the clips to be placed accurately and improve the clinical success.

The recently introduced OTSCs can close full thickness GI defects up to 2–3 cm in diameter. The design of OTSC is different and is mounted over-the-scope tip on a

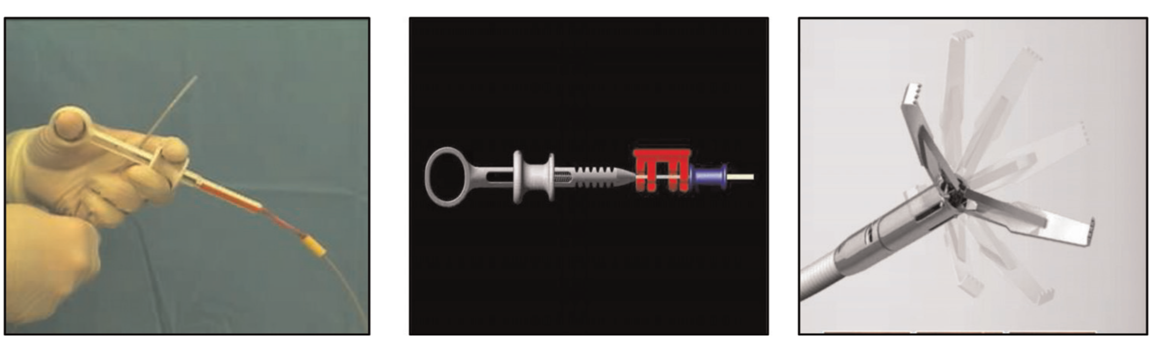

Figure 5.
Through-the-scope clips from different manufacturers.

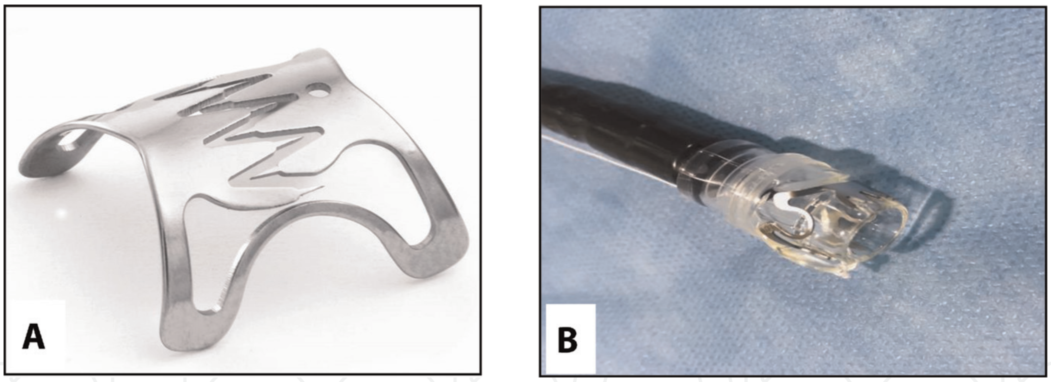

Figure 6.
(A) Ovesco clip and (B) ovesco loaded on tip of endoscope.

transparent cylinder somewhat akin to variceal band ligator device. OTSCs (**Figure 6A** and **B**) from Ovesco Endoscopy (Tübingen, Germany) are nitinol, biocompatible clips with teeth ends designed in the shape of a bear trap which can produce a full thickness closure. OTSCs have a greater tissue capture and compressive strength which gives it advantage over TTSCs to close chronic leaks and fistulae even in the case of inflamed or fibrotic tissue surrounding the defect. Accessories like anchor and twin grasper, which can pull the defective mucosa into the OTS cylinder or reduce the gap of the defect, can be used for larger defects. In a large muticenter study by Chavez et al. [28], 188 patients with GI leaks and fistula were treated with OTSCs. OTS was used as primary treatment in 97 patients and as rescue therapy in 64 patients (27 patients were lost on follow-up). The success rate was 75% in first group and 47% in second group with an overall success rate of 64%.

Padlock clip (Aponos Medical Corp., Kingston, NH, USA) is a recently introduced OTSC which uses somewhat different technique and design than Ovesco (**Figure 7A**). The six needles on the inner aspect point toward each other help in circumferential tissue approximation at 360° due to its radial compression technology. The Padlock clip is preassembled in an open position over the tip of endoscope and is deployed by its Lock-It delivery system with a trigger wire located parallel to the scope connected to a handle (**Figure 7B**). Recent studies have shown Padlock clip to be safe and effective in closing GI wall defects [29, 30]. However, data regarding its clinical use is still limited.

3.3 Sealants

Sealants have been used for a long time to close GI leaks and fistula, however the results are mixed with limited data. The most commonly used tissue sealants are cyanoacrylate and fibrin glue [31, 32]. The frequent sites of application include

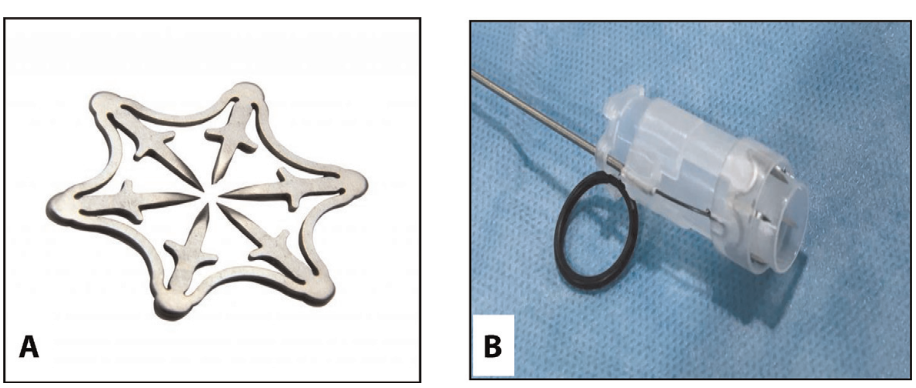

Figure 7.
(A) Padlock clip and (B) preassembled padlock clip.

endoscopically accessible areas of anastomotic leakage after esophagectomy and gastrectomy or after bariatric surgical procedures. The glue is applied via a double lumen catheter after removal of secretions or pus so that the targeted area becomes dry and it helps to form a fibrin clot. The underlying epithelium around the opening of the fistula is denuded with the aim of development of reactive inflammatory response around the opening. After application, the glue polymerizes on contact with moisture, causing tissue necrosis and an inflammatory response. Kotzampassi et al. used endoscopic tissue sealants (fibrin and cyanoacrylate glue) for anastomotic leakage after gastrointestinal operation and the success rate was 96.8% [33]. However, repeated sessions and large volumes of sealants may be necessary in many cases.

3.4 Sutures

Endoscopic suturing can be used for stent fixation and closure of larger defects including fistula and perforations, although the technique is more demanding and requires expertise. The Apollo Overstitch (Apollo Endosurgery, Austin, TX, USA) is US Food and Drug Administration (FDA) approved endoscopic suture device which offers full thickness plication. It is a single unit disposable device allowing continuous or intermittent suturing with a cinching device. The device is front loaded onto a double channel endoscope (**Figure 8**). The major advantage of Apollo Overstitch is that it can be reloaded inside the body without any need of removing it between stitches and allows one endoscopic channel to be free. In a large multicenter retrospective study by Sharaiha et al., endoscopic suturing used for management of GI defects and/or stent anchorage was found to be safe and efficacious [34]. The technical and clinical success rates achieved were 97 and 79%, respectively. Clinical success was high for perforations (93%) and fistulas (83%), however the results were disappointing for closure of anastomotic leaks (27%) [34]. Overstitch has also been used successfully in closure of iatrogenic esophageal perforations [35], endoscopic submucosal dissection (ESD) [36], and mucosal defect after Peroral Endoscopic Myotomy (POEM) [37] and stoma reduction post-bariatric surgery [38, 39].

3.5 Other techniques

Vacuum-assisted closure (VAC) device is a widely used treatment modality for management of cutaneous wounds [40]. It applies negative pressure to the wound through a vacuum-sealed sponge and helps in drainage of wound secretion which

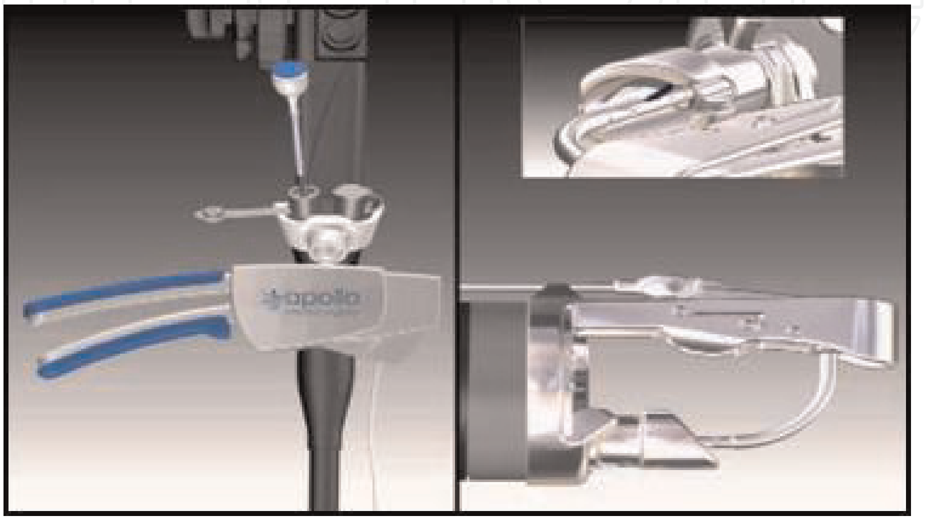

Figure 8.
Apollo overstitch device (Apollo Endosurgery, Austin, TX, USA).

promotes wound healing by increasing tissue vascularity and fresh granulation tissue. Endoscopic vacuum-assisted closure (EVAC) is a minimally invasive method which is mainly used in management of anastomotic leakage post-surgery [41, 42]. The sponge allows drainage of the leak by providing a gentle, continuous suction over tissue in contact with the sponge surface leading to a gradual reduction in the size of the wound cavity [43].

Atrial septal occluders (ASO) developed for the closure of atrial septal defects have been shown in case reports to be effective in treating GI fistulas including TEF [44, 45]. It consists of two self-expandable disks which are covered by polyester fabric and attached by a short connector that has various diameters. The other endoscopic methods used in management of GI leaks and fistula include fistula plugs [46], surgisis soft tissue grafts [47], and biodegradable stents [48]. However, more experience and data are required with these modalities to be included in routine clinical practice.

3.6 Limitations

The main limitations of endoscopic management are in situations with large perforation, difficult or inaccessible endoscopic location, fibrosis at the margins of the defect, presence of abscess or fecal contamination, etc. [49]. In these conditions,

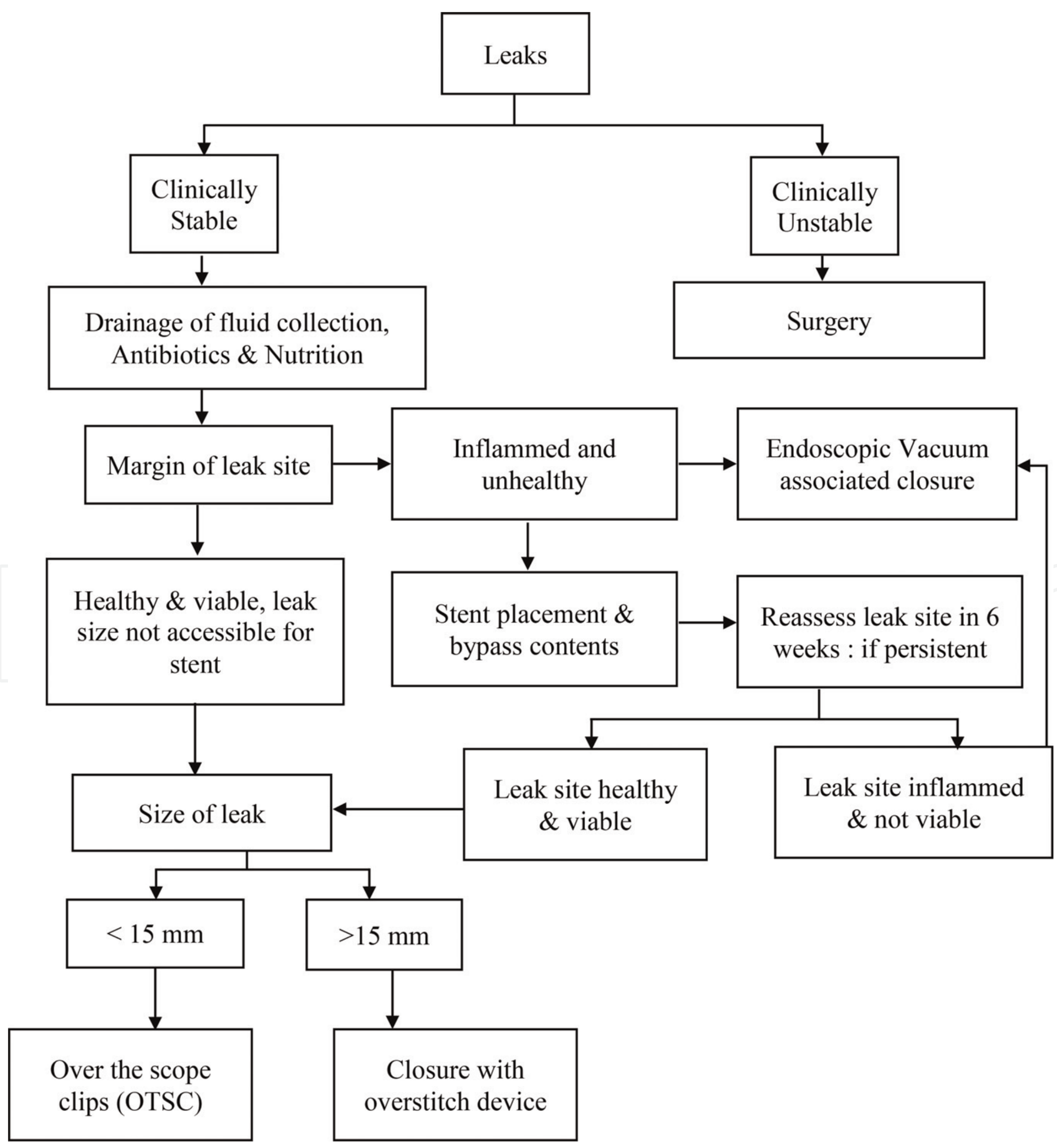

Figure 9.
Algorithm for management of leaks.

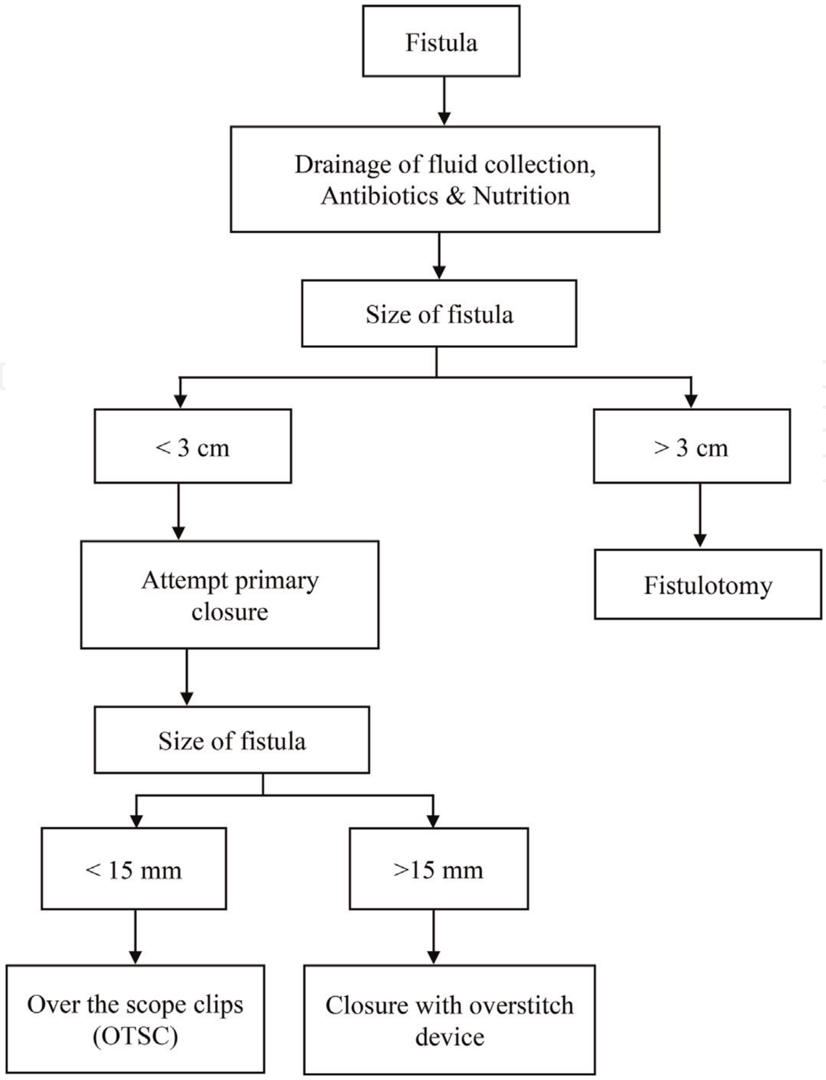

Figure 10.
Algorithm for management of fistula.

an additional procedure or surgical alternative should be considered. In cases with technical failure, where clip closure is unsuccessful, surgical intervention should be immediately considered to avoid sepsis [50]. Other complications such as perforation and bleeding are known with the endoscopic modalities.

3.7 Algorithm for management of leaks and fistula

Figures 9 and **10** (adapted [51]) give a systematic approach toward management of leaks and fistula.

4. Conclusion

The incidence of leaks and fistula involving the GI tract has increased in our routine practice. Only a small group of patient will respond to conservative management, while most of them will require either surgery or endoscopic management. Endoclips (TTSC and OTSC) and covered stents are the preferred endotherapy modalities to treat GI leaks and fistula. The small leaks (<10 mm) can be managed by traditional TTSCs, while the larger leaks require covered stents or OTSCs. In general, if the leak is located in proximal esophagus, distal-most esophagus, stomach, or in the right colon, clips are preferred over stents [52]. Results of

Endovac, Plugs and Grafts, and Biodegradable stents are promising. However, larger clinical studies are required before they can be used in routine clinical practice.

In view of availability of multiple endoscopic techniques, management according to the algorithm guides the endoscopist to select the best modality based on the location, size, and associated features.

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