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Review Article

The Role of Endoscopic Management in Afferent Loop Syndrome

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Afferent loop syndrome (ALS) is a morbid complication that may occur after gastrectomy and gastrojejunostomy reconstruction. The aim of this article is to review the different endoscopic treatment options of ALS. We describe the evolution of the endoscopic treatment of ALS and its limitations despite the overall propitious profile. We analyze the advantages of endoscopic ultrasound-guided entero-enterostomy (EUS EE) over enteroscopy-guided intervention, and the clinical outcomes of EUS EE. We expound on pre-procedural considerations, intra-procedural techniques and post-procedural care following EUS EE. We conclude that given the simplification of the technique and the ability to place a stent away from the tumor, EUS EE is a promising technique that will likely be established as the treatment of choice for ALS. **(Gut Liver 2023;17:351-359)**

Key Words: Afferent loop syndrome; Endoscopic ultrasonography; Enterostomy; Self expandable metal stent; Gastrojejunostomy

INTRODUCTION

Afferent loop syndrome (ALS) is a complication that may ensue in patients post gastrectomy and gastrojejunostomy reconstruction. The afferent loop represents the duodenojejunal limb upstream to the gastro-jejunal (GJ) anastomosis. Also termed the pancreaticobiliary limb, the afferent loop normally drains bile and pancreatic juices downstream towards the GJ anastomosis. Symptoms vary depending on the degree and the incipience of the obstruction. Complete obstruction at the GJ anastomosis creates a closed loop system that hinders natural drainage of secretions. Likewise, with acute obstruction, the cumulating and constrained secretions cause increased intraluminal pressure that precipitate a variety of complications such as pancreatitis, ascending cholangitis, and peritonitis secondary to afferent loop perforation.[1-3] In chronic ALS, there is partial or open loop obstruction where the impounded fluid is able to drain through a "pressure relief valve" mechanism. The sequelae of chronic ALS are generally more indolent and less catastrophic than with complete obstruction and include bacterial overgrowth, vitamin B_{12} deficiency, steatorrhea and malnutrition.[4,5]

ALS is a rare condition and its incidence ranges between 0.2% and 1% depending on the type of gastrectomy (distal vs total) and the type of reconstruction (Billroth II vs Roux-en-Y).[6-8] ALS can also occur after total gastrectomy with loop esophagojejunostomy with simple or pouch Roux-en-Y reconstruction and pancreaticoduodenectomy with conventional loop and Roux-en-Y reconstruction.[9]

Different surgical techniques can predispose to the development of ALS through different proposed mechanisms. In antecolic afferent loop of length longer than 30 to 40 cm, the bowel redundancy increases the risk of volvulus, kinking and entrapment by adhesions. On the other hand, improperly closed mesocolic defects create an aperture for a retrocolic afferent loop to develop internal herniation.[10]

Obstructing lesions engendering ALS can be secondary to benign or malignant etiologies. Benign causes arise from intraluminal, intramural or extrinsic pathologies. Intraluminal lesions include impacted foreign bodies, enteroliths or bezoars at an anastomotic stricture.[11] Intramural causes are secondary to scarring and fibrosis from marginal anastomotic ulcerations or radiation enteritis.[12,13] Postoperative adhesions, internal herniation, volvulus or intussusception of the afferent loop are the causes of extrinsic compression.[14,15] Recurrence of malignancy at the anastomosis or in the surgical bed, locoregional lymphadenopathy or peritoneal carcinomatosis can all be causes of malignant obstruction.[16,17]

NON-ENDOSCOPIC TREATMENT

Historically, surgical intervention has been the mainstay treatment for ALS. The type of surgical intervention depends on the location of the underlying pathology–intraluminal, intramural, or extrinsic. Depending on the predisposing cause, treatment options include lysis of adhesions, reconstruction of anastomoses, excision of redundant loops, and resection of malignant lesions with anastomosis re-do.[18,19] Furthermore, surgery has a principal role in the management of benign etiologies of ALS with repair of the primary cause, often paired with reconstruction.[17] One exception is anastomotic ulcerations and associated strictures which may be managed endoscopically with balloon dilations. For malignant etiologies, however, palliative approaches are preferred given the lack of survival benefit data favoring curative interventions over palliative ones.[17] As such, endoscopic treatment is the method of choice for patients with cancer recurrence.[17,20]

Patients with complete obstruction may present with significant illness rendering emergent surgical intervention risky. In these cases, radiologic procedures such as percutaneous enteral drainage or percutaneous biliary drainage are pursued to control ALS and stabilize the patients prior to surgery.[21] Available data on radiologic interventions stem from case series that have suggested the safety and feasibility of a bridging procedure prior to proceeding with a more definitive therapy via an endoscopic or surgical route.[7,21-23] Given the paucity of data regarding the optimal intervention for specific scenarios, the sequence of such procedures, or the timing thereof, future studies- albeit challenging- may help in answering these questions.

Both surgical and radiological treatment options have inherent advantages and disadvantages. Surgical interventions offer the possibility of definitive treatment but pose significant technical challenges for the operating surgeon due to the nature of the revision in general and to adhesions in particular.[17] Furthermore, patients with ALS tend to be sick and malnourished and thus more susceptible to infections and to poor wound healing.[9] On the other hand, when available, radiologic interventions can be performed more promptly and are less invasive. The main disadvantage, however, is that radiologic treatment is temporizing, and requires multiple re-interventions–making it more suitable as a bridge rather than destination therapy.

ENDOSCOPIC TREATMENT OF ALS

1. Endoscopic nasoenteral tube insertion

Endoscopic treatment has a propitious role in the treatment of afferent loop obstruction. Being minimally invasive and utilizing a natural orifice, endoscopy has considerable appeal over surgical or percutaneous methods of treating ALS. Endoscopic decompression was first used as a bridge to surgery. Paulsen *et al.*[24] first described the use of upper gastrointestinal endoscopy to insert a duodenal tube for urgent pre-surgical decompression of malignant afferent loop obstruction in a patient with previous Billroth II distal gastrectomy. The patient had immediate pain relief and subsequently underwent duodenojejunostomy uneventfully.

Endoscopic nasoenteral tube decompression has been employed for ALS in patients with a benign etiology in the absence of mechanical obstruction. In an observational study of 2,548 patients who underwent distal gastrectomy (either Billroth II or Roux-en-Y) for distal gastric cancer, Cao *et al.*[25] found that 23 patients (0.9%) developed ALS due to post-surgical inflammatory stricture. All 23 patients underwent successful endoscopic nasoenteral tube decompression, with relief of symptoms. The nasoenteral tube was removed after 3 to 14 days (median, 4 days). No patients required repeat endoscopy, however at 12-month follow-up, two patients (8.7%) required surgical intervention due to worsening adhesions.

2. Endoscopic lithotripsy and removal of phytobezoars

Endoscopic therapy offers a minimally invasive way of directly addressing intraluminal causes of ALS. Phytobezoars may result from delayed gastric motility post gastric surgery.[26,27] Migration of the phytobezoar into the afferent loop may result in obstruction. This obstruction can be relieved by endoscopic retrieval of the phytobezoar using a snare or retrieval net, or by fragmentation–either mechanically or by using electrohydraulic lithotripsy. Lee described the use of a retrieval basket to break down a phytobezoar to relieve afferent loop obstruction in a 44-year-old woman with a previous pylorus-preserving pancreaticoduodenectomy.[28] Kuo *et al.*[29] first described the use of endoscopic electrohydraulic lithotripsy in fragmenting large phytobezoars in a series of 11 patients with phytobezoars greater than 5 cm. Technical success was excellent, with phytobezoar fragmentation and clearance in 100% of patients.

3. Endoscopic stricture dilation

Benign enteral strictures may occur as a result of radiation enteropathy or fibrosis at the afferent limb GJ anastomotic site. Alves *et al.*[30] described the successful use of endoscopic balloon dilation to obliterate an anastomotic stricture in a patient with a previous gastrectomy with Roux-en-Y reconstruction.

Enteral stasis may result from both anastomotic strictures, as well as impaired enteral motor activity post gastrectomy.[31] Enteral stasis causes bacterial overgrowth and leads to bile salt precipitation, resulting in enterolith formation and afferent loop obstruction.[32] Both endoscopic basket retrieval and endoscopic electrohydraulic lithotripsy are effective means in removing enteroliths. Lim *et al.*[33] successfully treated a 77-year-old with afferent loop obstruction caused by both an anastomotic stricture and enterolith using both endoscopic balloon dilation and electrohydraulic lithotripsy.

4. Enteroscopy-assisted luminal stenting

Tumor recurrence is a frequent cause of afferent loop obstruction in patients who have undergone pancreaticoduodenectomy for pancreatic cancer.[20] Sakai *et al.*[34] described the use of endoscopic self-expanding metal stent (SEMS) in a small retrospective study involving seven patients with malignant afferent loop obstruction. Clinical success was achieved for all patients, with a median procedure time of 30 minutes (range, 15 to 50 minutes) and no procedure-related adverse events. The median survival period post SEMS placement was 155 days (range, 96 to 374 days), with reintervention required only for the patient who had the longest survival period (374 days).

Pannala *et al.*[20] described the use of double-pigtail plastic stents to relieve afferent loop obstruction resulting from local recurrence of pancreatic cancer after pancreaticoduodenectomy. In a retrospective study spanning 14 years at a tertiary referral center, malignant afferent loop obstruction occurred in 24 patients (13%) after a median follow-up of 1.2 years (range, 0 to 14 years). Eight of these patients (33%) underwent direct enteroscopy-assisted luminal stenting with a double-pigtail stent. In this technique, the stricture is traversed with two double-pigtail stents and drainage is achieved both via the stent lumen and also via a "wicking action" between the stents. Clinical success was achieved in six of these patients (75%).

1) Enteroscopy-assisted luminal stenting technique in ALS

Pre-procedure planning is essential to determine the feasibility of enteroscopy-assisted luminal stenting. The location of the afferent loop stricture and the length of bowel that needs to be traversed to reach it should be determined on both coronal and axial views on computed tomography.

The procedure is performed under general anesthesia to prevent the risk of aspiration. Both endoscopic and fluoroscopic guidance is utilized (Figs 1-4). A standard colonoscope is usually used as it provides adequate endoscope length to reach the lesion, and has a large 3.7 mm instrument channel to accommodate the 10-F delivery system of the enteral stent. The colonoscope is advanced to the lesion. A dilute contrast solution is instilled into the afferent loop to delineate the lesion. A 0.035-inch guidewire and extraction balloon catheter are advanced across the stricture and exchanged with enteral stent delivery system over the guidewire. The enteral stent is deployed under fluoroscopic guidance. We perform an abdominal X-ray

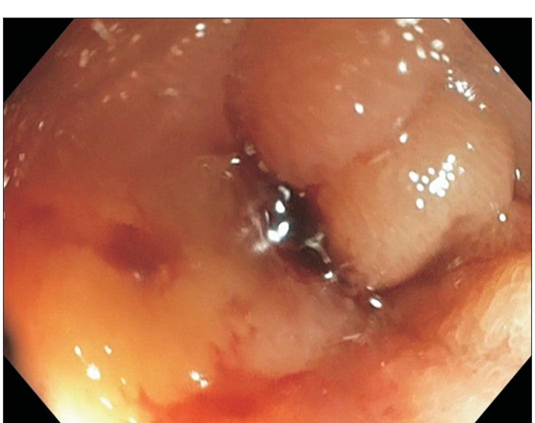

Fig. 1. A colonoscope was advanced to the afferent limb and a tight stricture was seen on endoscopic view.

Fig. 2. Instillation of dilute contrast showed a tight 3 cm stricture on fluoroscopic view.

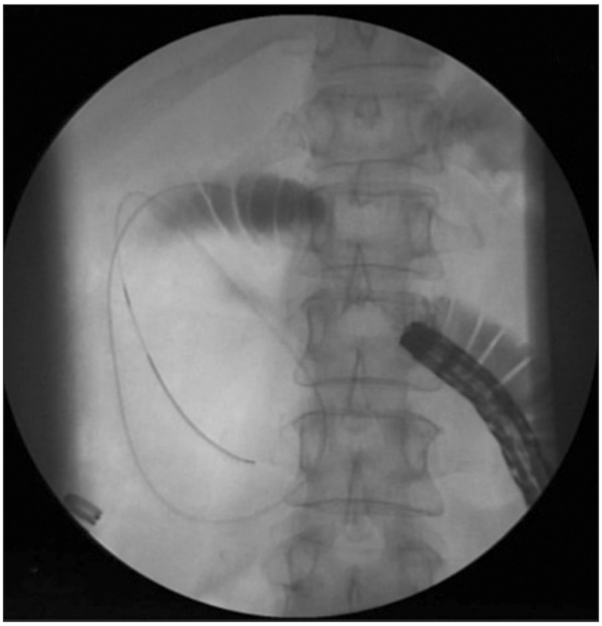

Fig. 3. The stricture was traversed with a 0.035-inch guidewire which was coiled in the dilated afferent loop.

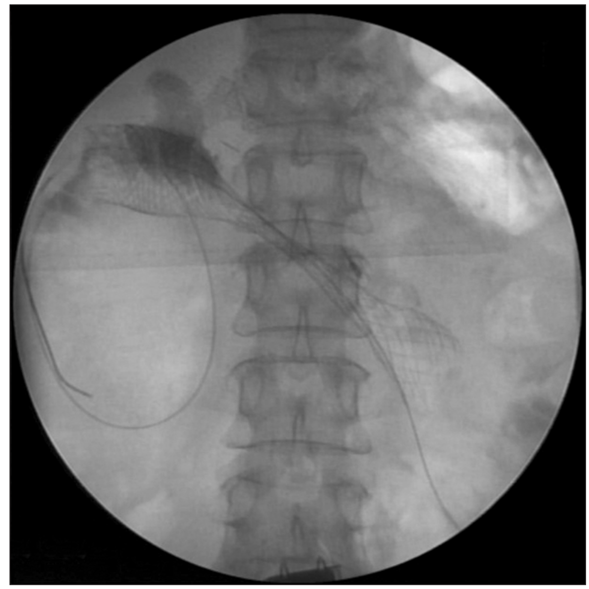

Fig. 4. A 22×90 mm WallFlex® uncovered self-expanding metal stent (Boston Scientific) was deployed under fluoroscopic guidance.

within 24 hours post-procedural to confirm adequate stent expansion and stable stent position. Serum biochemistry (including serum bilirubin and transaminases) is performed to confirm successful biliary drainage.

While endoscopic treatment options are favorable and attractive alternatives to percutaneous or surgical methods of treating ALS, there are several inherent limitations. Prior to the advent of endoscopic ultrasonography (EUS) entero-enterostomy, endoscopic treatment options were dependent on the ability to obtain direct endoscopic access to the afferent limb. This may not be possible in patients who have a long enteric segment preceding the lesion or tight angulation of the enteric segment–such as patients who have had a total gastrectomy. Furthermore, complete obstruction of the afferent loop precludes the passage of a guidewire and catheter, making SEMS insertion risky–if not impossible. Similarly, a long stricture of the afferent loop would affect the success of dilation or stent placement.

EUS ENTERO-ENTEROSTOMY IN ALS

Interventional EUS has introduced a new and "incisionless" alternative to surgery for patients with ALS. EUS provides a convenient means to take advantage of the compactness of the gastrointestinal tract. Obstructed small bowel loops can often be imaged from adjacent segments of the foregut, allowing for creation of an entero-enteric anastomosis which bypasses the obstruction. This is advantageous as it overcomes the problem of disease progression that may incur in patients post enteroscopy-assisted luminal stenting should the tumor recur; thus, attenuating the need for repeat procedure (Table 1).

Several considerations have to be made when assessing the suitability of EUS entero-enterostomy as a treatment modality for ALS (Table 2). EUS entero-enterostomy is one of the most challenging interventional EUS procedures with a significant learning curve and should preferably be performed in tertiary referral centers by experienced interventional endoscopists.[35] The distance between the planned puncture site on the afferent limb and the apposing foregut wall should not exceed 10 to 15 mm (the length of the saddle of the lumen apposing metal stent [LAMS]), so as to minimize tension on the LAMS post deployment reducing the risk of LAMS migration. Accessibility of the afferent loop (either via an existing percutaneous drain/fistula, or through direct intubation via endoscopy) would allow instillation of contrast and water into the obstructed afferent loop, if needed, to facilitate endosonographic confirmation of the target for needle puncture.

As previously stated, the presence of a long enteric segment preceding the lesion or tight angulation of the enteric segment, complete obstruction of the afferent loop, or a long stricture at the afferent loop, render direct endoscopic approach for ALS challenging–if not impossible. These are the same factors that merit consideration of EUS entero-enterostomy. Ascites, if present, should be drained to minimize the slippage of the afferent limb away from the

Table 1. Comparison of Treatment Modalities for Afferent Loop Syndrome

Procedure	Advantage	Disadvantage
EUS-guided entero-enterostomy	Short procedure time Bypass of tumor Prolonged stent patency Less painful procedure Shorter hospital stay	Technically challenging Expensive Potentially serious adverse events
Enteroscopy-assisted luminal stenting	Established procedure Less painful procedure Shorter hospital stay	Long procedure time Stent migration Stent occlusion
Percutaneous enterostomy	Short procedure time Bypass of tumor Prolonged stent Less painful procedure Shorter hospital stay	Potentially serious adverse events Morbidity associated with external draining tube
Surgical bypass	Bypass of tumor Permanent large anastomosis Established procedure	Invasive Long procedure time Longer hospital stay Contraindicated in critically ill patients

Table 2. Pre-Procedural Considerations for EUS Entero-Enterostomy

Operator-related factors
· Expertise in interventional EUS
· Learning curve for EUS entero-enterostomy
Disease-related factors
· Long enteric segment leading to stricture
· Tight angulation of afferent loop
· Presence of complete obstruction at afferent loop
· Long stricture afferent loop
· Accessibility of afferent loop for contrast injection
Patient-related factors
· Presence of ascites
· Coagulopathy

EUS, endoscopic ultrasonography.

apposing foregut wall during needle puncture and LAMS deployment. Coagulopathy should be corrected to attenuate bleeding risk.

1. EUS entero-enterostomy technique in ALS

Pre-procedure planning is crucial to the success of EUS entero-enterostomy. The location and distance between the stomach and the afferent loop need to be delineated on both coronal and axial views on computed tomography to obtain potential windows for intervention. Presence of intervening vessels and ascites should be determined to avoid complications.

The procedure is performed under general anesthesia to prevent the risk of aspiration. Prophylactic antibiotics are routinely administered although some patients are already on some due to underlying cholangitis. Under EUS guidance, the position of the dilated afferent loop is identified from the stomach or the proximal efferent limb (Figs

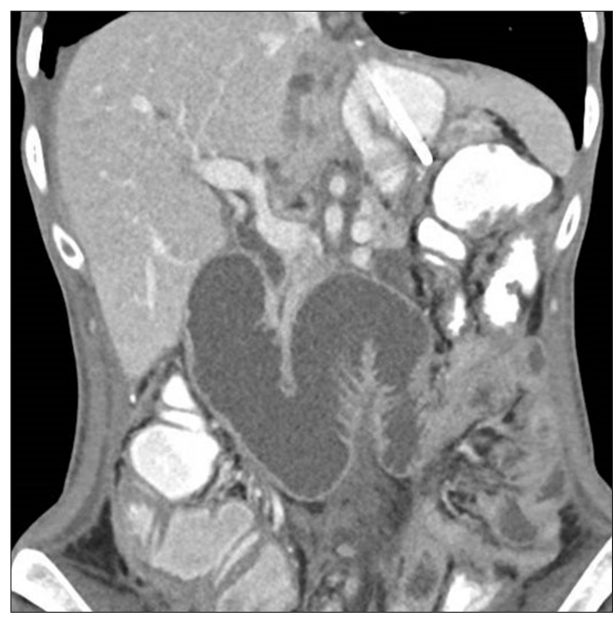

Fig. 5. Contrast enhanced computed tomography revealed dilated afferent limb due to obstruction from tumor recurrence.

5-10, Supplementary Video 1). The intervening distance between the stomach and afferent loop should be checked again and if it is >10–15 mm, an alternate site should be sought. If no optimal window is found, the procedure should be switched to an alternative treatment such as enteroscopy-assisted luminal stenting. If a percutaneous drain is absent, a pediatric colonoscope is used to intubate the afferent loop under endoscopic and fluoroscopic guidance. A mixture of contrast, normal saline, and methylene blue can be instilled into the afferent loop–to facilitate localization of the afferent loop on fluoroscopy and to enable

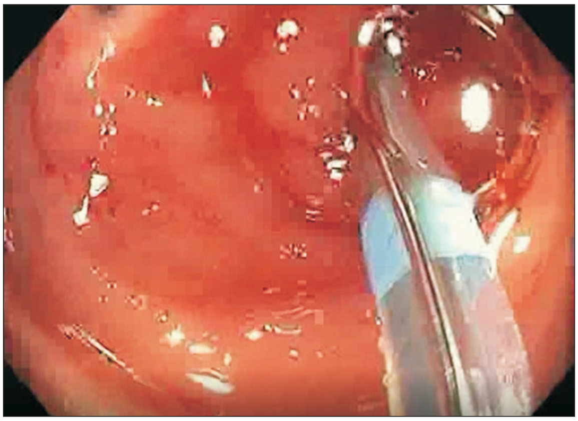

Fig. 6. A pediatric colonoscope was advanced and the afferent limb was cannulated under endoscopic and fluoroscopic guidance. A mixture of contrast, normal saline, and methylene blue was instilled within the obstructed limb, and the colonoscope was withdrawn.

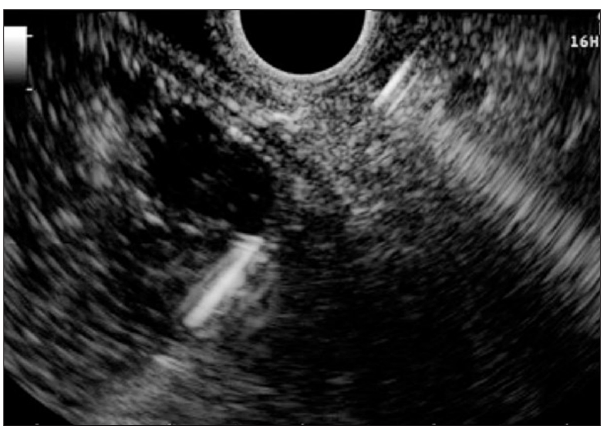

Fig. 7. The linear echoendoscope was advanced into the proximal efferent limb and the distended afferent limb was identified. A 19-gauge Flex fine needle aspiration needle (Boston Scientific) was advanced, and contrast, normal saline, and methylene blue were aspirated.

Fig. 8. A 3-cm stricture was observed with dilation of the upstream afferent limb under fluoroscopy.

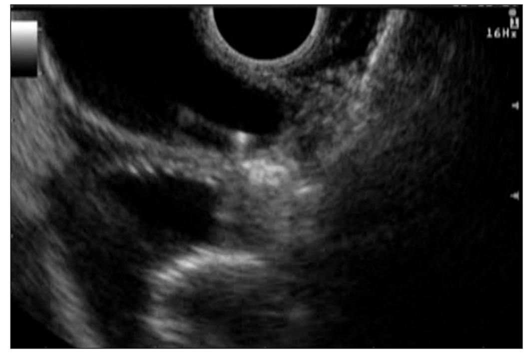

Fig. 9. An electrocautery enhanced lumen apposing metal stent was deployed into the obstructed limb. Endosonographic view of the distal flange into the obstructed afferent limb.

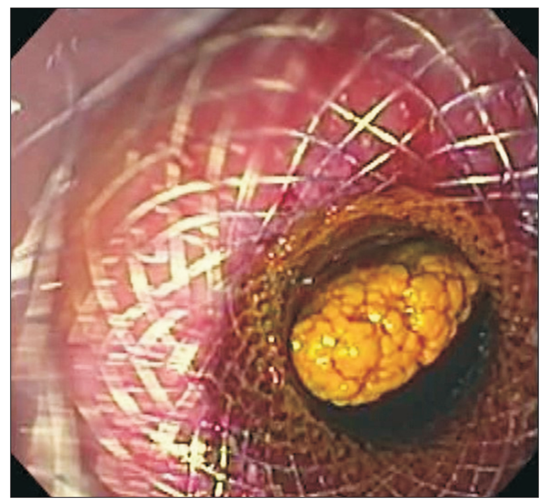

Fig. 10. The proximal flange was deployed. An enterolith was seen within the afferent limb.

easy verification of successful LAMS deployment. The pediatric colonoscope is then exchanged for a linear echoendoscope, and the distended afferent limb is identified. The above technique is not necessary in patients with severely distended afferent loops that can be easily visualized from proximal gastrointestinal tract. In addition, aggressive injection of fluid into the afferent loop in these patients with severely distended afferent loop risks perforation.

EUS entero-enterostomy can be performed using either a cautery or non-cautery-enhanced LAMS (Axios; Boston Scientific, Marlborough, MA, USA). The usage of a non-cautery-enhanced LAMS requires a 19-gauge needle puncture of the dilated afferent limb and aspiration of the contrast, normal saline, and methylene blue mixture in order to confirm access to the afferent limb. A 0.025-inch guidewire is advanced into the limb and exchanged with the needle over the guidewire. Dilation of the tract is then performed using a balloon catheter or a cystotome over a guidewire. This is followed by LAMS deployment to create the entero-enterostomy. Alternatively, a cautery-enhanced LAMS (Auto-Cut 100W, effect 5) can be deployed without the need for a guidewire, dilation or exchanging, shortening the procedure time, preventing the separation of the foregut wall, and potentially lowering risk of leakage after dilation of the tract. Endosonographic view should be used to confirm deployment of the distal flange in the dilated afferent limb. The proximal flange should be deployed within the echoendoscope channel, followed closely by concurrent advancement of the delivery system and gentle echoendoscope withdrawal to allow the proximal flange to spring open as the stent exits the echoendoscope. This avoids placing excessive traction on the LAMS, and does not compromise stability of the echoendoscope position during the procedure.

The use of a LAMS with a diameter of 10 mm is adequate for drainage of biliopancreatic secretions. A 15 mm diameter LAMS can be used if an endoscope needs to be advanced into the afferent limb post-deployment–however, the use of larger diameter LAMS may result in increased risk of reflux of food contents into the afferent limb. The placement of a double-pigtail stent through the stent has been described to help prevent stent occlusion by food and small bowel mucosal irritation from the distal flange.[36]

2. Post-procedure care following EUS entero-enterostomy

There is a lack of data examining post-procedure care for patients who have undergone EUS entero-enterostomy, and practice may differ between institutions. We recommend inpatient observation of the patient for at least 12 hours post-procedural. We perform an abdominal X-ray within 24 hours post-procedural to confirm adequate stent expansion and stable stent position. Serum biochemistry (including serum bilirubin and transaminases) is performed to confirm successful biliary drainage.

Data on the outcomes of EUS entero-enterostomy is constrained to small retrospective series. We summarized the clinical data from studies which had ≥3 subjects (Table 3). The overall technical and clinical success was 100%. The overall adverse event rate was 11.1% (three patients) and all three patients experienced mild abdominal pain. Likewise, in the largest reported series to date of 18 patients who underwent EUS entero-enterostomy for ALS, Brewer Gutierrez *et al.*[37] reported an adverse event rate of 16.7%. All adverse events were mild-moderate abdominal pain which resolved with conservative treatment (i.e., nil per os, intravenous fluids and analgesia). Several systematic reviews and meta-analyses of EUS entero-enterostomy in the setting of gastric outlet obstruction show a similar periprocedural adverse event rate of 11% to 12%.[38-40] Potential procedural-related adverse events include: (1) stent misdeployment resulting in perforation or leakage, (2) stent migration/dislodgement, (3) bleeding, and (4) aspiration of gastric contents.[41-44] Post-procedural adverse events include abdominal pain and erosion/ulceration of the contralateral wall due to the stent mesh.[45,46] Long-term adverse events in patients with lumen-to-lumen anastomoses include stent migration, obstruction by food residue and tissue ingrowth or overgrowth.[42,46,47]

CONCLUSION

ALS can occur after gastrectomy and gastrojejunostomy. It results in significant morbidity in patients who are already very frail. Endoscopy plays a vital role in the management of ALS, and is appealing as a minimally invasive and definitive treatment method. The advent of EUS entero-enterostomy with electrocautery enhanced LAMS has made endoscopic intervention simpler when compared to other minimally invasive methods such as enteroscopy-assisted luminal stenting. Retrospective studies have shown excellent results and an acceptable adverse event profile. Prospective randomized controlled trials will be important to establish EUS entero-enterostomy as the treatment of choice for ALS.

CONFLICTS OF INTEREST

M.A.K. is a consultant for Boston Scientific, Olympus, Pentax, GI Supply, Medtronic, and Apollo, has received re-

Table 3. Outcomes of EUS Entero-Enterostomy in Patients with Afferent Loop Syndrome (Only Studies with n≥3 Subjects Were Included)

Study (year)	No.	Stent	Technical success	Clinical success	Adverse events
Taunk *et al.* (2015)[48]	3	LAMS	3	3	0
Brewer Gutierrez *et al.* (2018)[37]	18	EC-LAMS (12) LAMS (6)	18	18	3 (abdominal pain)
De Bie *et al.* (2021)[49]	6	EC-LAMS	6	6	0
Overall, No. (%)	27		27 (100)	27 (100)	3 (11.1)

EUS, endoscopic ultrasonography; LAMS, lumen apposing metal stent; EC, electrocautery enhanced.

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SUPPLEMENTARY MATERIALS

Supplementary materials can be accessed at https://doi.org/10.5009/gnl220205.

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