Efficacy and safety of the Luso-Cor^{Ò} esophageal stent compared to other endoscopic techniques in the management of fistulas and anastomotic dehiscences after upper digestive tract surgery (ES-LCCE-UDFM)

21st February 2025

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Introduction

The global prevalence of obesity has prompted an increase in bariatric surgery, which is the only management strategy that provides long-term weight loss and improvement of obesity-related diseases.[1,2,3] Bariatric surgeries include sleeve gastrectomy(SG), Roux-en-Y gastric bypass(RYGB),and laparoscopically adjustable gastric banding(LAGB).[1] The incidence of adverse events depends on the type of bariatric surgery performed, with serious adverse events occurring in approximately 4% and mortality in 0.1% patients.[1,4,5] The incidence of fistulas after SG varies between 0.2% to 2.5% and between 1% and 4.9% in patients who have undergone an RYGB.[1,2,5,6,7,8] The incidence of strictures after SG is approximately 0.35%.[6] Older, more obese, and male patients with multiple comorbidities related to obesity are at increased risk for the development of fistulas and mortality following bariatric surgery.[7,9,10]Additionally, reoperative surgery after LAGB increases the risk of complications.[7,10]

The morbidity and mortality related to adverse events increases with surgical re-exploration at the site of a fistula orifice,[8,9,10,11]. For this reason, management of fistulas after bariatric surgery has shifted from a surgical to a primarily endoscopic approach, primarily with covered metallic stents, with fistula closure success rates between 75% and 100%.[1,2,12,13] However, a primarily endoscopic approach is demanding in terms of

resource use, and the high incidence of stent migration often requires multiple reinterventions — both endoscopically and surgically.[2,11,14,15]

The Luso-Cor® esophageal stent was designed to take into account altered anatomy after bariatric surgery and to overcome strictures in the gastric tube, which can be concomitantly present in patients with fistulas following SG. A pilot study involving 15 patients with fistulas after sleeve gastrectomy managed with the Luso-Cor® esophageal stent showed a 100% rate of fistula closure, low rate of adverse events with only one episode of stent dysfunction[16].

A recent meta-analysis suggested that endoscopic vacuum therapy (EVT) was associated with a 21% increase in successful fistula closure compared to self expanding metallic stents (RD 0.21, CI 0.10-0.32; P = 0.0003), a 12% reduction in mortality compared to stenting (RD 0.12, CI 0.03-0.21; P = 0.006) and an average reduction of 14.22 days in duration of treatment (CI 8.38-20.07; P < 0.00001). Additionally, EVT was associated with a 24% reduction in adverse events (RD 0.24, CI 0.13-0.35; P = 0.0001. There were no statistical differences between the studied therapies regarding the length of hospital stay[17].

Therefore, in this study, we aimed to evaluate and compare the success of the novel Luso-Cor esophageal stent® in the exclusion of fistulas, reinterventions, stent-related adverse events, duration of hospitalization and its efficacy in the management of fistulas after SG compared to other stents or EVT.

Hypothesis of the study

The novel concept of esophageal anchoring of a specially designed long stent may be useful in management of fistulas after gastric surgery with high success rate and minimal morbidity compared to conventionally available esophageal or bariatric surgery stents and EVT.

Objectives of the study

To evaluate and compare the performance of the Luso-Cor® oesophageal stent with other stents or EVT in management of fistulas after bariatric and oncologic surgery on the upper digestive tract with regard to:

- Technical success defined as successful deployment of the stent at the desired location and exclusion of the fistula orifice.

- Clinical efficacy defined as successful closure of the fistula orifice after stent removal.

- Safety – Early and late adverse events related to stent placement.

-Duration of hospitalization

- Number of endoscopic procedures required till fistula closure

- Mortality

Inclusion criteria

Patients undergoing endoscopic management of fistulas after bariatric surgery or dehiscences of esophago-jejunal or gastro-jejunal anastomosis after esophageal or gastric oncologic surgery will be included in the study.

Exclusion criteria

- Pregnancy

- Age < 18years

- Inability to give informed consent.

Type of study: Prospective observational multicentre study.

Materials and methods

Conventional covered metallic and bariatric surgery stents and EVT will be used as per standard of care.

Design features of the Luso-Cor® esophageal stent: This is a specifically designed stent to manage fistulas after sleeve gastrectomy, Roux-en-Y gastric bypass and esophago-jejunal anastomotic dehiscences after total gastrectomy. This metallic stent measuring 24 cm in length is covered with silicone and has three sections: 1) A proximal flared portion with diameters of 30, 34 and 36 mm measuring 6 cm in length; 2) Middle narrow portion with a

fixed diameter of 20 mm measuring 16 cm in length; and 3) Distal flared portion with a fixed diameter of 30 mm measuring 2 cm in length.

Esophageal anchoring, is achieved through the larger diameter of the proximal flared portion compared to conventional stents and a 5 mm uncovered portion located 1 cm below the proximal edge of the stent. The remainder of the stent is covered with a thin silicone coating. This contrasts with the conventional partially covered metallic esophageal stents which usually have at least 1 cm of uncovered portions near the proximal and distal edges.

There are two zones within the middle narrowed portion of the stent which allow articulation of the stent on itself up to 90°. This allows the stent to adapt to altered anatomy and peristaltic activity of the foregut. The distal flared portion of the stent is designed to be placed in the gastric antrum or in the proximal jejunum, to avoid peri-stent reflux of enteric fluid.

Radio-opaque markers are placed at the proximal and distal edge of the stent and at the junction of the proximal flared portion with the middle narrow portion, unlike conventional metallic esophageal where the radio-opaque markers are placed at the stent edges and in the middle.

Stent placement: Placement of the stent is done by over the wire technique and ideally with X-ray imaging control. It can also be done with endoscopic control by the bedside in emergencies. The distal edge of the stent should be placed at least 2 cm proximal to the pylorus and the proximal flared portion should be placed in the distal esophagus, at least 2 cm above the esophago-gastric junction or esophago-jejunal anastomosis. During stent delivery, after verifying opening of the distal flare of the stent near the pylorus, the endoscopist should focus on the radio-opaque markers in the proximal portion of the stent which are separated by 6 cm so that the proximal flare is liberated in the distal third of the esophagus.

Due to the usually smaller diameter of the esophagus in women, we recommend the use of the Luso-Cor^{Ò} esophageal stent with proximal flare of 30 mm diameter in women and 34 and 36 mm diameters in men. However, the endoscopist should choose the ideal diameter based on the endoscopic assessment of the esophageal lumen diameter prior to stent placement.

After deployment, the stent should be kept in place for at least 4 weeks and up to a maximum of 12 weeks. An oral contrast study should be done 48 to 72 hoursafter stent deployment to confirm effective exclusion of fistula orifice after which oral dietary intake may be commenced. All patients should receive proton pump inhibitors (PPIs) twice a day with a recommendation for head elevation in the supine position to decrease reflux esophagitis.

Stent Removal: Stent removal is easy compared to conventional stents. It requires ablation of the mucosal ingrowth in the 5mm uncovered portion near the proximal edge of the stent with argon plasma 50W/1L, followed by scraping of the tissue with a cap applied at the tip of the endoscope and capture of the drawstring at the proximal edge of the stent with a rat tooth forceps.

Clinical data and management strategy of patients with fistulas or anastomotic dehiscences:

The type of stent used or option for use of EVT as first line endoscopic option will be at the discretion of the endoscopist.

The Luso-Cor® esophageal stent was approved for clinical use in Portugal in 2016 by regulatory authorities (INFARMED).

After diagnosis of fistulas, whenever required, patients should undergo surgical peritoneal toillete either by laparotomy or laparoscopy with placement of abdominal drains.

Informed consent for endoscopic procedures to manage fistulas or anastomotic dehiscences will be obtained from all patients.

The location and size of the fistula orifice will be determined and the presence of concomitant stricture of the gastric tube noted endoscopically.

Fistulas will be considered as acute if endoscopy was performed within one month of surgery and chronic if performed >1 month after surgery.

Whenever possible, the fistula orifice will be closed with either through the scope clips(TTSCs) or the over the scope clips(OTSCs). Small fistula orifices measuring <5 mm will be initially managed with either TTSCs or OTSCs.

The Luso-Cor^{Ò} esophageal stent may be used as the first option in patients with fistula orifices >5 mm either alone or in combination with OTSCs or TTSCs, in those patients who have fistula persistence after initial application of TTSCs or OTSCs or in those with concomitant stricture in the gastric tube detected endoscopically.

Gastroesophageal reflux disease after stent placement will be managed with double dose PPI and sucralfate 1g up to 4 times a day.

Definitions

Technical success will be defined as correct placement and coaptation of the stent at the previously planned location under fluoroscopic imaging with radio-opaque markers with effective exclusion of fistula orifice.

Clinical efficacy will be defined as closure of the fistula orifice after Luso-Cor^{Ò} esophageal stent removal. Definitive closure of the fistula orifice should be confirmed by contrast injection during endoscopy and / or oral contrast study after Luso-Cor^{Ò} esophageal stent removal.

A secondary endpoint of clinical efficacy will be the effectiveness of the Luso-Cor^{Ò} esophageal stent or other stents in managing fistulas in the gastric tube after vertical gastrectomy.

Stent related adverse events will be defined as **early** (within 1 week of stent placement) and **late** (> 1 week after stent placement) and include stent migration, perforation, hemorrhage, stent fracture and mortality.

Primary outcome for this study will be closure of the fistula orifice after stent removal. **Secondary outcomes** will be effectiveness of the stent in managing strictures in the gastric tube, stent-related adverse events, number of endoscopies, motives for endoscopic reinterventions and the number of stents used, duration of hospitalization and fistula or stent-related mortality.

Simple fistulas will be defined as fistulas communicating between a hollow organ and the peritoneum or pleura (Gastro-pleural or gastro-peritoneal).

Complex fistulas will be defined as fistulas communicating between two hollow organs (Gastro-bronquial) or between a hollow organ and the skin (Gastro-cutaneous) or those with sub-divisions and multiple trajectories in continuity with a fistula orifice.

All procedures will be performed in accordance with the ethical standards of the institution and with the 1964 Helsinki declaration.

Statistical Analysis

Qualitative data will be presented as percentages and quantitative data as median (Min-Max). Factors at baseline predicting technical success, clinical success, clinical efficacy and development of adverse events will be evaluated using the Logistic regression analysis.

Qualitative data will be compared with the Chi-square test and quantitative data will be compared with the Student´s t test or Mann-Whitney test if the distribution is normal or non-normal.

Multivariate analysis will take into account all factors at baseline associated with the outcomes measured ($p<0,1$) and will be performed using the backward stepwise regression.

A p value <0,05 will be considered statistically significant.

Data will be analyzed using IBM® SPSS 21 (SPSS Inc., Chicago, IL, USA).

Parameters analyzed in the study: Please refer to Case Report Form (CRF)

Study Chronogram

December 2023 – Ethics committee approval

January 2024 to January 2025 – Implementation of the study.

January 2025 to April 2025 – Data analysis

May to October 2025 – Publication of the study results and presentation of data at national and international scientific meetings

Potential benefits from the study

- This observational study aims to compare the efficacy and safety of the main forms of endoscopic management of fistulas and anastomotic dehiscences after bariatric and oncologic surgery in the upper digestive tract.

- The new concept of esophageal anchoring of the Luso-Cor ® esophageal stent and the two articulated segments in the middle portion of the stent should improve the adaptability of the stent to altered anatomy and decrease the risk of migration.
- The new stent design will probably decrease the number of endoscopies required to manage fistulas after bariatric surgery and esophago-jejunal and esophago-gastric anastomotic dehiscences and may decrease the number of adverse events many of whom are related with migration of conventional esophageal stents.
- The reduction of endoscopies required to manage the fistulas and potential early resumption of oral feeding and shorter hospitalization with the Luso-Cor esophageal stent compared to conventional stents and EVT should improve the cost efficacy of fistula management.

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