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Lights and shadows of three endoscopic techniques as organ-sparing alternatives to surgery for anastomotic leaks after esophago-gastric surgery: results and data analysis of an Italian referral single center for gastrointestinal disease treatment

Anastomotic leak following upper gastrointestinal (UGI) surgery is one of the most fearsome complications, as it leads to a longer hospitalization and a significant increase in patients' morbidity and mortality.[1-3] Nowadays, endoscopy has gained more importance in healing of such defects, offering lots of minimally invasive repair techniques, such as over-the-scope clips, self-expandable-metal stents (SEMS), endoluminal suturing (overstitch devices), endoscopic internal drainage (EID) with double pigtail drains (Advanix®, Boston Scientific, Marlborough, MA, USA), or endoscopic vacuum-assisted (EVT) closure system device (Eso-SPONGE®, B. Braun Medical Ltd., Sheffield, UK).[1, 3, 4]

Since endoscopic modalities provide lower patients' mortality and morbidity, thus reducing significantly hospital stay and healthcare costs, they play a pivotal role in management of anastomotic leaks following UGI surgery.[3-5]

The aim of our article is comparing 3 endoscopic tools (EID, SEMS, EVT) for management of UGI post-surgical defects in 18 patients treated at our hospital institution from April 2018 to November 2022, reporting their impact on surgery-related outcomes. Patients had undergone a surgical operation for esophageal or gastric disease by either a robotic-assisted minimally invasive or a standard laparotomic incision method. Surgical operations included in our study are reported in Table I. Collected cases presented a fistula at the level of anastomosis, demonstrated by either contrast-medium computed tomography or esophagography.

When indicated, a percutaneous drainage of large fluid collections within mediastinum or peritoneum

TABLE I.—*Study population and surgery-related outcomes.*

Characteristics	SEMS	Not SEMS (EID or VAC)	Two devices (SEMS + not SEMS)	Overall	P value
Number of leakages, N.	7	4	7	18	
Type of disease, N. (%)					
Benign	0 (0)	1 (15.0)	1 (14.3)	2 (11.1)	0.30
Esophageal malignant	3 (42.9)	3 (75.0)	4 (57.1)	10 (55.6)	
Gastric malignant	4 (57.1)	0 (0)	2 (28.6)	6 (33.3)	
Surgical access, N. (%)					
Robotic-assisted minimally invasive	6 (85.7)	3 (75.0)	6 (85.7)	15 (83.3)	1.00
Laparotomic	1 (14.3)	1 (25.0)	1 (14.3)	3 (16.7)	
Surgical operation, N. (%)					
Ivor-Lewis esophagectomy	2 (28.6)	2 (50.0)	3 (42.9)	7 (38.9)	0.85
Fundoplication procedure for hiatal hernia	0 (0)	1 (25.0)	1 (14.2)	2 (11.1)	
Total gastrectomy	4 (57.1)	1 (25.0)	3 (42.9)	8 (44.4)	
Partial gastrectomy	1 (14.3)	0 (0)	0 (0)	1 (5.6)	
Surgical procedural time (minutes), median [IQR]	310.0 [302.5- 451.5]	482.5 [395.0-535.0]	455.0 [377.5-522.5]	432.5 [306.3-505.0]	0.69
Hospital stay (days), median [IQR]	31.0 [26.0-41.5]	37.5 [29.0-46.0]	57.0 [46.5-62.0]	45.0 [30.25-55.25]	0.02
Surgery-related complications, N. (%)					
Respiratory	3 (42.9)	1 (25.0)	3 (42.8)	7 (38.9)	0.92
Cardiac	0 (0)	0 (0)	1 (14.3)	1 (5.6)	
Sepsis	4 (57.1)	2 (50.0)	2 (28.6)	8 (44.4)	
Others	0 (0)	1 (25.0)	1 (14.3)	2 (11.1)	

SEMS: self-expandable-metal stents; EID: endoscopic internal drainage; IQR: interquartile range.

was preliminary achieved, as a fundamental prerequisite for a better outcome of endoscopic procedure. All cases were performed under deep sedation or general anesthesia.

Once directly visualized the leak through an UGI endoscopy (using a forward-view gastroscope), a fistulography was achieved, in order to assess the features of the defect (including communication with other cavities or organs). A debridement with clearance of necrotic tissue as well as lavages of cavity with fluids and hydrogen peroxide was achieved in all cases, in order to allow a better healing of the wound (reducing infection risks).

Selection of endoscopic closure approach was mainly related to the features of leakage (diameter, depth, necrotic tissue) and patients' characteristics, as well.[2, 3]

According to current literature, SEMS and EVT were preferentially chosen in case of leaks involving >30% of the circumference or in case of almost complete dehiscence, whereas EID was the approach of choice for small-size or initial disruptions.[2, 4] Regular sessions of endoscopic controls were accomplished, with an interval ranging from 2 days (for EVT) to 10 days (for SEMS), making further debridement and allowing replacement of the same tool or switching to a different device (Figure 1). Technical success was considered as a complete defect closure after endoscopic management, whereas clinical success was defined as a healing of leak and remission of systemic infection symptoms (Figure 2).

Statistical analysis was performed using R-software version 4.2.2 (The R Foundation, Vienna, Austria). Continuous variables were reported as median and interquartile range (IQR). Categorical variables were reported as numbers and percentages (%). Association

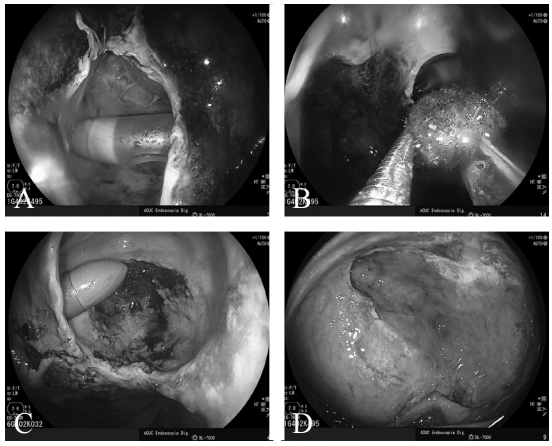

Figure 1.—Consecutive images temporally showing the progressive healing of a large anastomotic defect, effective treated by EVT. A) Early detection of the leak, with the thoracic drainage appearing through the defect. B) Forceps-assisted positioning of vacuum device at the level of the dehiscence. C) Endoscopic appearance of defect after a few regular sessions of EVT replacement. D) Complete healing of the anastomotic leak at the endoscopic control.

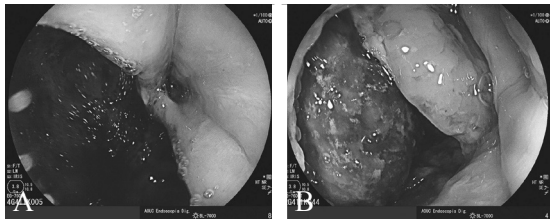

Figure 2.—Endoscopic appearance of a large anastomotic leak (>30 mm in diameter) resulting after an Ivor-Lewis esophagectomy. A) At the first detection, the wall of the cavity appears necrotic, with no evidence of granulation tissue. B) A progressive healing of the dehiscence with granulation of the wall is visible after some vacuum-device replacements.

between endoscopic devices and categorical clinical outcomes was evaluated by χ^2 test or Fisher Exact Tests, when appropriate. Association between endoscopic devices and continuous clinical outcomes was evaluated by One-Way ANOVA followed by Tuckey HSD Test, when a significant association emerged. Stratified survival analyses by endoscopic device were performed, as well. Visual inspection of survival curves was carried out with Kaplan-Meier method. Log-rank test was performed to evaluate the differences between the curves. In any case, a P value <0.05 was considered significant.

Overall, within the 18 patients collected, 16 experienced a complete healing of leak, one died during hospital stay due to a severe sepsis and one was referred to a further surgical operation (as a complete anastomotic disruption occurred). Patients were equally distributed among the following three cohorts (Table I): SEMS-group, not-SEMS group (experiencing either EID or EVT) and, finally, a combination of both SEMS and not-SEMS devices (since the endoscopist, during control sessions, considered the switch to a different device as the best choice to yield the healing process). Overall, all the 7 patients treating with two different tolls, experienced a complete repair of the dehiscence and none was re-operated.

We noticed that switching from EVT to SEMS provided an optimal healing, since the interim sponge-placement allowed an effective reduction of the cavity in diameter and depth, whereas the subsequent stent-placement sealed the residual wound.

According to univariable statistical data analysis, hospital stay was significantly shorter in the SEMS group (P=0.02). In addition, considering hospital stay as the reference continuous variable, Tuckey HSD Test (comparing cohorts between one-another) showed a significant P value whenever the switch of two different tools *versus* SEMS were compared. Mean and 95% confidence interval (CI) are reported in Table II.

Our data reaffirm Van Boeckel PGA's paper, in which temporary stent placement for esophageal leaks is described as an effective and safe endoscopic modality for management of anastomotic defects, regardless the features of the stent.[1, 2] Concerning the other parameters reported in Table I, no significant difference

TABLE II.—*Mean and 95% confidence interval.*

Groups of comparison	Mean (95% CI)	Adjusted P value
Not SEMS-SEMS	3.1 (-18.9–25.1)	0.93
Two devices (SEMS)	21.6 (2.8–40.3)	0.02
Two devices (not SEMS)	18.5 (-3.5–40.5)	0.11

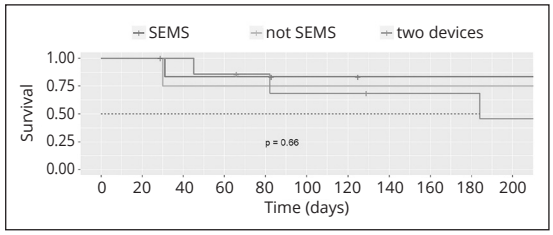

Figure 3.—Kaplan-Meier curve of follow-up time after surgery of the three cohorts included in Table I.
Log-rank test did not reveal a statistically significant P value among the groups (P=0.66).

among the three cohorts emerged from the univariable; this datum, still confirming Swinnen J's paper, may be affected by the small sample size of our single-arm retrospective study.[2] Log-rank test for follow-up did not reveal any statistically significant difference among the three groups (P=0.66) (Figure 3).

Concerning endoscopic EVT, a recently published review proposes a reliable flowchart as management algorithm for leaks.[3] In this decision-making flowchart, VAC-therapy can be adopted as interim approach in case of large diameter leaks associated to extraluminal collection, thus confirming our institutional approach, where EVT followed by stent-placement has been adopted in case of large defects.[3]

Dealing with EID, this tool is mainly accomplished in case of small defects, in which this toll may play an important role in reducing extra-luminal collections and stimulating the healing of the fistula thanks to a local traumatism.[3, 5]

In conclusion, considering our experience and literature data overview, we suggest SEMS use in case of large defect without any external fluid collection; EID may be an optimal strategy in case of very small defects, even in association to peri-anastomotic fluid collection. Literature more and more emphasize that EVT (alone or in combination with other devices) could serve as an organ-sparing alternative to surgery for large UGI anastomotic defects.[2, 3, 5]

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions
All authors read and approved the final version of the manuscript.

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