

Anastomotic Leakage after Gastrectomy for Gastric Cancer

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ABSTRACT

Anastomotic leakage (AL) constitutes a prominent cause of significant morbidity following gastrectomy for gastric cancer. The manifestation of AL typically occurs within 7 to 10 days post-surgery, with reported incidence rates of 5.8-6.7% for open gastrectomy and 3.3-4.1% for laparoscopic gastrectomy. Various predisposing risk factors have been identified, including the individual nutritional status (excluding obesity) and preoperative corticotherapy. Interestingly, the administration of neoadjuvant therapies appears to reduce the AL occurrence. In the context of distal gastrectomies, the rates of AL are comparable between laparoscopic, robotic, and open approaches. The total gastrectomies have higher AL rate compared to distal gastrectomies, which are considered the preferred approach. Prophylactic drainage measures have not demonstrated efficacy in preventing AL. As for postoperative management, conservative treatment is indicated for patients presenting with mild clinical symptoms and increased inflammatory blood tests. This approach involves fasting, enteral or parenteral nutrition, administration of antibiotics, and percutaneous drainage. For small AL, endoscopic therapies such as stents, vacuum therapy, clips, suturing devices, and injections are appropriate treatment options. In cases of high-volume fistulas, severe sepsis or failure of previous therapies, surgical reoperation becomes the ultimate solution.

Key words: anastomotic leakage – gastrectomy – gastric cancer – complications – surgery – endoscopy – stenting – vacuum therapy.

Abbreviations: AL: anastomotic leakage; CRP: C-reactive protein; CT: computed tomography; EVT: endoscopic vacuum therapy; GC: gastric cancer; RCT: randomized controlled trial; SEMS: self-expandable metallic stent.

INTRODUCTION

Gastric cancer (GC) ranks sixth in terms of incidence and fourth as a leading cause of cancer-related mortality [1, 2]. In 2020, it contributed to 8% of cancer-related deaths, with the incidence of GC reported at 3.8 cases per 100,000 inhabitants, rising to 70.1 cases per 100,000 inhabitants among those over 60 years old [3]. While there has been a decline in *Helicobacter pylori* infection, the incidence of GC has shown an increase in younger individuals (below 50 years old) due to dietary habits

and obesity [2]. Managing GC requires a multidisciplinary approach, but surgery remains the cornerstone treatment modality, despite being associated with considerable morbidity (ranging from 9.1% to 46%) and mortality (up to 13%) [4]. Patients who experience postoperative complications have a lower 5-year overall survival rate compared to those without complications, with reported rates of 27-47% versus 43-85%, respectively [5, 6]. Additionally, the severity of these postoperative complications is directly correlated with increased mortality rates [7].

Gastric surgery is indicated in resectable T1b-T3 tumors using distal or total gastrectomy, based on the location and extent of the tumor. Gastrectomy with celiac branch vagus nerve-preserving technique has demonstrated benefits in early gastric cancer, leading to a reduced incidence of gallstones, bile reflux, shorter time of first flatus and shorter hospital stay, though AL rate remained similar [8]. Minimally invasive approaches, such as laparoscopic or robotic procedures can

be suitable for early and advanced gastric cancer, but caution is advised for T4b tumors requiring en bloc resection of involved structures. Reconstruction after distal gastrectomy can be achieved using Roux-en-Y procedures (the gold standard reconstruction procedure) and, when this is not feasible, Billroth II procedures are viable options.

In stage II/III CG, severe postoperative complications have been reported at rates of 11.6-13.3%, leading to a decrease in the completeness of adjuvant therapy (37.6% in cases with complications vs 64% in cases without complications) [6] and 5-year survival (58% in patients with complications vs. 73.4% in patients without complications) [9]. Distal laparoscopic or open gastrectomy for operated T1 tumors yields similar prognostic outcomes, with a 5-year survival rate of 94-95% and a low complications rate of 1-2%, associated with bowel obstruction [10].

The purpose of this narrative review is to provide a comprehensive description of the current postoperative management of anastomotic leakage (AL) after surgery for GC.

A literature search was performed in PubMed, Embase, and Cochrane Library for eligible randomized controlled trials (RCTs) in English until July 2023. The search used broad search terms containing “anastomotic leakage”, “gastric cancer”, “gastric carcinoma”, “stomach cancer”, “laparoscopic”, “laparoscopy”, “open gastrectomy”, “RCT”, “endoscopic treatment”, “stenting”, “vacuum therapy”, “injection”, “clipping”, “suturing” and “conservative treatment”.

DEFINITION AND EPIDEMIOLOGY

Anastomotic leakage is a full thickness defect of esophago-jejunal, gastro-jejunal, and jejuno-jejunal anastomoses. Irrespective of presentation or method of identification, AL has clinical consequences, and sometimes is associated with an abscess close to the anastomosis [11]. It usually occurs 7 to 10 days (range 3-26) after surgery [12, 13], at the level of suture or staple lines [14], with a rate of 5.8-6.7% after open gastrectomy and 3.3-4.1% after laparoscopic gastrectomy [15, 16].

Anastomotic leakage is associated with 7-9.8% mortality and 38.5% of all surgery-related mortality after gastrectomy [15], decreasing the overall survival (HR: 2.36, $p < 0.001$) [16, 17], but not the recurrence free survival [18].

Duodenal stump leak is the most feared anastomotic complication after partial gastrectomy with Billroth II or Roux-en-Y procedure. It represents a full thickness duodenal defect; it could associate an abscess close to the duodenal stump [12]. This complication was reported in 1.17% of 1537 patients with radical gastrectomy [19] up to 7.7% in more recent studies [20], although older studies reported up to 18.3% [21].

DIAGNOSIS

Patients with AL present fever, tachycardia, abdominal pain and/or acute abdomen. The presence of digestive fluids in surgical drains is unequivocal for AL. Computed tomography (CT) scan reveal pneumoperitoneum with contrast leakage outside the gut lumen and fluid perianastomotic collections. Elevated C-reactive protein (CRP) and leukocytosis are early indicators, but systemic inflammation response index (defined

as neutrophil count \times monocyte/lymphocyte count) was found to be an independent predictive factor for developing an AL [22]. Endoscopy can be indicated in the early postoperative setting, 7 to 8 days after surgery, with high sensitivity in detection of minor leaks [23] (Fig. 1).

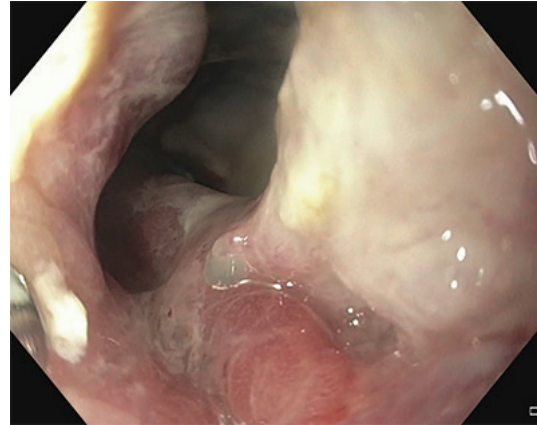


Fig. 1. Endoscopic aspect of a large anastomotic leakage after proximal gastrectomy for gastric adenocarcinoma

Routine upper gastrointestinal contrast agent examinations on day 5 postoperatively should be avoided because some AL occur after the day 5 and the sensitivity of the examinations is low (53%) [24]. When the clinical suspicion of AL exists (eg. fever), CT scan should be performed first, followed by contrast swallow and/or endoscopy [25].

CLASSIFICATION

The Clavien-Dindo classification revisited in 2004 is the most used for characterizing the postoperative complications. It categorizes complications into grades I to V based on their severity, with grade I/II representing less severe complications and grade III or higher indicating more serious complications. However, patients experiencing grade I/II complications but remaining in the hospital for 15 days or longer may exhibit similar clinicopathologic characteristics as those with grade III or higher complications [6].

There are other less common classifications such as Accordion Severity Classification of Postoperative Complications, which included four levels of severity, or Comprehensive Complication Index [25].

RISK FACTORS

Anastomotic leakage can occur due to various factors, including ischemia, impaired blood supply or oxygen delivery, anastomotic tension, operation time and surgical technique. Several studies have shown different factors associated with the occurrence of AL.

- Site of anastomosis: esophagojejunostomy was the most frequent AL site (73.8%, 59 from 80 patients) with 2.5% mortality and no influence on 5-year survival [26]. The Roux-en-Y and Billroth-I anastomosis had an AL incidence of 0.6% and 1.4%, respectively [27].

- Patient factors: low albumin concentration, diabetes, laparoscopic method, total gastrectomy, and proximal gastrectomy were predictive factors for AL [28]. The presence of a low level of albumin was associated with a late leakage closure [28].

- Body mass index (BMI) ≥ 24 kg/m², elevated preoperative CRP level, and unreinforced duodenal stump [29] or a shortened duodenum due to duodenal ulcer or previous operations were associated with duodenal stump leakage [21].

- Adiposity: intramuscular adipose tissue content was more frequent in AL patients, and visceral adipose tissue index was higher in patients with a pancreatic fistula and infectious complications [29]. Obesity did or increase the risk of AL [30].

- Preoperative medication: corticosteroids increased the postoperative AL to 11.8% (compared to 2.1% in patients without corticosteroids) and increased with prednisone dose [31]. The nonsteroidal anti-inflammatory drugs (NSAIDs) administered preoperatively increased the rate of anastomotic and duodenal leakage compared to non-NSAIDs group (2.1% vs. 0.7%, $p=0.005$ and 1.5% vs. 0.4%, $p=0.008$, respectively) [32].

- Neoadjuvant therapy was not associated with an increased risk (OR=0.53) of developing AL [33] (Table I) [34-46]. The 5-year overall survival (57 vs. 63%; $p=0.77$) or disease-free survival (52 vs. 52%; $p=0.52$) were similar, no matter the presence or absence of complications in patients with neoadjuvant therapy [6]. However, the major postoperative complications in patients without neoadjuvant therapy led to inability to complete the multimodal postoperative adjuvant therapy and they had a lower 3-year overall survival (OR=2.76, $p=0.011$) [47].

Type of Gastrectomy

The choice of surgical technique, whether open, laparoscopic, or robotic, can also impact the occurrence of AL.

Open or Laparoscopic?

- Open versus laparoscopic gastrectomy showed that open surgery had similar AL rate compared to laparoscopic surgery (OR=1.17, without statistical significance), with similar overall survival rates [48].

- Laparoscopic proximal gastrectomy versus total gastrectomy. A meta-analysis indicated no difference for AL rate between the two methods (OR=1.13) for proximal gastric cancer [49]. The double tract reconstruction of proximal gastrectomy had a similar complications rate and an overall survival, but a less need of vitamin B12 supplementation [50] and a lower incidence of reflux symptoms [51].

- Distal gastrectomy versus total gastrectomy (open and laparoscopic). A meta-analysis showed better 5-year survival for distal gastrectomy compared to total gastrectomy (55-67% vs 24-61%) and lower AL rate (OR=3.38, $p=0.02$), despite similar TNM stages [52], suggesting that distal gastrectomy should be preferred whenever possible.

- Laparoscopic distal versus open distal gastrectomy showed no difference for AL rate in one meta-analysis including 5 randomized controlled trials (RCTs) and 2,746 patients (OR=1.77, $p=0.10$) [53].

Robotic or Laparoscopic?

- Robotic versus laparoscopic distal gastrectomy. A meta-analysis indicated no difference between the two methods concerning AL rate (OR=0.73, $p=0.49$) and the postoperative complications, but the robotic surgery had more retrieved lymph nodes and a more rapid postoperative recovery, with a longer operative time [54].

Robotic or Open?

- Robotic versus open. Similarly, to laparoscopic gastrectomy, robotic distal gastrectomy was associated with similar rate of AL compared to open distal gastrectomy. No

Table I. The leakage rate in patients with neoadjuvant therapy

Author, year, reference	Type of study	Aim of study	Number of patients	Leakage rate
Xu, 2021, [34]	R	NACS vs. S	221 vs. 221 matched analyses	1.35% vs. 4.07%
Umeda, 2021, [35]	R	NACS vs. S	64 NACS vs. 128 S	1.6% vs. 6.3%
Ma, 2020, [36]	R*	NACS vs. S	20 NACS vs. 49 S	5% vs. 4.1%
Wu, 2020, [37]	R	NACS vs. S	86 paired matched	1.2% vs. 1.2%
Terashima, 2019, [38]	RCT	NACS+A vs. S+A	139 NAC vs. 147 S+A	2.72% vs. 1.36%
Ramachandra, 2019, [39]	RCT	NACS vs. S	27 NACS vs. 24S	0% vs. 4%
Kano, 2019, [40]	R	NACS vs. S	39NACS vs 37 S	2.6% vs. 2.7%; $p=0.970$
Haskins, 2017, [41]	R	NACS vs. non-NACS RT vs non-RT	121 NAC, 58 RT	NACS 15% vs. non-NACS 10%, $p=0.12$ RT 3.1% vs. non-RT4.8%, $p=0.58$
Fuentes, 2016, [42]	R	NACS vs. S	145 NACS vs. 308 S	2.1% vs. 3.6%
Feng, 2015, [43]	R	NACS vs. S	80 NACS vs. 90 S+A	0% vs. 2.2%; $p=0.49$
Teoule, 2015, [44]	R	NACS vs. S	30 NAC vs. 105 S	6.6% vs. 14.28% duodenal stump (13.3 vs. 1.9%; $p=0.022$)
Ruf, 2014, [45]	R	NACS vs. S	26 NAC vs. 38 S	11.53% vs. 10.52%
Ahn, 2014, [46]	R	NACS vs. S	58 NACS vs. 92 S	2.08% vs. 2.17%; $p=1.00$

*neuroendocrine tumors; A: adjuvant therapy, DFS- disease free survival; NACS: neoadjuvant chemotherapy plus surgery; OS: overall survival; R: retrospective study; RCT: randomized controlled study; RT: radiotherapy; S: surgery alone.

differences were found in the total number of harvested lymph nodes, tumor-free resection margins, 5-year overall, and disease-free survival [55].

Surgeon Experience

No learning curve effect for avoiding AL in gastrectomy performance [56] or in laparoscopic gastrectomy [57] were found in some large retrospective series, while in other retrospective group the surgeon's initial 100 cases had higher AL incidence than in later cases (2.4 vs. 1.3%; $p < 0.001$), especially when the minimally invasive surgery was used [14].

Reconstruction Type

Eso-jejuno-anastomosis

- Hand-sewn technique for esophago-jejunal anastomosis in total gastrectomy seemed similar with stapler anastomosis in terms of mortality, morbidity and postoperative complications [58].

- Seromuscular layer sutures after esophagojejunostomy in simple anastomosis patients reduced the AL from 9.21% to 1.72% [59].

- The overlap method of eso-jejuno-anastomosis (closure of anastomosis with a linear stapler, and double-stapling reconstruction of jejunojejunostomy) proved the same value as standard laparoscopic approach, using a 25-mm sized circular stapler via minilaparotomy, while jejunojejunostomy was performed in a hand-sewing manner (OR=1.23, $p=0.50$), with longer procedure duration [60] and lower incidence of anastomotic stenosis (OR=0.19, $p < 0.001$) [61].

- The use of modified overlap method did not modify the outcome [62].

- Mechanical linear-stapled or circular-stapled anastomoses did not influence the rate of AL [63].

- The jejunal interposition did not influence the rate of AL [64].

- The transorally inserted anvil (OrVil) is frequently selected for esophagojejunostomy after laparoscopic total gastrectomy because of its versatility. During anastomosis with OrVil, the double stapling technique or hemi-double stapling technique had similar AL rate, although only one AL of Clavien-Dindo classification grade \geq IIIa was observed in the double stapling technique [65].

- The overlap guiding tube-assisted oesophagojejunostomy shortened the operation, the postoperative recovery and decreased the rate of AL (2.8% vs 4.8% in conventional group) [66].

- Preservation of mesentery of jejunum reduced the frequency of AL (1.4% vs. 13.0%, $p=0.017$) compared to dividing mesentery of jejunum group during laparoscopic gastrectomy [67].

- Fibrin-glue in the operative bed reduced postoperative lymphatic leakage after gastrectomy and D2 dissection and the patients were discharged earlier [68].

A recent meta-analysis including 3,177 patients found similar AL rate, no matter the technique of anastomosis after laparoscopic gastrectomy [69].

Gastro-jejuno-anastomosis

One meta-analysis including 12 studies found that Roux-en-Y anastomosis was more beneficial than Billroth-II in

reducing the incidence of remnant gastritis, reflux disease and dumping syndrome, but the AL rate was similar [70]. Delta-shaped Billroth I anastomosis in totally laparoscopic distal gastrectomy had an advantage in postoperative gastrointestinal function recovery [71].

The uncut Roux-en-Y gastrojejunostomy was preferred to Billroth II with Braun anastomosis in distal gastrectomy because it reduced the reflux gastritis [72].

Other Surgical Preventing Techniques

- Intraoperative test with blue-methylene for checking the anastomotic discontinuity, despite increasing the total length of operation with 30 minutes, found 4.9% leakage in a group of 82 patients, which was repaired intraoperatively. No postoperative leakage was found in these patients compared to 7.3% in non-tested patients, although the total hospital stay was not statistically different (15.8 vs. 17 days, $p=0.16$) [73].

- An indocyanine green-based blood flow evaluation might be an effective method of preventing anastomotic complications of delta-shaped anastomosis, especially for highlighting the aberrant left gastric artery [74].

- The use of prophylactic abdominal drainage after gastrectomy is still widely used worldwide for the early diagnosis and management of post-operative bleeding, AL, and intra-abdominal infections. A metaanalysis including 7 RCTs (783 patients) and 14 observational studies (4,359 patients) suggested that lack of use of prophylactic drainage had a lower total complications rate (OR=0.68; $p=0.04$), earlier time to soft diet and shorter length of hospital stay. Also, they reported no impact on AL rate, duodenal stump leakage, pancreatic leakage compared to drainage group [75], as sustained by the Enhanced Recovery After Surgery protocols implementations trials.

TREATMENT

The fundamental principles include identification of the site of leak, drainage of any leaked contents, and controlling the flow of luminal contents with either diversion of luminal contents or closure of the disruption. This could use endoscopic methods (similar to leaks after bariatric surgery) or surgery if the patient is hemodynamically unstable for drainage and control the abdominal sepsis.

Additionally, the conservative management includes bowel rest, broad spectrum antibiotic therapy, fluid and electrolyte management, parenteral nutritional support, and drainage of any fluid collections and/or abscesses.

A multidisciplinary effort should be done for the correct management involving surgery, interventional radiology, and endoscopy.

Conservative treatment is applicable in case of mild clinical symptoms and laboratory signs (fever, leukocytosis and abnormal C-reactive protein), low output fistulas from the drains and small radiologic leaks. Fasting, parenteral or enteral nutrition, and antibiotics are needed [76]. The placement of a gastrointestinal decompression tube is a safe treatment. For example, in case of the defect size is \geq 4 mm, the time to clinical success, length of hospital stay, and hospital cost can be reduced [77]. Jejunostomy might be necessary for nutritional purposes.

Percutaneous radiologic-guided drainage is mandatory in presence of undrained fluid collections.

Endoscopic Therapy

Endoscopic treatment is suitable for recent leaks of small size <2 cm and <50% of circumference [78]. It is highly effective (80-90%) and can avoid surgical revision (Fig. 2).

Endoscopic stenting

European Society of Gastrointestinal Endoscopy recommends that temporary self-expandable metallic stent (SEMS) placement can be considered for the treatment of leaks, fistulas, and perforations. No specific type of stent can be recommended, and the duration of stenting should be individualized [79].

A multicentric retrospective study including 68 patients with AL (40% of them with total gastrectomy and the rest of them with esophageal surgery), showed that within a median 9 days after surgery, SEMS using covered stents and internal drainage were successful in 90% of cases [80].

One study of 85 AL (using 63 clipping and 23 covered stents) showed that the closure rate was lower for duodenal/jejunal site compared to gastric site or esophageal site (60%, 86.1%, 94.1%, p=0.031). Together with intraabdominal abscesses, the duodenal stump site of leakage represented factors of unsuccessful closure [81].

One of the complications of SEMS is embedding into the esophageal mucosa by the 4th–6th week after stent placement. Massive granulation tissue can result in partial esophageal stricture by the 8th week or later, and for this reason the partially covered stents should be avoided in such patients.

Another complication is migration because the stent is not anchored. Fixation of stents could be done with clips or suturing systems, but migration cannot be completely avoided: 13% for anchoring with clips method [82] and 17% for suture fixation [83].

The external fixation of stents by using of special covered stents with silk thread fixed to the patient’s ear lobe using tape was associated with 85.7% success rate [15], but this is uncomfortable for the patient.

The “Niti-S Beta” stent is a novel stent designed to minimize the risk of stent migration and to simplify the removal of

stents for leakage or fistula after bariatric surgery. They have 92% healing rate from the first stent placement, higher than for thread-fix stents (53.8%), with a 7% migration rate [84].

Sometimes the stent is situated far from the gut wall, cannot cover the entire fistula tract and it allows liquids and saliva to access into the anastomotic defect. If the perianastomotic collections develops, especially if this is infected, an internal drainage using double pigtail stents should be used for controlling sepsis [82], mainly if endoscopic vacuum therapy is not available.

Endoscopic Vacuum Therapy

The principle of endoscopic vacuum therapy (EVT) consists in the placement intra- or extra-luminally of a polyurethane foam connected via a tube to a vacuum device by applying continuous negative pressure. The aim is of cleaning the anastomotic site, producing shrinkage of the peri-anastomotic cavity. The direct effect of negative pressure to the wound surface has been termed “micro-deformation” and it can be observed as small granulation tissue nodules after removal of the porous connecting material [85].

A polyurethan sponge is tailored to the size of leakage and it is attached to a naso-gastric tube connected to an electronic vacuum device and continuous suction pressure (100 to 125 mm Hg). The sponge is changed endoscopically in 3 to 5 days. The possible complications are bleeding, avoided by wrapping the sponge with a non-adhesive, permeable foil [86] and postinterventional stricture of the gut lumen [87].

In a retrospective study of 39 patients with gastrectomy for GC, followed-up for 17 months, there were 11 EVT patients who healed successfully and two cases (7.1%) from 28 patients treated with SEMS who failed to heal. Anastomotic stricture occurred one case (9.1%) in EVT and four cases (14.3%) in SEMS within 1 year after endoscopic treatment. The median treatment duration of EVT was shorter than that of SEMS (15 days vs 36 days; p<0.001) [86]. Similar results were obtained in other retrospective small study [88].

Another retrospective study included patients who received SEMS (n=76) or EVT (n=35) for oncologic gastroesophageal surgery. The overall closure rate in the final treatment analysis was 85.7% for EVT and 72.4% for SEMS (p=0.152). Intensive care stay ranged from 0 to 60 days (median 6 days) for EVT

Anastomotic leakage occurrence Day7-10 after gastrectomy Rate=5.8-5.7% (open gastrectomy), 3.3-4.1% (laparoscopic gastrectomy)		
Diagnosis • fever, tachycardia, abdominal pain and/or acute abdomen, high CRP, leukocytosis • CT scan± contrast swallow ± endoscopy	Risk factors • patient characteristics: low albumin, diabetes, corticotherapy, NSAIDs, visceral adiposity • surgical technique : open >laparoscopic/robotic, total gastrectomy only for distal gastric tumors • lack of neoadjuvant therapy	
Treatment		
Conservative In low volume leakage+ mild symptoms • Fasting • Parenteral or enteral nutrition • Antibiotics • Percutaneous drainage	Endoscopic of small size< 2cm • Stenting • Vacuum therapy • Clipping • Suturing	Surgical In severe sepsis or failure of other treatments

Fig. 2. Management of anastomotic leakage after gastrectomy

and from 0 to 295 days (median 9 days) for SEMS ($p=0.704$), proving no difference between the two methods [89]. Long duration of treatment was associated with neoadjuvant treatment and a large leakage opening [90].

A more recent system EsoSponge (Braun, Aescula AG, Tuttlingen, Germany) was successful in 74% of 28 patients with AL after upper gastrointestinal surgery [91]. Another small retrospective study included nine patients successfully treated with EVT in eight patients (88%), with six mean number of endoscopies, 14 mean days of therapy, and 38 mean days of hospitalization [92].

A meta-analysis including four retrospective studies with esophagectomy and gastrectomy for oncologic reasons including 164 patients compared the EVT to stenting showed the same success rate ($OR=1.59$) and the same duration of hospitalization, but lower number of devices in SEMS group and lower short-term complication rate in EVT group ($OR=0.25$) [93]. Another meta-analysis including 559 patients with gastrectomy and esophagectomy proved 81% closure defect for EVT and 65% for SEMS, with lower mortality for EVT patients, although many confounders were encountered in the selected studies [94]. A previous meta-analysis including AL after esophageal surgery proved that EVT was significantly associated with a higher rate of leak closure ($OR=3.14$), more endoscopic device changes, a shorter duration of treatment (pooled median difference: -11.90 days), and a lower mortality rate ($OR=0.39$) [95], but no meta-analysis exists for vacuum therapy in AL after gastrectomy for gastric cancer.

The stent-over-sponge procedure is a technical variant of EVT that combines polyurethane sponges with covered SEMS placement, with 75% successful rate [96]. Main advantages are that it maintains the gastrointestinal lumen opened after the insertion of sponge into the extraluminal cavity, protecting the periluminal cavity from the saliva contamination and it prevents the SEMS migration due to the negative pressure applied on the foam. An esophageal hybrid SEMS (VACStent®) was used in a small number of cases and seems promising [97]. The device consists of a sponge cylinder around the stent which fixes the device to the intestinal wall like a suction cup and seals it against the intestinal lumen > it is preferred once the extraluminal cavity is contained and granulated. The main benefit is that it avoids the gastrointestinal obstruction of the standard EVT, and it allows to feed the patient, with 76% success rate (38 of 50 patients included) [98].

Endoscopic Injection

Histoacryl injection at the AL after total gastrectomy was successful in 87.5% (7 of 8 patients) with a mean hospital stay after injection of 13.8 days [99]. Also, fibrin glue injection in conjunction with stenting was reported as successful [100].

Endoscopic Clipping

If the fistula is not too large and fibrous, placing hemoclips around the fistula and tightening them with a detachable snare or endoloop could be a good solution. Clips alone are efficient in 50% of cases [101]. Over-the scope clips are difficult to be used after gastrectomy due to difficult position of the endoscope, but in old studies the rate of technical success was 86.7% and the need for surgical correction after clip placement was 7.4% [102].

Endoscopic Suturing

The Overstitch Endoscopic suturing system allows full-thickness placement of interrupted or continuous sutures using a double-channel therapeutic endoscope (Overstitch) or alongside a single-channel endoscope (Overstitch SX) [103]. Limited experience exists with its use for AL after gastrectomy due to AL position which limits the movement of the device.

Surgical Treatment

Surgical treatment is indicated as early reintervention in high-volume fistulas with clinical impact before systemic inflammatory response syndrome and sepsis to appear, for patients with severe sepsis or when conservative and/ or endoscopic treatment has failed. It is necessary in about 10% of cases, with mortality rate up to 62% [80]. The clinical success for surgical treatment of AL was 87%, similar to 80% for endoscopic treatment, but the in-hospital mortality was lower for endoscopic treatment compared to surgery (6.4% vs. 35.8%) [104]. The surgical bail out treatments (esophageal exclusion/spit fistula/J-tube placement) is recommended only in very frail patients.

PREVENTION

Preventing AL is crucial, and good preoperative nutrition, precise surgical techniques, and proper understanding of anastomotic devices are essential. The integrity of the ring of tissue retained in the circular stapler after completion of the anastomosis should be confirmed and additional suturing is required to reinforce the anastomosis. Supplementary reinforcement materials such as fibrin or a degradable extracellular matrix scaffold derived from porcine urinary bladder were used in small series with good results [105, 106].

CONCLUSIONS

Anastomotic leakage after gastrectomy for GC represents an important postoperative complication. Early recognition and treatment in multidisciplinary team is compulsory. Most of the cases respond to conservative or endoscopic therapy. Surgery is indicated as early reintervention in high-volume fistulas, or when conservative and/ or endoscopic treatment has failed.

Conflicts of interest: None to declare.

Authors' contribution: R.S. and A.S. conceived the study. D.P. and A.G. collected data. R.S. and G.D. analysed the data. A.S. and C.P. drafted the manuscript. G.D. revised the manuscript. All the authors read and approved the final version of the manuscript.

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