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ABSTRACT

Introduction: different endoscopic procedures have been proposed for the management of surgical leaks. Endoscopic internal drainage using trans-fistulary double-pigtail plastic stents has emerged as an alternative strategy, especially in fistulae presenting after laparoscopic gastric sleeve.

Methods: a retrospective case series was performed at a single tertiary care center including all upper gastrointestinal post-surgical leaks primarily managed with endoscopic trans-fistulary insertion of double-pigtail plastic stents. Clinical success was defined as the absence of extravasation of oral radiographic contrast and radiological resolution of the collection with adequate oral intake.
Results: nine patients were included, six (66.6 %) females with a median age of 52.6 years (IQR 47-60). Five cases presented after laparoscopic gastric sleeve, two cases after distal esophagectomies, one after a Roux-en-Y gastric bypass and another one after a pancreaticoduodenectomy. Fistulae measured < 10 mm in five patients (55.6 %) and 10-20 mm in four patients (44.4 %). Six were early leaks. Technical and clinical success was achieved in nine (100 %) and seven (77.8 %) cases, respectively. Seven (77.8 %) patients required ≤ 3 endoscopic procedures. The median hospital stay after the first endoscopic procedure was 12 days (IQR 6.5-17.5 days), while the overall median time until leak healing was 118.5 days (IQR 84.5-170). One patient with a post-esophagectomy intrathoracic leak developed an esophageal-tracheal fistula 37 days after stent deployment.

Conclusions: our results support the use of endoscopic internal drainage in postsurgical abdominal leaks, regardless of the type of surgery. Although only two patients with intrathoracic dehiscence were included.

Keywords: Double-pigtail stents. Endoscopic internal drainage. Gastrointestinal surgery complications. Leaks.

INTRODUCTION
Anastomotic leaks are among the most severe complications following upper gastrointestinal surgery. Their incidence ranges between 2 % after laparoscopic sleeve gastrectomy (1), 5.3 % after Roux-en-Y gastric bypass (RYGBP) (2) and 5-30 % after esophageal anastomoses (3), with mortality rates of up to 18.9 % (3). Clinical presentation of anastomotic leaks includes perianastomotic collections, pneumothorax or pneumoperitoneum, abscess formation and mediastinitis (4).

Surgery has historically been the preferred management strategy to control the infection and close the dehiscence. Surgery is still the preferred management strategy in cases of mediastinitis, severe sepsis or a large fistula involving more than 50 % of the anastomotic circumference. However, less invasive endoscopic approaches have been proposed for cases presenting with milder symptoms (4). Reported endoscopic procedures include deploying covered self-expandable metal stents (cSEMS) (5,6),
fibrin glue (7), endoscopic suturing (8), endoluminal vacuum therapy (9) and fistula closure with over-the-scope clips (OVESCO) (10). These techniques have achieved variable clinical success rates, ranging from 37 to 86 % (1,3,6-9).

Endoscopic internal drainage (EID) has recently been proposed as a promising alternative to treat anastomotic leaks. It consists of deploying double-pigtail stents (DPS), with one end inside the collection and the other in the intestinal lumen. It drains the collection diverting the flow into the empty intestinal lumen, while also inducing the growth of granulation tissue. Thus, promoting the closure of the fistula. This procedure can be performed with a gastroscope or duodenoscope. Most available studies of EID assess laparoscopic sleeve gastrectomy (LSG) leaks, achieving leak closure rates of 74.6 % (11) and up to 85 % when employed after other failed endoscopic treatments (12). Studies that assess its results in non-LSG related upper gastrointestinal leaks are scarce. Bouchard et al. reported a case series including 28 LSGs and five patients with a Roux-en-Y gastric bypass with an overall clinical success rate of 78.8 % (13). Whereas another case series showed optimal results in four anastomotic leaks following upper and lower gastrointestinal surgeries (14).

Thus, we decided to report our experience treating upper gastrointestinal leaks using EID with DPS insertion, assessing its efficacy and adverse events.

METHODS
The present study is a retrospective case series performed at a single tertiary care center in Spain. All patients or their next of kin provided informed consent for all the procedures performed. The study was approved by the local Institutional Review Board (PI008-20).

Participants
All patients undergoing endoscopic treatment of postsurgical anastomotic leaks or fistulae after upper gastrointestinal surgeries between May 2017 and June 2019 were included. Patients were identified using a prospective database of the Endoscopy Unit, including all subjects undergoing advanced therapeutic procedures. After identifying all patients undergoing endoscopic management of fistulae, medical records were
reviewed to include those with a previous upper gastrointestinal surgery. Since May 2017, we use the EID with transmural DPS as first line treatment of postsurgical anastomotic leaks in our endoscopic units.

**Inclusion criteria**
The only inclusion criterion was the endoscopic treatment of upper abdominal abscesses secondary to post-surgical leak or fistulae with trans-fistulary insertion of DPS.

**Exclusion criteria**
Patients with at least one previous attempt of surgical treatment.

**Procedures**
All endoscopic procedures were performed under sedation by the interventional endoscopist with propofol +/- midazolam, without oro-tracheal intubation, unless critically ill. Broad-spectrum antibiotic treatment was started at the time of diagnosis. A gastroscope (Olympus GIF 160 Gastroscope) was used to evaluate the leak (Fig. 1), cannulate the orifice and insert one or more 5-7 cm 7 Fr DPS (Advanix™, Boston Scientific, Massachusetts or Visio® G.Flex Europe, Belgium) after guidewire insertion (Jagwire™ 0.035in, Boston Scientific) (Fig. 2A). The stents were deployed through the leak, placing one end inside the collection and the other inside the gastrointestinal lumen, in order to achieve drainage. The size of the DPS was chosen at the discretion of the endoscopist. We used the 5 cm DPS for smaller collections and the 7 cm DPS for the larger ones. Furthermore, we chose to insert one or more DPS according to the size of the fistula orifice.

Systematic endoscopic follow-up was performed to assess the fistula and consider the removal or exchange of the DPS (Fig. 2B). Timing was decided at the discretion of the attending physician. In the case of a persistent abscess or collection, further endoscopies were performed until complete resolution of the leak.

**Definitions and outcomes**
Postsurgical leaks were defined as the extravasation of radiographic contrast in the computed tomography (CT) scan confirmed by upper gastrointestinal endoscopy. The time until onset and location of the fistula were defined according to the United Kingdom surgical infection study group (15). Briefly, the time until onset was classified as acute (onset on post-operative day [POD] 1 to 7), early (POD 8 to 48), delayed (POD 49 to 84) and chronic (presenting beyond 12 weeks after surgery). Technical success was defined as the correct trans-fistulary deployment of at least one DPS. Clinical success was defined as the absence of extravasation of oral radiographic contrast accompanied by the radiological resolution of the collection and adequate oral intake. Leak healing was defined as leak closure observed on endoscopy with withdrawal of the DPS, with no need for further exchange and the absence of collections on CT scan. Treatment failure was defined as the need for surgery, other endoscopic treatments or death. Adverse events were graded according to the American Society for Gastrointestinal Endoscopy (ASGE) recommendations (16).

Data retrieval
Endoscopic data were retrieved from the advanced endoscopic procedures database, which includes patient’s demographics and variables describing the procedure. Other patient data (demographics, radiological findings, clinical outcomes and adverse events) were retrospectively retrieved from medical electronic records. Clinical management and follow-up were performed according to the attending physician’s decision. Patient data were collected into a newly created database. In cases of unclear or contradictory statements in the medical records, a consensus decision was made.

Statistical analysis
The statistical analyses were performed using IBM SPSS Statistic version 15.0 (Inc. IL. USA). Continuous variables were presented as the mean and standard deviation or median with interquartile range (IQR), as appropriate. Categorical variables are presented as numbers and percentages.

RESULTS
Participants
Between May 2017 and June 2019, a total of nine patients presenting post-surgical anastomotic leaks presented to our Endoscopy Unit. Two patients underwent urgent laparotomy after the leak diagnosis without finding its exact location. Therefore, they did not receive surgical treatment. Thus, all patients were included in the final analysis. Six (66.6 %) patients were female and the median age was 52.6 years (IQR 47-60). Most leaks were secondary to LSG (five cases). However, there were also two cases after distal esophagectomy and lymphadenectomy with gastric pull-up, one presenting after a RYGBP and another after a pancreaticoduodenectomy (Whipple procedure) with gastrojejunostomy. The comorbidity assessment via the ASA system were five ASA III patients, three ASA II patients and one ASA IV patient. One third of patients were in the Intensive Care Unit at the time of the procedure, due to the severe clinical conditions.

Characteristics of leaks and fistulae
The diameter of the fistula was measured as < 10 mm in five patients (55.6 %) and 10-20 mm in four patients (44.4 %). In the two patients with previous esophagectomy, the location was intra-thoracic in the esophagogastric anastomosis. Regarding locations, in the patient with a previous Whipple procedure it was a gastrojejunal anastomosis and in the patient who underwent a RYGBP it was in the gastric pouch. In the remaining LSG, the location was in the proximal gastric staple line. Anastomotic leaks were identified a median of nine days (IQR 3-31) after surgery. Most fistulae (66.6 %) were classified as early leaks; the remaining three (33.3 %) were acute. The median time between surgery and the first endoscopic procedure was 14 days (IQR 7-34 days). The number of endoscopic procedures per patient was as follows: one procedure (n = 1), two procedures (n = 5), three procedures (n = 1) and four procedures (n = 2).

Endoscopic procedures
Fluoroscopic control for cannulation and insertion of the guidewire to deploy the DPSs was used in all patients. Most procedures were performed with a gastroscope but an
Endoscopic ultrasound was used in two cases to deploy the DPS. Seven patients received two DPS, the remaining two received only one. In four out of five patients with a previous LSG, an antral balloon dilation to allow an adequate gastric emptying was performed due to postsurgical distal staple line stenosis. Further postsurgical collections besides those communicating through the fistulae were observed in two cases who required simultaneous percutaneous drainage of synchronous collections, not amenable to endoscopic drainage. Both were cases following LSG; the first case was a 50-year-old female presenting a 10 x 7 cm collection and the other case was a 36-year-old female who presented a 4 x 7 cm collection.

Outcomes
Technical and clinical success was achieved in nine (100 %) and seven (77.8 %) cases, respectively. Two patients were deemed to be treatment failures. A 68-year-old female who underwent a Whipple procedure for an ampullary adenocarcinoma developed a 10 to 20 mm leak in the gastrojejunostomy anastomosis. Subsequently, she presented an intraperitoneal hemorrhage from a ruptured gastroduodenal aneurysm, causing hemorrhagic shock seven days before the endoscopic procedure. Despite initial clinical improvement, the patient died 38 days after surgery due to multiple organ dysfunction. This adverse event was not considered to be related to the endoscopic procedure, as the aneurysm was not in the vicinity of the collection and it presented before placing the DPS. The second case of treatment failure was due to the development of an esophageal-tracheal fistula (see below).

The median hospital stay after the first endoscopic procedure was 12 days (IQR 6.5-17.5 days). The median time until the first follow-up endoscopy was 87 days (range: 21-171 days, IQR 40-146 days). The overall median time until leak healing was 118.5 days (IQR 84.5-170), ranging from 71 to 208 days.

Adverse events related to the endoscopic procedure
Two patients developed stent-related adverse events. A patient with a LSG presented moderate upper gastrointestinal bleeding due to a mucosal erosion by a DPS 128 days after the index endoscopy. Neither endoscopic treatment nor blood transfusions were
required. Another patient with a previous esophagectomy and gastric pull up developed a tracheoesophageal fistula. The patient was readmitted 37 days after stent deployment, complaining of fever, cough and chest pain. On endoscopy, a persistent fistula was noted, so the DPS was removed and a SEMS (Wallflex®) was deployed. Despite the endoscopic intervention, the patient persisted with cough and purulent sputum. A bronchoscopy confirmed a 1-cm-size orifice of an esophageal-tracheal fistula 2 cm above the carina (Fig. 3). We hypothesized that the proximal end of the DPS was responsible for the tracheal perforation. Two attempts of endoscopic suture of the orifice were unsuccessful. Repeated bronchoscopies were performed with the instillation of ethanol with an endoscopic needle and BioGlue® (CryoLife Inc., Kennesaw, Georgia). Complete healing of the fistula was achieved after three months.

**DISCUSSION**

Our study is the first single center retrospective case series assessing the outcomes of EID in upper gastrointestinal postsurgical anastomotic leaks or fistulae in Spain. Apart from LSGs, we also included other different upper gastrointestinal surgeries. Overall, clinical success was achieved in seven cases (77.8 %), although it reached 100 % in LSG but dropped to 50 % in non-LSG cases.

The endoscopic approach in post-surgical leaks seems to be widely accepted. The deployment of SEMS remains the most popular endoscopic approach, but a poor tolerance and high migration rate of up to 83 % have been reported (17). EID has shown excellent results in post-LSG leaks. A recently published systematic review of 385 patients with gastric leaks following LSG, reported overall clinical success rates of 83.4 % and 84.7 % when only first line treatment was included. Furthermore, a low complication rate (13.7 %) and good tolerance have been reported (18). Reported adverse events include bleeding, drainage migration, perforation, gastrobronchial fistula, splenic hematoma, stricture, bleeding ulcer, peritonitis and wall incarceration (18). In addition, this rate seems to vary greatly when used as first line or second line treatment. Gonzalez et al. reported a 47 % overall adverse event rate when used as a second line treatment, while it was only 4.7 % when only first line treatment was considered (19).
We included four patients with surgeries different from LSG, two cases after distal esophagectomy and lymphadenectomy with gastric pull-up, one presenting after a RYGBP and another after a Whipple procedure with gastrojejunostomy. In these patients, the clinical success was achieved in only two cases. One failed case presented a severe adverse event (esophageal-tracheal fistula requiring various endoscopic treatments and prolonged hospital stay) and the second one did not reach clinical success as she died due to complications unrelated to the endoscopic treatment (rupture of a gastroduodenal artery aneurysm which presented seven days before the endoscopic procedure). Three studies assessing the use of EID with DPS in leaks presenting after surgery different from LSG have been published. Firstly, Donatelli et al. reported nine cases with previous upper gastrointestinal surgeries other than LSG (three total gastrectomies, three cholecystectomies, tumorectomy of retroperitoneal cancer, distal esophagectomy and esophageal diverticulotomy). However, only five cases were anastomotic leaks. There were only two (22.2 %) clinical failures, both following total gastrectomy with esophageal-jejunal anastomosis; one presented a perforation on POD 1 and the other a persistent gastric leak (14). Secondly, Bouchard et al. reported five cases after GPB with another 28 LSGs, observing a combined clinical success rate of 78.8 % (13). Lastly, the largest case series published to date by Donatelli et al. included exclusively patients following RYGB using EID by DPS. Thirty-three patients were included and clinical success was achieved in 31 (93.9 %) (20). The median length of stay after the procedure (12 days) and the need for intensive care in three patients demonstrates the complexity of these patients. The median time until leak healing was prolonged (118.5 days), but patients were attended in the outpatient clinic. This is similar to the interval to leak healing data reported by Giulani et al. (118.1 days, range: 55.5-227) (18).

The paucity of published reports in supradiaphragmatic postsurgical leaks is even higher than in non-LSG procedures. Donatelli et al. reported five cases (three leaks in the esophagojejunal anastomosis following a total gastrectomy, one case in the esophagogastric anastomosis and one case in the esophageal staple line) (14). Only three (60 %) achieved clinical success. In our series, we identified a severe esophageal-tracheal fistula and a success rate of 50 %. Interestingly, Meunier et al. reported an
esophago-pericardial fistula following EID using a DPS in a LSG, requiring surgical treatment (21). Including the two cases from our series, DPS has achieved clinical success in four (57.1 %) patients, with two (28.6 %) severe adverse events among the seven reported cases. These results raise serious concerns regarding the use of DPS in intrathoracic fistulae.

In our protocol, the endoscopist decided to remove the DPS. According to our experience, it should not be done before three months. In our series, the median time until the second endoscopist procedure was 87 days. In the case of good clinical evolution, no radiological images were required for the removal. Furthermore, if no replacement was needed due to successful leak closure, no additional endoscopic procedure was used for the closure of the orifice.

There are several limitations to our study. Firstly, the limited number of patients included did not allow us to draw firm conclusions. Secondly, the retrospective design misses interesting data, especially regarding the endoscopic procedure. However, the strict clinical follow-up allowed us to adequately retrieve all primary and secondary outcomes. Thirdly, there might be a selection bias, as the decision to refer patients for endoscopic therapy was made by the attending surgeon. Finally, as concluded by other case series and retrospective studies, the lack of prospective multicenter studies precludes the assessment of the role of the expertise of the endoscopist. This aspect could be determinant in the feasibility and use of this technique (13,18).

In summary, our results support EID with transmural double-pigtail stents in leaks and suture-line dehiscence as a highly effective method for abdominal postsurgical fistulae, regardless of the gastrointestinal surgery involved. However, we included only two cases of intrathoracic leaks.

REFERENCES


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LSG: laparoscopic sleeve gastrectomy; PD: pancreaticoduodenectomy; GBP: Roux-en-Y gastric bypass; E: esophagectomy and lymphadenectomy with gastric pull-up.
Fig. 1. Post-surgical leak following a laparoscopic gastric sleeve in a 45-year-old female. A suture dehiscence in the proximal staple line in the gastroesophageal junction is seen.
Fig. 2. A. Endoscopic image of a fistula in a laparoscopic gastric sleeve in a 45-year-old female. A double-pigtail plastic stent can be observed accessing the collection through the fistula, while a guidewire is inserted to deploy a second double-pigtail stent. B. Endoscopic view of the same patient obtained 95 days after stent placement and just after stent removal, where the fistula is completely closed.
Fig. 3. Bronchoscopic view of an esophageal-tracheal fistula secondary to an endoscopic internal drainage of a postsurgical leak in a patient with previous esophagectomy and gastric pull up using double-pigtail stents. The plastic stent can be observed through the fistula.