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REVIEW

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Exploring the boundaries of anastomotic leak: experience in a high-volume center

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Abstract

Background Gastric cancer remains a major global health challenge, ranking fourth in cancer-related deaths. Total gastrectomy with lymphadenectomy is the standard treatment, with advancements in surgery shifting towards minimally invasive techniques to reduce surgical trauma and metabolic response. Esophagojejunal anastomotic leak is a frequent complication of gastrectomy, significantly increasing morbidity and mortality rates by up to 64%.

Materials and methods A retrospective cohort study reviewed adults undergoing total gastrectomy for gastric cancer who developed esophagojejunal anastomotic leaks. The study described patient characteristics, diagnostic methods, and management at Clinica Universitaria Colombia from 2013 to 2023.

Results Among 500 patients who had total gastrectomy, 54 developed esophagojejunal leaks. The cohort was 64.8% male, average age 55.2 years (± 14.87), and average BMI 24.5 kg/m^2. Notably, 18.5% smoked, 11.1% had lung disease, and 9.3% had heart disease or diabetes. Chest tomography was used in 60% of cases, followed by endoscopy in 35.2%. Endoscopic management with fully covered stents was the main strategy, used in 84% of cases. Average hospitalization was 18 days, with 33% needing intensive care, and overall hospital stay was 23.31 ± 16.33 days. Patients undergoing neoadjuvant and elective laparoscopic surgeries had a significant 30-day mortality risk.

Conclusions Despite advances in surgical techniques and perioperative management, esophagojejunal anastomotic leaks continue to represent a serious complication, increasing morbidity and mortality. Therefore, early postoperative detection, based on the patient's clinical signs that allow confirmatory studies to be performed, is crucial. This facilitates the implementation of timely treatments, whether conservative, through the use of endoscopic or percutaneous strategies, or surgical procedures. The next step for the scientific community will be to conduct studies with long-term follow-ups to ensure consistency of the high-quality results reported so far.

Keywords Anastomotic leak, Gastric cancer, Esophageal stent, Gastrectomy, Endoscopy

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Introduction

Gastric cancer remains a global public health challenge, ranking as the fourth leading cause of cancer-related death in both sexes, being one of the most lethal malignant tumors, and the foremost nationally, with a five-year survival rate of 20% [1]. Despite therapeutic advances that have allowed for chemotherapy and targeted molecular therapy regimens, the current gold standard treatment remains gastrectomy with lymphadenectomy [1, 2].

Advancements in surgery have led to the evolution of minimally invasive surgical techniques, allowing for radical resection followed by esophagojejunostomy in cases of total gastrectomy, thus restoring gastrointestinal tract integrity, minimizing surgical trauma, and attenuating the metabolic response to trauma [3]. Despite advances in perioperative care in gastrointestinal surgery, some postoperative complications appear unavoidable; among these is esophagojejunal anastomotic leak following total gastrectomy, with reported incidences varying from 4 to 31% across different high-volume centers in the East and West, directly increasing morbidity and mortality rates up to 64% [3, 4].

The occurrence of an anastomotic leak negatively impacts patients by reducing quality of life, prolonging hospital stays, increasing costs, and raising morbidity and mortality associated with surgical interventions, potentially doubling mortality rates to 50% [5, 6]. Therefore, identifying risk factors for esophagojejunal anastomotic leaks is crucial, as is identifying different management strategies to influence these outcomes [7]. Patient-specific characteristics such as nutritional status, preoperative anemia, age over 65 years, decreased physiological function at the time of surgery, sarcopenia, smoking, obesity, steroid use, as well as tumor-related factors, and intraoperative and anatomical factors like tissue perfusion, degree of invasion, anastomotic tension, minimally invasive surgical techniques, and surgical team experience, are all relevant factors to consider [7–9].

Standardization of surgical technique has facilitated the implementation of intraoperative methods and strategies to assess anastomotic integrity, such as intraoperative endoscopic evaluation, air leak tests, or methylene blue tests. Early identification postoperatively based on clinical signs allows for confirmatory studies and timely institution of conservative treatments or through endoscopic, percutaneous, or surgical procedures [8, 9].

To date, there is no consensus on the diagnostic or therapeutic approach; reintervention, which involves the creation of a new anastomosis poses a high risk of morbidity and mortality. Additionally, due to tissue fragility, present inflammation, adherence formation distorting anatomy, and overall patient deterioration, there is a high risk of repeated leaks; esophageal diversion is now considered a last resort procedure. The development of endoscopic and minimally invasive techniques, utilizing covered stents, endoscopic clips, negative pressure endoscopic therapy, has allowed for a growing percentage of successfully treated anastomotic leaks [10, 11].

The objective of this study is to describe the diagnostic and therapeutic approach with percutaneous, endoscopic, and/or surgical interventions for patients with esophagojejunal anastomotic leaks following radical laparoscopic total gastrectomy, identifying related factors that may characterize patients requiring close monitoring and early treatment to prevent progression to potentially fatal complications.

Methods

Population

An observational cross-sectional cohort study was conducted, including adult patients who underwent laparoscopic total gastrectomy with a histologically confirmed diagnosis of gastric cancer by the gastrointestinal surgery group at Universidad Colombia Clinic in Bogotá, D.C. The study period spanned from 2013 to June 2023.

Inclusion criteria comprised patients with clinical suspicion, imaging or endoscopic diagnosis of esophagojejunal anastomotic leak following total gastrectomy. Esophagojejunal anastomotic leak was defined by clinical findings characterized by changes in surgical drainage characteristics associated with inflammatory response, secondary acute abdomen due to peritonitis, radiological findings indicating anastomotic dehiscence such as perianastomotic collections or contrast medium leakage, and endoscopic findings demonstrating disruption of the esophagojejunal anastomosis.

Exclusion criteria included patients who underwent subtotal gastrectomy, gastric tumors deemed inoperable, loss to follow-up within the first 30 days, or incomplete information on the studied variables.

Review of medical records was conducted individually by investigators using the SOPHIA version 7.0.4 clinical records management system for hospitalization data, with auditing by a second investigator.

Since 2016, Universidad Colombia Clinic has implemented an early rehabilitation and recovery program targeting patients scheduled for gastrointestinal surgery. This approach aimed to prepare patients across all perioperative phases to optimize their physical, functional, and nutritional status before surgery, thereby facilitating a faster and more effective recovery post-operation.

Statistical analysis

For continuous variables, descriptive measures such as mean and standard deviation were calculated. These measures provide a general understanding of the central tendency and dispersion of the observed values in the

dataset. Regarding discrete variables, they were analyzed individually by determining frequencies and percentages.

Results

After reviewing the medical records of 500 patients who underwent laparoscopic total gastrectomy with esophagojejunostomy L-L in PI, all surgeries were performed with curative intent; a sample of 54 patients was selected based on specific inclusion and exclusion criteria. Of the total, 64.8% ($n = 35$) were male, with a mean age of 55.2 years (± 14.87) and a mean body mass index (BMI) of 24.5 kg/m² (range: 15.2–34). It was observed that 18.5% had a history of smoking, followed by pulmonary disease (11.1%), cardiovascular disease and diabetes mellitus (9.3%). These general characteristics are detailed in Table 1.

Regarding histopathological analysis, 29 patients presented with intestinal-type adenocarcinoma, followed by 14 patients with the diffuse subtype. Among these, 38.9% were classified as stage 3, while 25.9% and 24.1% corresponded to stages 1 and 2, respectively. Additionally, 60.7% of the patients received neoadjuvant chemotherapy, given the data collection period over the last 10 years, patients were initially treated with the MAGIC protocol and later with FLOT, based on studies demonstrating superior overall survival rates. Currently, FLOT is the standard perioperative chemotherapy regimen at our institution. Analysis of the population showed that 15.2% received the MAGIC regimen, while 48.5% of patients were treated with FLOT. Finally, 64% of the patients received some form of adjuvant therapy.

Regarding intraoperative characteristics, gastric mobilization and lymph node dissection were performed laparoscopically, following the Japanese guidelines for gastric cancer treatment. The technique for creating the esophagojejunal anastomosis was a Pi latero-lateral approach, as described by Xing J [12].

Eighty-seven percent (87%) of the patients underwent laparoscopic total gastrectomy, with only 5.6% requiring conversion to open surgery. Roux-en-Y reconstruction was the most commonly used anastomosis technique, performed in 93% of cases.

During the study follow-up, a higher incidence of anastomotic leaks was observed in the years 2023, 2019, and 2021, possibly due to an increase in surgical procedures performed during those periods Fig. 1.

Average surgical time was 252 ± 74 min, with intraoperative bleeding averaging 264.8 ± 260 cc. In our population, an average of 27.18 ± 13.6 lymph nodes were retrieved. All patients underwent total gastrectomy with esophagojejunostomy. The JGCA guidelines recommend a D1 or D1-plus lymphadenectomy for cases with clinically negative lymph nodes, which involves the removal of perigastric lymph nodes and station 7. When lymph nodes are clinically positive, the JGCA treatment guidelines recommend a D2 lymphadenectomy, which includes

Table 1 Demographic characteristics, nutritional status, and pathological history of patients with anastomotic leak

Demographic Characteristics	
Variable	N = 54
Age (years)	58 (44, 67) [a]
Sex	
Female	19 (35%) [b]
Male	35 (65%) [b]
Body Mass Index (BMI) (kg/m²)	25 (21, 44) [a]
Nutritional Status	
Underweight	5 (9.3%) [b]
Obesity	3 (5.6%) [b]
Normal weight	35 (65%) [b]
Overweight	11 (20%) [b]
History	
Smoking	10 (19%) [b]
Cardiovascular disease	5 (9.3%) [b]
Type 2 diabetes	5 (9.3%) [b]
Pulmonary disease	6 (11%) [b]

[a] Median (Interquartile Range), [b] n(%)

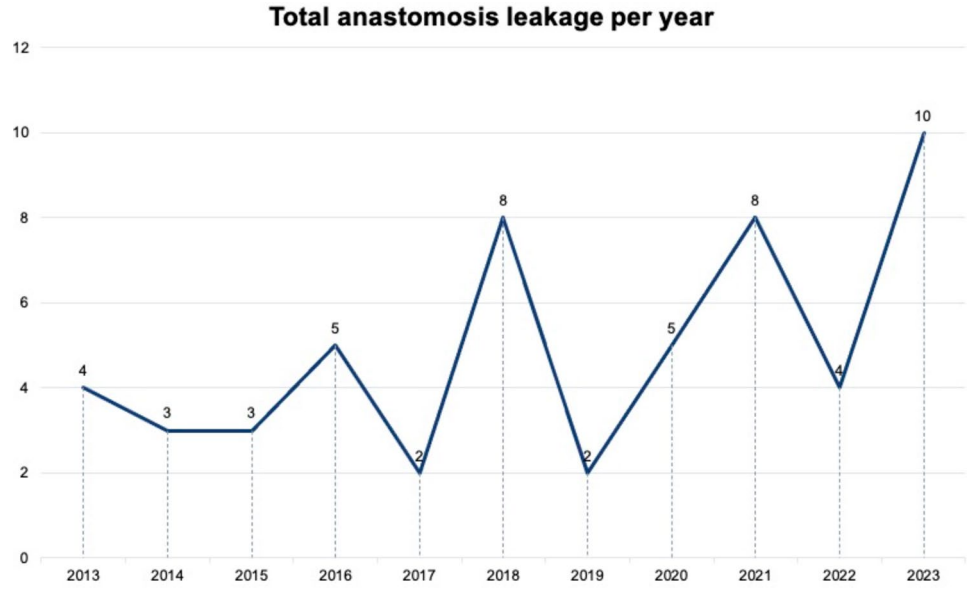

Fig. 1 Estimation of the percentage of anastomotic leaks by year. *Source*: Authors' own creation

the removal of stations 12a, 11d, and 10 during total gastrectomy. In our population, 72.7% of patients underwent D2 lymph node dissection.

Additionally, 37% of patients required intraoperative drainage placement, and 33.3% were managed in the Intensive Care Unit postoperatively. In 5.6% of cases, intraoperative leak was diagnosed using methylene blue testing, leading to reinforcement of the corresponding suture Table 2.

During the 10-year data collection period, in the first 3 years prior to oral intake initiation, a gastrointestinal tract study was conducted as part of the protocol. The diagnostic suspicion of anastomotic leak was based on clinical signs, such as documented tachycardia in 61% of patients ($n = 33$), and changes in drainage characteristics observed in 16.7% of patients ($n = 9$). Chest CT scan was the most commonly used diagnostic method, accounting for 60%, followed by gastrointestinal endoscopy in 35.2% of cases; Among the latter, 45 patients required stent placement and of these, 73.3% ($n = 33$) were managed jointly with a laparoscopic revision and an endoscopic prosthesis. The median time to diagnosis was 5 days after gastrectomy (range 1–13 days) Fig. 2.

The primary therapeutic strategy employed in these patients was endoscopic management, specifically the placement of fully covered self-expandable esophageal stents, used in 84% of cases ($n = 45$) (Fig. 3). The average length of hospital stay was 18 days, and only 33% of patients required postoperative intensive care ($n = 18$), with a mean stay of 3.33 ± 7.2 days in the unit. The average overall hospital stay was 23.31 ± 16.33 days.

Various therapeutic strategies were implemented, including: (1) conservative treatment, involving measures such as fasting, administration of antibiotics, nutritional support (enteral or parenteral), placement of nasojejunal tube, and the option of percutaneous drainage; and (2) surgical treatment, encompassing drainage, repair, or reoperation to correct the anastomosis.

In our series, 7.4% of patients required percutaneous drainage, while 72.2% required surgical reintervention. The primary reason for reintervention was esophagojejunal anastomotic leak, observed in 50% of cases. Among patients with anastomotic leak, 35.2% were classified as Clavien-Dindo grade 3B, followed by 16.7% classified as 3 A and 11.1% as 4 A. Finally, mortality associated with anastomotic leak was 25.9%. Figure 4 illustrates the different therapeutic approaches employed in our patient cohort.

Finally, Chi-square tests were conducted, determining that patients with anastomotic leak who underwent neoadjuvant therapy and scheduled surgeries, especially those performed laparoscopically, showed a significant association ($p < 0.05$) with mortality within the first 30 days of follow-up. This variable did not show a significant association with the histological type of gastric cancer, tumor stage, type of gastrectomy, or type of reconstruction ($p > 0.05$).

Discussion

Surgical resection remains the curative treatment for gastric cancer but is still affected by high rates of postoperative morbidity and mortality. The incidence of complications associated with gastric cancer gastrectomy ranges from 19.9 to 40% [13]. A French study reported a postoperative leakage incidence of 7.1%, while a German study reported 7.5% following total gastrectomy [9, 14].

Table 2 Systemic and Surgical Treatment Characteristics in Patients Diagnosed with Anastomotic Leak

Perioperative and Surgical Treatment	
Variable	**N = 54**
Neoadjuvant Therapy	34 (63%) [b]
Adjuvant Therapy	9 (21%) [b]
Scheduled Surgery	49 (92%) [b]
Laparoscopy	47 (87%) [b]
Conversion	3 (5.7%) [b]
Type Gastrectomy	
Total	50 (93%) [b]
Subtotal	2 (3.7%) [b]
Atypical	2 (3.7%) [b]
Type of Reconstruction	
Roux-Y	50 (93%) [b]
Billroth I	2 (3.7%) [b]
Billroth II	1 (1.9%) [b]
Surgical Time	240 (205,293) [a]
Bleeding	200 (100, 300) [a]
Lymph Nodes	26 (17, 32) [a]
Drain	20 (38%) [b]

[a] Median (Interquartile Range), [b] n(%)

Various strategies have been implemented to prevent these complications. Preoperatively, emphasis has been placed on nutritional replenishment and control of comorbidities. Intraoperatively, adequate tissue perfusion has been prioritized to ensure sufficient blood supply to the gastric remnant. In cases of total gastrectomy, preserving mesenteric vessels around the Roux limb is considered essential. Additionally, efforts have been made to reduce excessive tension at the anastomosis and minimize factors that predispose to suture failure or stapling technique [15].

In 2015, consensus was reached on standardizing complications associated with esophagectomy, providing an infrastructure for data collection and facilitating future comparative studies. It classifies leaks into Type 1, where the defect is local and treatment is medical/conservative; Type 2, where the defect requires interventionist treatment but not reoperation (percutaneous puncture, endoscopy, stent placement); and Type 3, where the defect necessitates reoperation to resolve [16].

During intraoperative procedures, various methods have been employed to assess anastomotic integrity, such as air (pneumatic) testing and methylene blue testing. Studies have shown that intraoperative diagnosis of leakage with methylene blue varies between 3.2% and 7.4%, with sensitivity of 60% (95% CI: 14.7–94.7%) and specificity of 93.4% (95% CI: 87.2–97.4%), respectively [17, 18]. However, intraoperative diagnosis of leakage allows for additional intraoperative interventions. Kanaji et al. [19] demonstrated that patients with positive intraoperative methylene blue tests who received additional suturing did not develop postoperative anastomotic leaks. However, anastomotic leakage occurred in nine patients (4.9%) with negative leak tests. Factors independently predicting a positive leak test included history of gastrectomy ($p < 0.01$), blood loss ≥ 500 g ($p < 0.05$), and age ≥ 75 years ($p < 0.05$). In our cohort, the average surgical

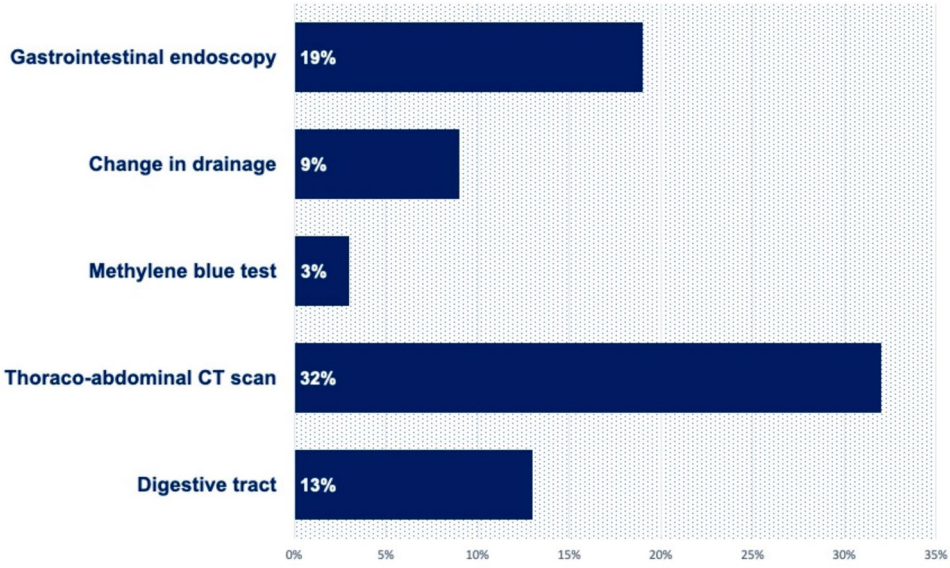

Fig. 2 Diagnostic Methods for Esophagojejunostomy Leak. *Source* Authors' own creation

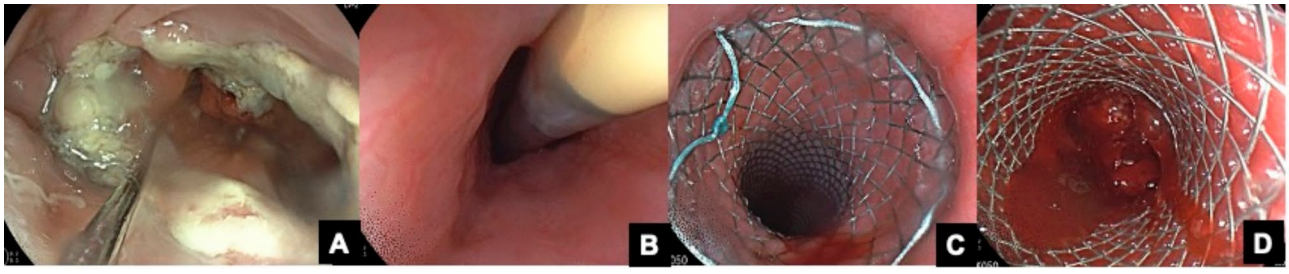

Fig. 3 Digestive tract endoscopy A. Esoenteric anastomosis covered with fibrin with an 8mm discontinuity. B. C. and D. Insertion of a partially covered esophageal stent (18mmx123mm)

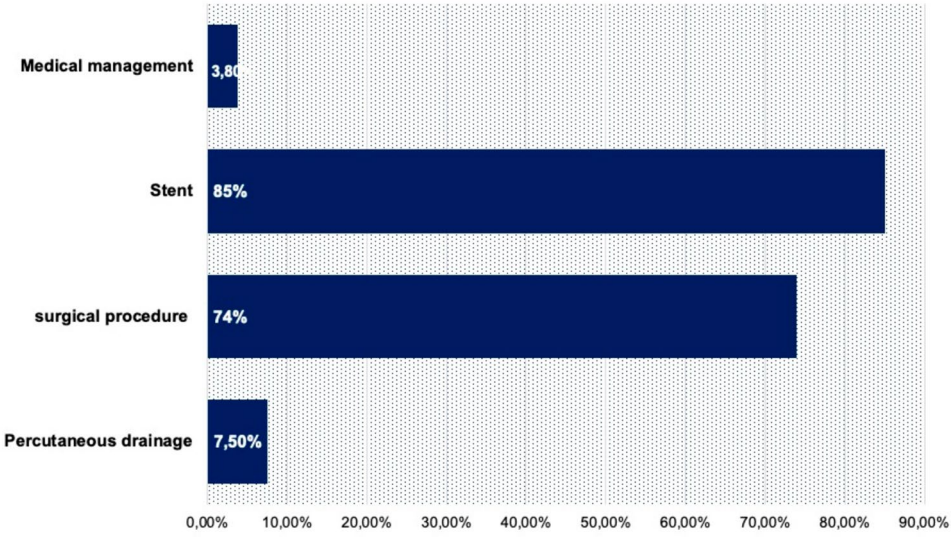

Fig. 4 Distribution Diagram According to Management

time was 252 ± 74 min, and intraoperative bleeding was 264.8 ± 260 ml. Intraoperative diagnosis of leakage with methylene blue was performed in 5.6% of patients, with suture reinforcement performed accordingly.

Numerous studies have attempted to establish different biomarkers for diagnosing anastomotic leakage following total gastrectomy with esophagojejunostomy, including C-reactive protein (CRP) and leukocytes, prealbumin, procalcitonin, albumin, and interleukin (IL)-6. Ji et al. used CRP and achieved an area under the curve of 0.99 with very high cut-off points [20]. The neutrophil-to-leukocyte ratio (NLR) has been studied as a predictor of leakage, as it increases early in patients with esophagojejunostomy who developed leaks, achieving an area under the curve of 0.78 on postoperative day 3, making it a suitable test [5].

In our series, the most prevalent histological diagnosis was intestinal-type adenocarcinoma followed by diffuse-type adenocarcinoma, respectively. Regarding oncological stage, 38.9% were classified as stage 3, followed by stages 1 and 2 at 25.9% and 24.1%, respectively. Diagnosis of leakage was suspected based on clinical signs, such as tachycardia documented in 61% of patients. Additionally, 16.7% of patients showed changes in drainage characteristics. The most commonly used study for diagnosing anastomotic leakage was chest CT, followed by upper digestive endoscopy Fig. 5.

Early diagnosis of anastomotic leakage is based on a high index of suspicion leading to endoscopic, fluoroscopic, and/or tomographic studies. Radiological findings confirming clinical suspicion may include pneumoperitoneum, contrast medium extravasation, fluid collection and/or abscesses, as well as detection of air bubbles in the perianastomotic fluid collection and thickening of the wall at the anastomosis site [16]. In some reports, upper digestive endoscopy has demonstrated 100% sensitivity and specificity for detecting anastomotic leakage [17].

While several researchers have classified the degree of anastomotic leakage, there is no universally accepted classification. However, the Clavien-Dindo classification is currently used, considering the type of required treatment. In our series, 35.2% were classified as Clavien-Dindo 3B, followed by 3 A and 4 A grades at 16.7% and 11.1%, respectively. Finally, mortality associated with anastomotic leakage was 25.9%.

Treatment strategies

Treatment measures are categorized into three categories: conservative treatment, endoscopic treatment, and surgical treatment. The choice is based on the patient's clinical condition, the level of anastomotic leakage, the extent of the discontinuity, and the timing of diagnosis [12]. In situations of early leakage with sepsis, multi-organ failure, signs of peritonitis, or jejunal loop ischemia, surgical treatment is recommended. In contrast, if the leakage is late, asymptomatic, or minimally symptomatic, conservative management with intensive

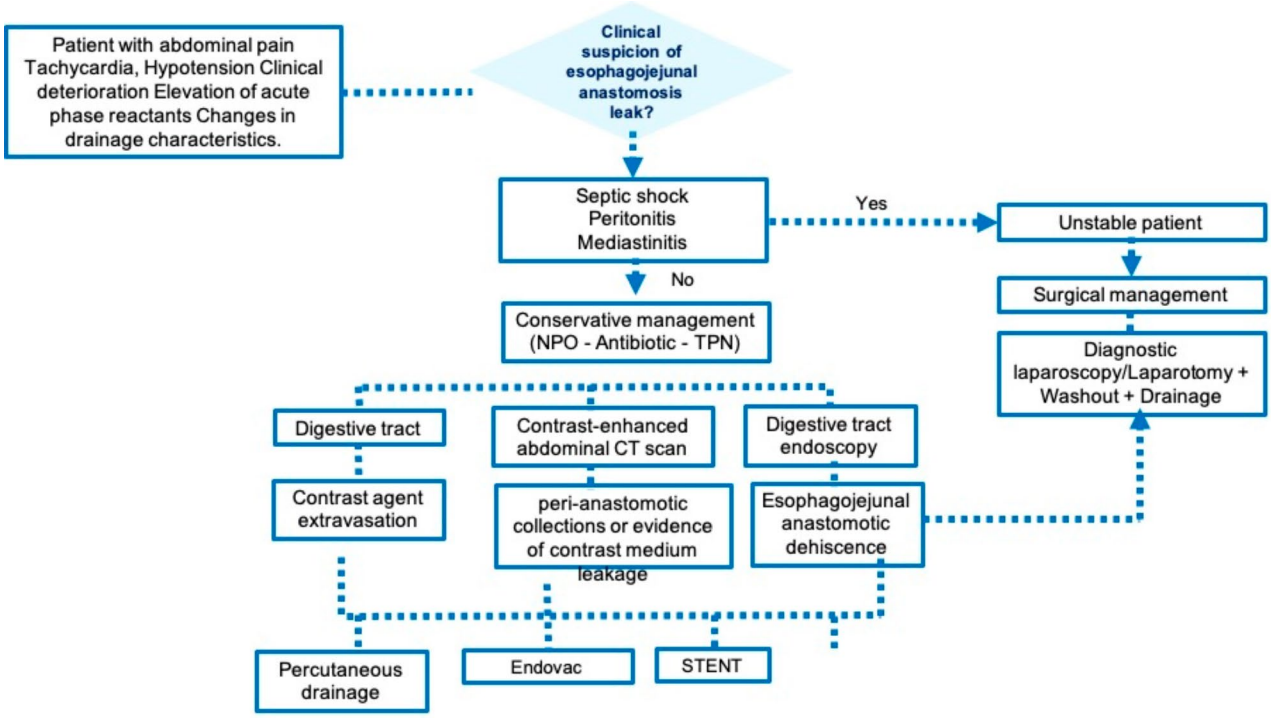

Fig. 5 Evaluation and treatment algorithm for managing esophagojejunal anastomotic leakage. Developed by the authors

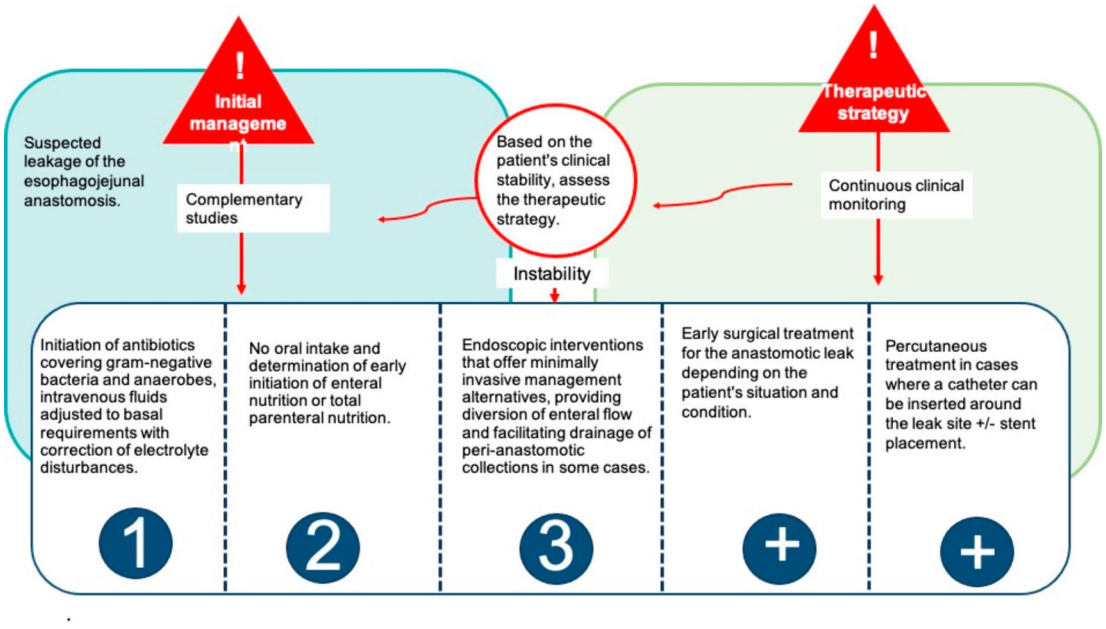

Fig. 6 Therapeutic approach for esophagojejunal leaks. *Source* Authors' own work

monitoring may be considered. In cases of perianastomotic collection, percutaneous drainage or endoscopic management aimed at draining the collection should be considered. If conservative treatment fails, surgery should be performed without delay [13] Fig. 6.

Regarding endoscopic management, there are different interventions that offer minimally invasive management alternatives. The choice of intervention will depend on both patient characteristics and the leak itself; however, in general, endoscopic management is indicated for leaks smaller than 2 cm and involving less than 70% of the anastomotic circumference [21].

In the scenario of acute presentation leaks, primary closure methods are preferred, such as the use of fully covered self-expandable metal stents, clips, or endoscopic sutures, although the latter are not widely available in our setting. The use of fully covered self-expandable metal stents and plastic stents has demonstrated a success rate of approximately 87.7%, with removal within 4 to 8 weeks after insertion [22]. While adverse event rates are not negligible, most can be managed conservatively, making this technique widely accepted for managing these patients.

Adhesive sealants may also be used as adjunct therapy, which can be glues like cyanoacrylate or protein derivatives of coagulation, with fibrin sealants being the most commonly used in this scenario. These mechanically occlude the defect in the wall and promote healing by inducing a cellular response to tissue damage and promoting extracellular matrix formation. Adhesive sealant success has been described between 55.7% and 96.8% and is often used adjunctively with other techniques [21].

When leakage is chronic, these primary closure techniques are less effective due to the presence of epithelialized fibrotic tissue. Therefore, management should focus on optimizing cavity pressure gradients to allow proper drainage of collections, where present, and second-intention closure of the cavity through granulation tissue formation. In this case, vacuum-assisted closure endoscopic therapy and fully covered self-expandable metal stents are often used.

Endoscopic vacuum-assisted closure therapy (E-VAC) involves endoscopically placing a polyurethane dressing connected to a suction device at the fistula level, providing continuous drainage of perianastomotic collections, promoting microcirculation, and supporting granulation tissue development for proper healing. It is considered a minimally invasive, safe, and effective technique [23]. Initially developed for managing leaks and fistulas in colorectal anastomoses, its use has expanded over time to other parts of the gastrointestinal tract. Recent studies have demonstrated its efficacy, particularly in esophageal cancer, with ongoing attempts to explore its use following gastric cancer surgery [24, 25].

In our population, the most commonly used endoscopic therapeutic approach was the placement of fully covered self-expandable esophageal stents, based on the availability of this procedure in our institution and institutional experience.

In 2017, Kuehn et al. [8] published a review on endoscopic vacuum therapy for various upper gastrointestinal tract defects, including 210 patients treated with E-VAC. The overall resolution rate was achieved in 180/210 patients (90%), with lower mortality, a lower incidence

of stenosis, and no difference in treatment duration compared to stent treatment.

In cases requiring emergency surgery, a laparoscopic and/or open approach is determined for irrigation, drainage, and closure of the leak site or revision of the anastomosis to control the infectious focus. However, surgical treatment invariably correlates with a higher mortality rate compared to conservative and endoscopic approaches [26–29]. During the study follow-up, the years with the highest anastomotic failures were 2023, followed by 2019 and 2021, respectively, which may be explained by the increased number of surgical procedures performed in those years.

This study has several limitations. First, it is a single-center study with a relatively small sample size. Additionally, its retrospective and observational design, combined with the limited sample size, constrains the generalizability of the findings. To address these limitations and confirm the safety and effectiveness of standardized management for esophagojejunal leaks in patients with gastric cancer, multicenter studies are needed.

The relevance of this manuscript contributes to the development of a more effective diagnostic approach for managing anastomotic leaks and creating a diagnostic algorithm that facilitates the implementation of strategies for early management of these situations.

Conclusions

Despite advances in surgical techniques and perioperative management, anastomotic leakage at the esophagojejunal junction remains a serious complication that significantly increases morbidity and mortality. A key prognostic factor is early postoperative detection, based on clinical signs and supplemented by confirmatory studies. In our cohort, intraoperative tests such as the use of methylene blue were implemented, allowing for the detection of leaks in 5.6% of cases intraoperatively, in which the anastomotic suture was reinforced. Clinically, the presence of a leak was suspected with signs such as tachycardia, documented in 61% of patients, and changes in drainage characteristics, observed in 16.7% of cases. This facilitated timely intervention, whether through endoscopic or percutaneous strategies or surgical procedures. In our series, 7.4% of patients required percutaneous drainage, while 72.2% required surgical reintervention. These findings support the development of a diagnostic and therapeutic algorithm that considers all available strategies to reduce the morbidity and mortality associated with esophagojejunal anastomotic leakage in patients undergoing radical total gastrectomy.

Author contributions

The authors declare that there is no conflict of interest or plagiarism and attach the completed conflict of interest declaration forms, as well as, the sources of financing for this project. We have reviewed and edited the submission to omit any identifying information. I hereby submit this self-blinded manuscript for consideration in World Journal of Surgical Oncology.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The protocol (042 – 24 UNV) *"Characterization of the diagnostic approach for the treatment of patients with esophagojejunal anastomotic leakage following total gastrectomy at Clínica Universitaria Colombia during the period from 2013 to 2023"* was evaluated and approved by the Research Ethics Committee of Fundación Universitaria Sanitas.

Consent for publication

Not applicable.

Informed consent

The research protocol was evaluated and approved by the institution's research and ethics committee. According to Resolution 008430 of 1993 from the Ministry of Health, this is considered a low-risk investigation. Given that it is a retrospective study involving analysis of administrative data from medical records, obtaining informed consent was not necessary.

Use of artificial intelligence

No artificial intelligence (AI) technologies were used in the development of this research.

Competing interests

The authors declare no competing interests.

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