



Self-Expanding Metal Stents Versus Endoscopic Vacuum Therapy in Anastomotic Leak Treatment After Oncologic Gastroesophageal Surgery

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Received: 26 May 2018 / Accepted: 28 September 2018 / Published online: 29 October 2018
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Abstract

Background Anastomotic leak after gastroesophageal surgery is a life-threatening complication. Self-expanding metal stent (SEMS) implantation or endoscopic vacuum therapy (EVT) have been established as alternatives to reoperation. This study compares the outcome of both interventions for anastomotic leak clinical management.

Methods In this retrospective study, we identified all patients who received SEMS or EVT for anastomotic leaks after oncological gastroesophageal surgery between January 2007 and December 2016. Only patients with type II leaks according to the Esophagectomy Complications Consensus Group were included. Sealing rates, intervention-related complications, demographic characteristics, clinical history, leak characteristics, therapy duration, and in-hospital mortality were analyzed.

Results One hundred eleven patients who received SEMS ($n = 76$) or EVT ($n = 35$) were identified and categorized by primary and final treatment. The overall closure rate in the final treatment analysis was 85.7% for EVT and 72.4% for SEMS ($p = 0.152$). ICU stay ranged from 0 to 60 days (median 6 days) for EVT and from 0 to 295 days (median 9 days) for SEMS ($p = 0.704$). EVT patients were hospitalized for 19–119 days (median 39 days) and SEMS patients for 13–296 days (median 37 days; $p = 0.812$). Demographic factors, comorbidities, and surgical parameters did not correlate with treatment or treatment success.

Conclusions SEMS and EVT show comparable results for anastomotic leak management after oncologic gastroesophageal surgery. No superior outcome could be found for either one of the two treatments options.

Keywords Anastomotic leak · Self-expanding metal stent · Endoscopic vacuum therapy · Esophagectomy · Complication management

Felix Berth and Marc Bludau contributed equally to this work.

DDW 2018 SSAT PLENARY PRESENTATION, Washington D.C

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s11605-018-4000-x>) contains supplementary material, which is available to authorized users.

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Abbreviations

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Introduction

Anastomotic leaks remain one of the major clinical challenges of postoperative care in patients undergoing surgery for malignancies of the upper gastrointestinal tract. Especially in surgery for esophageal cancer, anastomotic leaks carry a significant risk for the patients. For minimal-invasive esophagectomy, the leak rate is reported to range from 15.9 to 21.2% in nationwide databases and worldwide cohorts of high-volume centers.^{1–3} In a Dutch cohort including 1282 patients who underwent esophagectomy, anastomotic leak was identified

as the predominant specific complication associated with 30-day and 90-day mortality, which was accounted for 2.9% and 7%.⁴ Furthermore, anastomotic leak was found to be an independent prognostic factor for even long-term survival after gastrectomy and esophagectomy in multicenter studies.^{5,6} Several endoscopic treatment options for leak after upper gastrointestinal surgery are clinically implemented, and mostly, retrospective studies are published evaluating the success of each therapy.⁷ A widely performed endoscopic interventional treatment is the application of self-expanding metal stents (SEMS) that are designed to cover the leak and remain in position until the leak site has healed and the success rate is reported to range between 69.3% and 91%.^{8,9} In recent years, the application of an endoscopic vacuum therapy (EVT) has become an alternative treatment option in the management of upper gastrointestinal leaks or perforations.^{10–13} So far, four studies aimed to compare outcome of SEMS and EVT treatment for upper gastrointestinal leaks or perforations. The largest cohort is presented by Brangewitz et al. including 71 patients overall and presenting favorable results for EVT in terms of sealing rate and stricture rate but included benign perforations as well as anastomotic leaks.¹⁴ The other three studies included very low number of EVT patients.^{15–17} For this reason, there is no consensus so far on whether in the specific finding of anastomotic leak after upper gastrointestinal surgery for malignancies, SEMS or EVT is to be preferred. Therefore, this retrospective study is to compare the clinical outcomes of SEMS and EVT in overall 111 patients with anastomotic leak after surgery for gastric, junctional, or esophageal cancer in a single high-volume center.

Materials and Methods

Patient Cohort

This retrospective study was performed at the Department of General, Visceral and Cancer Surgery at the University Hospital Cologne, which is a national referral center for tumor entities of the upper gastrointestinal tract (Chairman Prof. Dr. med. A.H. Hölscher until 04/2016). Only patients who underwent surgery for malignant diseases and experienced postoperative leaks of esophagojejunal or esophagogastric anastomoses were included in the analysis. The total number of oncological resections between 2007 and 2016 were $n = 1361$ esophagectomies and $n = 454$ gastrectomies. All patients with type II anastomotic leaks according to the Esophagectomy Complications Consensus Group (ECCG) classification for anastomotic leaks were identified.¹⁸ This definition considers postsurgical leaks that require interventional but not surgical therapy and was also used for gastrectomy in this study. Patients who received a self-expanding metal stent (SEMS) treatment or endoscopic vacuum therapy

(EVT) in the study period were included. The study period was chosen so that all patients that ever received EVT treatment in this institution were included. Data were collected retrospectively from our endoscopic database “Clinic WinData” (version 8.05; E&L medical system GmbH, Erlangen, Germany) and from our hospital database “Orbis” (version 08042702; Agfa HealthCare N.V., Belgium) and comprised the following information: demographic and clinical patient characteristics, details of the disease, surgical outcome data, leak characteristics, stent specification, and stent-related complications. Furthermore, clinical data from our follow-up care and the department’s quality management was included. The current study was performed by adhering to the criteria of the Local Ethics Committee (No. 17-319).

Surgery

The surgical procedures being included in this study were D2 gastrectomy and D2 gastrectomy with distal esophagus resection as well as Ivor-Lewis esophagectomy and McKeown esophagectomy. In other words, leaks of esophagojejunostomy (abdominal or mediastinal) or esophagogastrostomy (cervical or thoracic) were included. All surgical procedures were performed in a single institution in highly standardized manner. The detailed surgical procedure is explained in detail elsewhere.^{19,20}

Leak Detection and Management

In the event of a clinically suspected anastomotic leak, we performed a flexible video esophagogastroduodenoscopy (e.g., Pentax Medical, Japan; Olympus Corporation, Tokyo, Japan). If a leak could not be diagnosed with certainty, the diagnosis was followed up with other diagnostic tools (e.g., CT scan and contrast swallow). All endoscopic procedures were performed by senior endoscopic surgeons. All surgical endoscopists (H.S., T.H., S.C.) together had experience of more than 10,000 examinations in total and more than 200 esophageal cancer staging procedures per year each. The examination was performed using general anesthesia (for intubated intensive care unit patients), or a combination of midazolam (e.g., Roche Pharma AG, Germany) and propofol (e.g., Fresenius Kabi Germany GmbH) or only propofol. Anesthesiological procedures were similar for EVT and SEMS, no patient was intubated exclusively for SEMS or EVT treatment, neither in first place nor in the follow-up sessions. Any procedural decision for EVT or SEMS treatment was done by the surgeon and endoscopist when a leak was diagnosed. In the study period and after, there was no institutional preference for one therapy or the other.

SEMS

A SEMS was endoscopically inserted over a guidewire, and an introducer was used so that the stent could be inserted into the esophagus and, subsequently, released over the leak. Either a swallow x-ray, computed tomography (CT), or endoscopy was performed after the endoscopic insertion to eliminate the possibility of a persisting leak. If the diagnostics showed successful leak closure, the patient was able to drink clear fluids as water or tea. We utilized the following SEMS models: fully covered “aixstent® OEL” (Leufen Medical GmbH, Germany), “Ultraflex Covered Esophageal NG Stent” (Boston Scientific, USA) and fully covered “Niti-S™ Esophageal Stent” (TaeWoong Medical, South Korea). As clinical routine in our institution, patients stayed in hospital for the duration of SEMS treatment.

EVT

An open-pore polyurethane foam was individually adapted to the size of the leak. Using an endoscope to ensure constant observation, the polyurethane foam drainage tube was then moved to the desired location. Once the correct position had been verified, the drainage tube was moved from the oral to the nasal cavity and the endoscopist connected the drainage tube to an electric vacuum pump (e.g., VivanoTec®, Hartmann AG, Germany) and applied a defined vacuum of 125 mmHg. There was no routinely performed additional diagnostic check after the insertion of the sponge. Only if the vacuum pump shows dysfunction, an endoscopy was performed immediately to check a sponge replacement. The size of the anastomotic leak and the wound cavity behind the leak determined the treatment duration. Therapy was only considered concluded when the leak was closed or the wound cavity lined with granulation tissue. Endoscopic interval for changing the EVT was 3 to 5 days. The patients with EVT could not have any oral intake. When removing the EVT for interval change, the leak site was endoscopically evaluated for persisting or healed defect. In case of successful healing, the therapy was determined, and patient was put on oral diet starting with drinking water on the same day. For the duration of EVT treatment, patients stayed in hospital. The details of the endoscopic procedure were published beforehand.⁴

Additional Treatment

Furthermore, the endoscopist performed additional nonoperative management. A double-lumen nasogastric feeding tube (e.g., Freka® Sonde, Fresenius Kabi Germany GmbH) or a triple-lumen diverted nasogastric feeding tube (e.g., Freka® Trelumina, Fresenius Kabi Germany GmbH) was endoscopically placed directly before (EVT) or after (SEMS) intervention. The gastric lumen was to decompress the anastomotic

region and to evacuate the gastric/duodenal reflux. Enteral caloric nutrition was provided via the duodenal lumen. The nasogastric tube was left, if tolerated, until the leak was sealed successfully. Further additional treatments involved intravenous antimicrobials (including antifungals). In the event of mediastinal, pleural, or abdominal fluid collection, an external drainage of the leaks was interventionally applied, either ultrasonically guided or CT-guided.

Outcome Detection

Short-term complications were defined by the technical success of the treatment. Uneventful and successful application of the endoscopic treatment was considered a technical success. Long-term complications were defined as complications occurring after the end of endoscopic treatment: stenosis, fistula or persistent leak, and death or reoperation. To achieve a homogeneous comparison, for this analysis, we only examined patients that exclusively received SEMS or EVT. Patients that received both therapies consecutively were excluded from the complication analysis, as the complications could not clearly be connected to one therapy. Successful closure of the leak was defined as the state in which the endoscopy confirmed complete healing and the patient no longer had any clinical signs of persistent leak. We did not routinely perform contrast esophagograms for the evaluation of the definitive successful closure since there is conflicting data about their value within the diagnosis of anastomotic leaks.²¹

A failure to seal the leak was defined as one or more of the following: persistent leak or fistula at the end of the treatment or, when changing the treatment strategy, death before confirmation of healing; the need for surgical reoperation of the esophageal or anastomotic leak after the SEMS treatment or EVT; and the referral of the patient to another hospital before the stent or sponge was extracted. It was not considered as failure of treatment but as short-term complication if the SEMS or EVT needed replacement or repositioning. The secondary outcomes evaluated time to clinical success, duration of hospital stay, and complication rate.

Statistics

Distributions of quantitative variables are described as means (\pm SD) or by median and interquartile range and compared with the use of the Mann–Whitney *U* test. Qualitative variables are summarized by count and percentage and compared with the use of Fisher’s exact test. A two-sided $p < 0.05$ was considered statistically significant. Due to the small number of cases, multivariate analysis was not performed. Data were managed with the SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA) for Windows (Microsoft Corp., Redmond, WA) and Microsoft Excel version 2013 for Windows (Microsoft Corp., Redmond, WA).

Results

Demographic and Treatment Group Results

In total, we identified 111 patients who underwent SEMS treatment (63 male and 14 female; median age, 64 years) or EVT (29 male and 5 female; median age, 65 years). Ninety-three patients underwent Ivor-Lewis esophagectomy, and 18 patients D2-gastrectomy or D2-gastrectomy with distal esophageal resection. Details of the patient characteristics are shown in Table 1. The size of the leak ranged from 1/4 ($n = 63$, 81.8%), 1/3 ($n = 10$, 13%) up to 1/2 ($n = 2$, 2.6%) of the circumference of the esophagus and no description ($n = 2$, 2.6%) in the SEMS group and from 1/4 ($n = 22$, 64.7%), 1/3 ($n = 2$, 5.9%), 1/2 ($n = 5$, 14.7%) up to 2/3 ($n = 1$, 2.9%) of the circumference of the esophagus in the EVT group with 4 other leaks ($n = 11.7%$) in the pulled-up gastric tube along the longitudinal staple line or ischemia (Fig. 1). These differences in proportion of circumferential leak for SEMS and EVT were statistically significant ($p = 0.001$). Eleven out of 111 patients (10%) died as a direct consequence of leak, and 3 out of 111

patients (3%) died while the anastomosis was completely healed due to septic complications ($n = 1$) or severe pneumonia ($n = 2$), resulting in an in-hospital mortality of 14 out of 111 (12.6%) for all type II leak patients.

Details of Treatment Groups

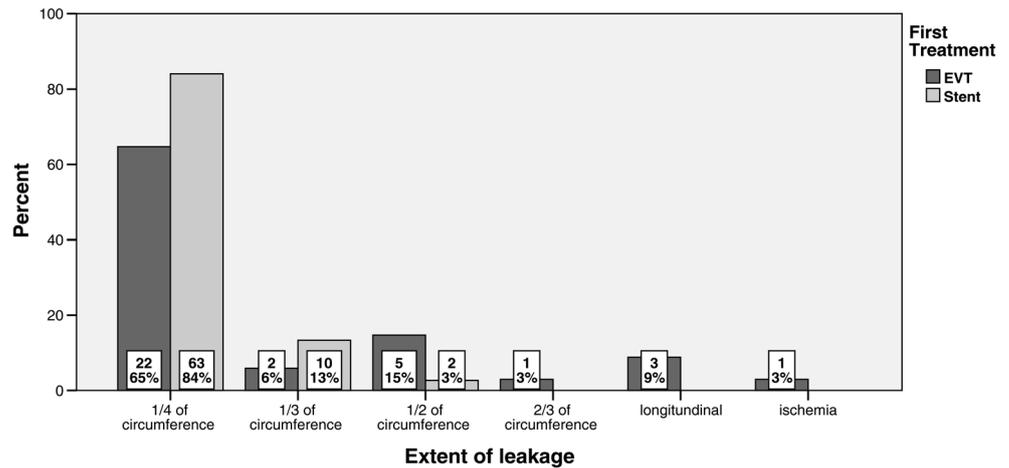
Primarily, 77 patients received SEMS and 34 patients EVT for the treatment of their leak (Fig. 2, Table 3). During the treatment period, 7 out of 8 patients in the SEMS group changed their treatment to EVT because of a failure of SEMS. In 1 out of 8 patients, the treatment was switched more than once, and the patient was finally treated with SEMS again. Failure of the primary treatment led in 6 out of 7 primarily EVT patients to ultimately switch their treatment to SEMS. In 1 out of 7 patients, the treatment was switched more than once, and the final treatment was EVT again. The reason for the switch between EVT and SEMS treatment in all of these cases was found in a persisting leak with clinical deterioration of the patient despite sealing therapy.

Table 1 Study population by primary endoscopic therapy. Values given as a number (percentage), or median (range)

	SEMS	EVT	<i>p</i> value
Number of patients	77	34	
Gender (male:female)	63:14	29:5	0.654
Age	64 (43–88)	65 (43–84)	0.732
Smoker (yes:no)	31:46	16:18	0.504
BMI	26 (16–46)	26 (17–38)	0.944
ASA score	3 (1–4)	3 (2–4)	0.792
Neoadjuvant therapy (yes:no)	50:26 [†]	18:16	0.200
Histopathology			0.054
Adenocarcinoma	46 (59.7)	28 (82.4)	
Squamous cell carcinoma	29 (37.7)	5 (14.7)	
Neuroendocrine	2 (2.1)	1 (2.9)	
Resection type			0.159
Esophagectomy	68 (88.3)	25 (73.5)	
Gastrectomy + distal esophagus resection	5 (6.5)	4 (11.8)	
Total gastrectomy	4 (5.2)	5 (14.7)	
Reconstruction type			0.091
Esophagogastrostomy	68 (88.3)	25 (73.5)	
Esophagojejunostomy	9 (11.7)	9 (26.5)	
Level of anastomosis			0.228
Neck	0 (0.0)	1 (1.3)	
Mediastinum	29 (85.3)	72 (93.5)	
Abdomen	5 (14.7)	4 (5.2)	
Days between surgery and leak detection	8 (1–23)	8 (0–58)	0.511
Days between diagnosis of leak and stenting	0 (0–37)	0 (0–7)	0.288
Number of stents/sponges	1 (1–3)	3 (1–9)	<0.001

[†] Information about prior treatments was not available for one patient

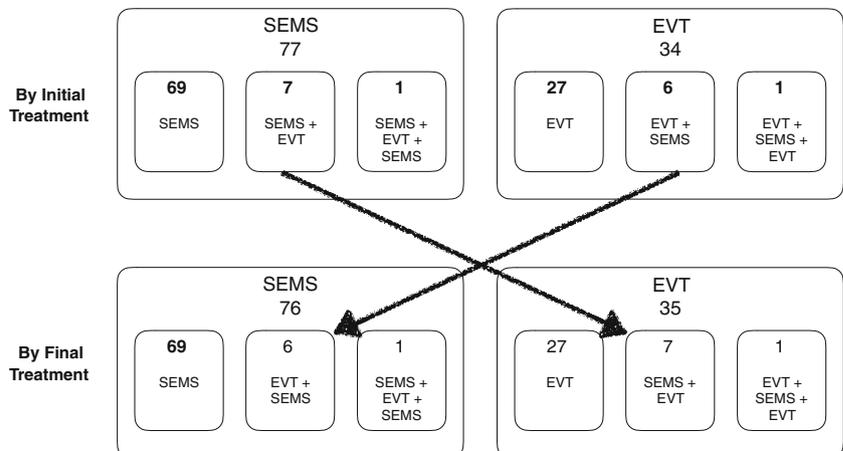
Fig. 1 Extent of leak in each treatment group (*p* value, *p* = 0.001)



SEMS Treatment

Primarily, 77 patients received a SEMS for the management of an anastomotic leak. In 8 out of 77 patients, the treatment strategy was switched, and 69 patients remained in the group until the end of the treatment. One out of 8 patients received SEMS again as a final treatment even though SEMS and EVT had not been successful in the beginning. Technical success of stenting in anastomotic leak was achieved in 51 out of 69 patients (74%). Short-term complications occurred in 18 out of 69 patients (26%), which were categorized as dislocation (*n* = 14, 20%), leak persistence (*n* = 3, 4.3%), or esophagotracheal fistula (*n* = 1, 1.4%). With regard to short-term complications, there was no significant difference between both groups (*p* = 0.614). Eighteen out of 69 patients (26%) developed long-term complications. The most frequent complications were persistent leak (*n* = 8, 11.6%), stenosis (*n* = 5, 7.2%), esophagotracheal fistula (*n* = 4, 5.7%), and perforation (*n* = 1, 1.4%). With regard to long-term complications, there was no significant difference to the EVT group (*p* = 0.137). Patients were treated with a median of one stent (range, 1–3).

Fig. 2 Graphic illustration of the composition of the groups



EVT

Thirty-four patients received EVT as their primary treatment. Seven patients switched their treatment strategy, and 27 patients remained in the group until the end of the treatment. One out of 7 patients received the EVT again as final treatment even though EVT and SEMS were not successful in the beginning. Technical success of EVT in anastomotic leak was achieved in 23 out of 27 patients (85%). Short-term complications, which were all categorized as dislocation, occurred in 4 out of 27 patients (15%) treated with EVT. Long-term complications occurred in 1 out of 27 patients (3.7%). This patient developed a stenosis in the successfully sealed anastomotic region and was treated with endoscopic dilatation (Table 2). Patients were treated with a median of three sponges (range, 1–9).

Results After Primary and Final Treatment

To compare the results of both treatment options, patients were allocated to groups according to their primary and final treatment (Fig. 2, Table 3).

Table 2 Long-term complications of the group

	SEMS	EVT	<i>p</i> value
Persisting leak	8 (11.6%)	0	0.101
Perforation	1 (1.5%)	0	1.000
Gastrotrachael fistula	4 (5.8%)	0	0.326
Stenosis	5 (7.2%)	1 (3.7%)	0.673
None	51 (73.9%)	26 (96.3%)	
Total	69	27	

The results analyzed by primary treatment are shown in Table 2. Patients were allocated based on the primary therapy, and 77 patients in the SEMS group and 34 patients in the EVT group were identified. As a significant difference, the duration of treatment was found to be significantly higher for SEMS treatment than for EVT (27 days vs. 12 days, $p < 0.001$). The statistics for ICU stay, length of hospital stay, success of treatment, and 30-day mortality were not significantly different between both treatment groups.

To analyze the difference between the two treatment groups according to the final treatment, patients were allocated according to the endoscopic treatment ultimately applied. Seven out of 77 patients from the primary treatment stent group were switched to the EVT group, and 6 out of 34 patients from the primary treatment EVT group were switched to the SEMS group (Fig. 2). One key consideration is that not all patients being switched from SEMS to EVT were recognized as a SEMS failure and patients being switched from EVT to SEMS were not recognized as EVT failure for the final treatment analysis as these cases of treatment failure were incorporated into the primary treatment group analysis. The sealing rate in the final treatment group was 72.4% in the SEMS group and 85.7% in the EVT group ($p = 0.152$). There were no significant differences with regard to ICU stay, length of hospital stay, and 30-day mortality between the two groups (Table 2).

Discussion

Management of anastomotic leak after upper gastrointestinal surgery for malignancies remains a clinical challenge, and

different therapeutic options for endoscopic treatment are under discussion. The two recently most applied treatments are SEMS and EVT. Other options such as endoscopic suture techniques and clipping are only reported in selected cases.^{7,22} Single-arm studies showed promising results for both SEMS and EVT.

Limited studies were able to compare both treatment options in order to identify which clinical findings are more suitable for one or the other treatment or even to show superior outcomes.^{9,23} Brangewitz et al. compared 39 stent (SEMS and plastic stent)-treated patients with 32 EVT cases for intrathoracic leaks. The closure rate was found to be significantly higher for EVT (84.4%) than that for SEMS (53.8%), and a higher stricture rate was found after SEMS treatment.¹⁴ This study included the highest number of patients so far, but the patients' cohorts were found to be heterogeneous, as patients after esophagectomy, fundoplication, endoscopic perforation, and Boerhaave syndrome were included. Three further studies compared outcomes of SEMS and EVT for esophagectomy or gastrectomy patients and found significant differences, but with a small cohort ($n = 20$). Schniewind et al. found a lower mortality for 17 EVT cases than for 6 matched SEMS cases in systemically ill patients (12% vs. 83%), Mennigen et al. found a higher success rate for 15 patients treated primarily with EVT in terms of anastomotic healing (93.3% vs. 63.3%), and Hwang et al. reported a lower complication rate for 7 EVT cases than that for SEMS (0% vs. 54.5%).^{15–17} In terms of the rather limited patient cohorts in these studies, the results have to be confirmed by larger studies. A recently published review and meta-analysis pooled the patients of the four studies for “esophageal leaks” and found significantly higher sealing rates, shorter treatment duration, and lower complication rates and mortality for EVT compared to SEMS.²⁴

However, our study only included patients after upper gastrointestinal surgery for malignancies. It compared 77 patients treated primarily with SEMS with 34 patients undergoing EVT for anastomotic leak and revealed a success rate of 63.3% for SEMS compared to 70.6% for EVT by primary treatment. Given the treatment strategy was changed in several patients, the analysis by final treatment shows a success rate of 72.4% for SEMS and 85.7% for EVT. Although the difference in success rate became larger in favor of EVT, it was not found to be significant in either of the analyses (Table 2). The outcome analyses were performed for primary and for final

Table 3 Groups of therapy

	SEMS	EVT
By primary therapy	$n = 77$	$n = 34$
	$n = 7$ switched to EVT	$n = 6$ switched to SEMS
	$n = 1$ switched back to SEMS	$n = 1$ switched back to EVT
By final therapy	$n = 76$	$n = 35$

Table 4 Short-term complications of the group

	SEMS	EVT	<i>p</i> value
Dislocation	14 (20.3%)	4 (14.8%)	0.581
Persisting leak	3 (4.3%)	0	0.557
Gastrotrachael fistula	1 (1.5%)	0	1.000
None	51 (73.9%)	23 (85.2%)	
Total	69	27	

treatment because 7 patients were switched from SEMS to EVT and 6 patients were switched from EVT to SEMS (Fig. 2). As this modified analysis did not reveal differences in the outcome, it can be concluded that the patients being switched to the other treatment group were neither extremely successful nor unsuccessful cases in favor of SEMS or EVT. Based on our data, we cannot confirm superiority for EVT compared to SEMS. We believe that reasons for diverging results from other studies might be found in the patient selection. Our study is the only one to specifically classify the leaks of each treatment group, reflecting the complexity of the cases as endoscopic parameter. The differences in circumferential extend of the leak might lead to the assumption that EVT was used in bigger leaks that naturally result in worse outcome. Although there is no scientific evidence for such an assumption, we performed a subgroup analysis towards the patient with leaks of 1/3 of the circumference or less and also found no difference in the major outcome parameter such as treatment success, mortality, or ICU stay (Supplementary). As all retrospective studies carry a high risk of selection bias, it could be assumed that first experiences of other institutions using EVT would be collected in cases in which a favorable outcome was expected; hence, studies with very small EVT groups might overestimate EVT results.

Another important point to be addressed is the definition of treatment success and the inclusion criteria. In the study of

Brangewitz et al., all patients that received the endoscopic treatment and were discharged somewhat later with a healed leak/perforation were counted as treatment success.¹⁴ In our study, only if the leakage was healed in the moment of SEMS or EVT removal, it was counted as a success for the therapy. Mennigen et al. allowed additional endoscopic treatments like clipping or fibrin application in the treatment groups, which was not performed in our study.¹⁶

Generally, our data can confirm a shorter treatment duration for EVT even though being used in larger leaks, but it did not result in a shorter in-hospital stay for this group (Table 2). The complication rate was calculated for patients receiving only one treatment option in order to assuredly assign the complication to the treatment. Short-term complications were found in 26% of the SEMS group and in 14.8% of the EVT group without statistical significance (Table 4). Interestingly, only one patient (3.7%) of the EVT group developed a long-term complication (after finishing treatment), which was a stenosis. In the SEMS group, long-term complications were found in 26.1% (Table 5). However, this difference did not appear statistically significant either. Even without statistical significance, it may be pointed out that none of the EVT patients developed any kind of fistula, but gastrotracheal fistula was found in the SEMS group as a short-term complication in one case (1.4%) and in 4 cases as a long-term complication (5.8%). As these kinds of fistula practically always occur together with anastomotic leak, it cannot definitely be attributed to the SEMS, but on the other hand, there is no evidence that the negative pressure of the EVT provokes a higher fistula rate.²⁵

The findings of this study in discussion with the previously published data suggest a greater focus on the appropriate selection of patients for each treatment, where there is no definite consensus or concept on this so far. The EVT group in our study, although smaller in number, included a larger variety of leaks in terms on circumferential proportion of leak. Additionally, longitudinal defects and one case of ischemia

Table 5 Outcome of endoscopic therapy. Values given as median (range)

		SEMS	EVT	<i>p</i> value
By primary treatment	Days on ICU	9 (0–295)	6 (0–60)	0.097
	Hospitalization	38 (13–296)	37 (19–118)	0.393
	Duration of treatment	27 (1–152)	12 (3–58)	<0.001
	Success	49/77 (63.6)	24/34 (70.6)	0.522
	In-hospital mortality	11/77 (14.3)	3/34 (8.8)	0.544
	30 day mortality	4/77 (5.2)	2/32 (6.3)	0.883
By final treatment	Days on ICU	7 (0–295)	8 (0–60)	0.704
	Hospitalization	37 (13–296)	39 (19–119)	0.817
	Duration of treatment	28 (1–152)	12 (3–46)	<0.001
	Success	55/76 (72.4)	30/35 (85.7)	0.152
	In-hospital mortality	10/76 (13.2)	4/35 (11.4)	0.799
	30 day mortality	3/76 (3.9)	3/35 (8.6)	0.377

were only found in the EVT group (Fig. 1), and these differences appeared significant. This finding, which has also to be mentioned as a limitation of this study in terms of potential selection bias by the endoscopist and surgeon, might also reflect the somewhat divergent treatment strengths of SEMs and EVT.

Thus far, in our opinion, no clear superiority for SEMs or EVT is identified for a specific type of upper gastrointestinal leak, while further investigation should also address the issue of discomfort and pain for the patient as well as cost-effectiveness, neither of which were part of this study. With regard to the retrospective design, our study has certain limitations, including the potential selection bias (of treatment) by the endoscopist and still limited number of patients included. Only prospective trials can minimize these biases and then achieve a comparison of both treatments within an almost identical patient group. On the other hand, no prospective randomized or comparative trials for this topic have been published, and our study presents the largest single-center cohort of SEMs and EVT patients for comparison that can be found so far. Furthermore, our study includes a more homogenous population of patients and specifically describes the leaks being treated.

Conclusion

In conclusion, we identified both SEMs and EVT to be feasible options in endoscopic interventional therapy of anastomotic leaks after oncological surgery resulting from upper gastrointestinal cancer. There was no superiority of one therapeutic modality within our study since the rates of successful leak sealing were not significantly different. EVT was associated with shorter treatment times although being applied for a larger variety of circumferential leak. Prospective trials are highly recommended for further evaluation and identification of selection criteria for each treatment option.

Acknowledgments We would like to thank all the nurses in our surgical endoscopy department for their expert technical assistance. We thank Lisa-Maria Teubler for proofreading. We thank Dr. Thomas Dratsch for the statistical consultation. We thank Hartmut Schäfer for his technical expertise and his guidance as interventional endoscopist.

Authors' Contributions

- Felix Berlth:
- Conception and design
 - Acquisition of data
 - Analysis of data
 - Interpretation of data
 - Drafting the work
 - Final approval of the manuscript
- Marc Bludau:
- Conception and design
 - Acquisition of data
 - Analysis of data
 - Interpretation of data

- Revising the work
 - Final approval of the manuscript
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- Acquisition of data
 - Interpretation of data
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 - Final approval of the manuscript
- Hildegard Christ:
- Analysis of data
 - Interpretation of data
 - Revising the work
 - Final approval of the manuscript
- Hakan Alakus:
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 - Final approval of the manuscript
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 - Acquisition of data
 - Analysis of data
 - Interpretation of data
 - Drafting the work
 - Final approval of the manuscript

References

1. Low DE, Kuppasamy MK, Alderson D, Cecconello I, Chang AC, Darling G, Davies A, D'Journo XB, Gisbertz SS, Griffin SM, Hardwick R, Hoelscher A, Hofstetter W, Jobe B, Kitagawa Y, Law S, Mariette C, Maynard N, Morse CR, Nafteux P, Pera M, Pramesh CS, Puig S, Reynolds JV, Schroeder W, Smithers M, Wijnhoven BPL. Benchmarking Complications Associated with Esophagectomy. *Ann Surg* 2017. <https://doi.org/10.1097/SLA.0000000000002611>
2. Seesing MFJ, Gisbertz SS, Goense L, van Hillegersberg R, Kroon HM, Lagarde SM, Ruurda JP, Slaman AE, van Berge Henegouwen MI, Wijnhoven BPL. A Propensity Score Matched Analysis of Open Versus Minimally Invasive Transthoracic Esophagectomy in the Netherlands. *Ann Surg* 2017;266(5):839–846. <https://doi.org/10.1097/SLA.0000000000002393>.
3. Schmidt HM, Gisbertz SS, Moons J, Rouvelas I, Kauppi J, Brown A, Asti E, Luyer M, Lagarde SM, Berlth F, Philippon A, Bruns C, Hoelscher A, Schneider PM, Raptis DA, van Berge Henegouwen MI, Nafteux P, Nilsson M, Räsänen J, Palazzo F, Rosato E, Mercier S, Bonavina L, Nieuwenhuijzen G, Wijnhoven BPL, Schröder W,

- Pattyn P, Grimminger PP, Gutschow CA. A Multicenter Analysis of Total Minimally Invasive Esophagectomy in Low Risk Patients. *Ann Surg*. 2017;266(5):814–821. <https://doi.org/10.1097/SLA.0000000000002445>.
4. Talsma AK, Lingsma HF, Steyerberg EW, Wijnhoven BPL, Van Lanschot JJ. The 30-day versus in-hospital and 90-day mortality after esophagectomy as indicators for quality of care. *Ann Surg* 2014;260(2):267–273. <https://doi.org/10.1097/SLA.0000000000000482>
 5. Sierzega M, Kolodziejczyk P, Kulig J. Impact of anastomotic leak on long-term survival after total gastrectomy for carcinoma of the stomach. *Br J Surg* 2010;97(7):1035–1042. <https://doi.org/10.1002/bjs.7038>
 6. Markar S, Gronnier C, Duhamel A, Mabrut JY, Bail JP, Carrere N, Lefevre JH, Brigand C, Vaillant JC, Adham M, Msika S, Demartines N, Nakadi IE, Meunier B, Collet D, Mariette C. The Impact of Severe Anastomotic Leak on Long-term Survival and Cancer Recurrence After Surgical Resection for Esophageal Malignancy. *Ann Surg* 2015;262(6):972–980. <https://doi.org/10.1097/SLA.0000000000001011>
 7. Rogalski P, Daniluk J, Baniukiewicz A, Wroblewski E, Dabrowski A. Endoscopic management of gastrointestinal perforations, leaks and fistulas. *World J Gastroenterol* 2015;21(37):10542–10552. <https://doi.org/10.3748/wjg.v21.i37.10542>
 8. Aryaie AH, Singer JL, Fayeizadeh M, Lash J, Marks JM. Efficacy of endoscopic management of leak after foregut surgery with endoscopic covered self-expanding metal stents (SEMS). *Surg Endosc Other Interv Tech* 2017;31(2):612–617. <https://doi.org/10.1007/s00464-016-5005-8>
 9. Dasari BV, Neely D, Kennedy A, Spence G, Rice P, Mackle E, Epanomeritakis E. The Role of Esophageal Stents in the Management of Esophageal Anastomotic Leaks and Benign Esophageal Perforations. *Ann Surg* 2014;259(5):852–860. <https://doi.org/10.1097/SLA.0000000000000564>
 10. Loske G, Mueller C. Vakuumentherapie einer Anastomoseninsuffizienz am Ösophagus – ein Fallbericht. *Zentralbl Chir* 2009;134(3):267–270. <https://doi.org/10.1055/s-0028-1098764>
 11. Bludau M, Fuchs HF, Herbold T, Maus MKH, Alakus H, Popp F, Leers JM, Bruns CJ, Hoelscher AH, Schroeder W, Chon SH. Results of endoscopic vacuum-assisted closure device for treatment of upper GI leaks. *Surg Endosc* 2018;32(4):1906–1914. <https://doi.org/10.1007/s00464-017-5883-4>.
 12. Kuehn F, Loske G, Schiffmann L, Gock M, Klar E. Endoscopic vacuum therapy for various defects of the upper gastrointestinal tract. *Surgical Endoscopy and Other Interventional Techniques* 2017:1–10.
 13. Laukoetter MG, Mennigen R, Neumann PA, Dhayat S, Horst G, Palmes D, Senninger N, Vowinkel T. Successful closure of defects in the upper gastrointestinal tract by endoscopic vacuum therapy (EVT): a prospective cohort study. *Surg Endosc Other Interv Tech* 2017;31(6):2687–2696. <https://doi.org/10.1007/s00464-016-5265-3>
 14. Brangewitz M, Voigtländer T, Helfritz FA, Lankisch TO, Winkler M, Klempnauer J, Manns MP, Schneider AS, Wedemeyer J. Endoscopic closure of esophageal intrathoracic leaks: stent versus endoscopic vacuum-assisted closure, a retrospective analysis. *Endoscopy* 2013;45(6):433–438. <https://doi.org/10.1055/s-0032-1326435>
 15. Schniewind B, Schafmayer C, Voehrs G, Egberts J, von Schoenfels W, Rose T, Kurdow R, Arlt A, Ellrichmann M, Jürgensen C, Schreiber S, Becker T, Hampe J. Endoscopic endoluminal vacuum therapy is superior to other regimens in managing anastomotic leak after esophagectomy: a comparative retrospective study. *Surg Endosc Other Interv Tech* 2013;27(10):3883–3890. <https://doi.org/10.1007/s00464-013-2998-0>
 16. Mennigen R, Harting C, Lindner K, Vowinkel T, Rijcken E, Palmes D, Senninger N, Laukoetter MG. Comparison of Endoscopic Vacuum Therapy Versus Stent for Anastomotic Leak After Esophagectomy. *J Gastrointest Surg* 2015;19(7):1229–1235. <https://doi.org/10.1007/s11605-015-2847-7>
 17. Hwang JJ, Jeong YS, Park YS, Yoon H, Shin CM, Kim N, Lee DH. Comparison of Endoscopic Vacuum Therapy and Endoscopic Stent Implantation With Self-Expandable Metal Stent in Treating Postsurgical Gastroesophageal Leak. *Med* 2016;95(16):e3416–e3416. <https://doi.org/10.1097/MD.00000000000003416>
 18. Low DE, Alderson D, Ceconello I, Chang AC, Darling GE, D Journo XB, Griffin SM, Hoelscher AH, Hofstetter WL, Jobe BA, Kitagawa Y, Kucharczuk JC, Law SY, Lerut TE, Maynard N, Pera M, Peters JH, Pramesh CS, Reynolds JV, Smithers BM, van Lanschot JJ. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG). *Ann Surg* 2015;262(2):286–294. <https://doi.org/10.1097/SLA.0000000000001098>
 19. Hoelscher AH, Schneider PM, Gutschow C, Schroeder W. Laparoscopic ischemic conditioning of the stomach for esophageal replacement. *Ann Surg* 2007;245(2):241–246. <https://doi.org/10.1097/01.sla.0000245847.40779.10>
 20. Schroeder W, Hoelscher AH, Bludau M, Vallböhrer D, Bollschweiler E, Gutschow C. Ivor-lewis esophagectomy with and without laparoscopic conditioning of the gastric conduit. *World J Surg* 2010;34(4):738–743. <https://doi.org/10.1007/s00268-010-0403-x>
 21. Strauss C, Mal F, Perniceni T, Bouzar N, Lenoir S, Gayet B, Palau R. Computed tomography versus water-soluble contrast swallow in the detection of intrathoracic anastomotic leak complicating esophagogastrectomy (Ivor Lewis): a prospective study in 97 patients. *Ann Surg* 2010;251(4):647–651. <https://doi.org/10.1097/SLA.0b013e3181c1aeb8>
 22. Hampe J, Schniewind B, Both M, Fritscher-Ravens A. Use of a NOTES closure device for full-thickness suturing of a postoperative anastomotic esophageal leak. *Endoscopy* 2010;42(7):595–598. <https://doi.org/10.1055/s-0030-1255518>
 23. Ahrens M, Schulte T, Egberts J, Schafmayer C, Hampe J, Fritscher-Ravens A, Broering DC, Schniewind B. Drainage of esophageal leak using endoscopic vacuum therapy: a prospective pilot study. *Endoscopy* 2010;42(9):693–698. <https://doi.org/10.1055/s-0030-1255688>
 24. Rausa E, Asti E, Aiolfi A, Bianco F, Bonitta G, Bonavina L. Comparison of endoscopic vacuum therapy versus endoscopic stenting for esophageal leaks: systematic review and meta-analysis. *Dis Esophagus* (2018), 1–8. <https://doi.org/10.1093/dote/doy060>
 25. Lambertz R, Hoelscher AH, Bludau M, Leers JM, Gutschow C, Schroeder W. Management of Tracheo- or Bronchoesophageal Fistula After Ivor-Lewis Esophagectomy. *World J Surg* 2016;40(7):1680–1687. <https://doi.org/10.1007/s00268-016-3470-9>