



Long-Term Quality of Life Assessment After Successful Endoscopic Vacuum Therapy of Defects in the Upper Gastrointestinal Tract Quality of Life After EVT

Sameer A. Dhayat¹  · Rosanna Schacht¹ · Rudolf Mennigen¹ · Daniel Palmes¹ · Thomas Vogel¹ · Thorsten Vowinkel¹ · Norbert Senninger¹ · Mike Georg Laukoetter¹

Received: 13 June 2018 / Accepted: 25 October 2018 / Published online: 14 November 2018
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Abstract

Background Accumulating evidence indicates that anastomotic leakages and perforations of the upper gastrointestinal tract (uGIT) can be treated successfully with endoscopic vacuum therapy (EVT). So far, no data is available regarding the long-term quality of life (QoL) after successful EVT of defects in the uGIT.

Methods We present a prospective survey on long-term QoL of 52 patients treated by EVT for defects of the uGIT. Results are compared with 63 of 221 patients treated by esophagectomy without anastomotic insufficiency (w/o EVT) between 12/2011 and 12/2015. The Gastrointestinal Quality of Life-Index (GIQLI) score was determined by a 36-item questionnaire of 25 respondents with EVT and 50 respondents w/o EVT.

Results The response rate was 78.95% (75/95) including 25 survey respondents who were treated with EVT for anastomotic insufficiency secondary to esophagectomy or gastrectomy ($n = 19$), iatrogenic esophageal perforation ($n = 4$), and Boerhaave syndrome ($n = 2$) and 50 respondents with complication-free esophagectomy w/o EVT. The median follow-up was 19 months for EVT patients and 21 months for patients w/o EVT. Except for “social function” ($p = 0.009$) in favor for patients w/o EVT, the median GIQLI score did not differ significantly between both study groups concerning the categories ‘symptoms’, ‘emotions’, ‘physical functions’, and ‘medical treatment’ resulting in a total median GIQLI score of 83 in EVT versus 96.5 in patients w/o EVT ($p = 0.185$). Spearman Rho analysis revealed that a high GIQLI score correlated with a low ASA score ($p < 0.001$), a benign pathology ($p = 0.001$), and a hospital stay less than 21 days ($p < 0.001$).

Conclusion EVT in the uGIT is well tolerated by the patients and accompanied by a satisfactory long-term QoL.

Keywords Negative-pressure wound therapy · Upper gastrointestinal tract · Anastomotic leakage · Quality of life

Abbreviations

BMI	Body mass index
EVT	Endoscopic vacuum therapy
GI	Gastrointestinal
GIQLI	Gastrointestinal Quality of Life Index
r	Spearman’s rank correlation coefficient

w/o EVT	Without endoscopic vacuum therapy
QoL	Quality of life

Introduction

Failures of the esophageal continuity are diverse. Esophageal perforation, particularly anastomotic leakage after esophagectomy or gastrectomy, remains a serious postoperative hazard with reported mortality rates up to 50%.^{1–5} Competing treatment modalities including conservative, endoscopic, or surgical treatment have been proposed for its management. Over the past decades, there has been a distinguishable shift in the management of anastomotic leaks from surgical interventions to conservative management strategies, and more recently to endoscopic interventions. The establishment of endoscopic

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s11605-018-4038-9>) contains supplementary material, which is available to authorized users.

✉ Mike Georg Laukoetter
laukoetter@uni-muenster.de

¹ Department of General and Visceral Surgery, University Hospital Muenster, Albert-Schweitzer-Campus 1, Bldg. W1, 48149 Muenster, Germany

vacuum therapy (EVT) as a new treatment modality for the management of esophageal leakages allows the containment of the leak, drainage of the contaminated para-esophageal and mediastinal space, and finally the closure of the defect by promotion of perfusion and granulation. EVT can be regarded as a safe, promising, and successful minimally invasive approach in the management of spontaneous, iatrogenic, or postoperative leaks in the upper GI tract.^{6–17} Mounting evidence suggests that EVT is also superior to surgical revision and stent therapy in managing of major esophageal leaks, especially in septic patients.^{18–21} Since the successful implementation of EVT into our clinical routine, we have extended its application to complication management and therapy for substantial wall defects of any etiology in the upper GI tract on the basis of existing literature data.⁶ However, data concerning quality of life (QoL) assessment after EVT of upper gastrointestinal (GI) leaks are not available to date. Thus, it remains unclear to what extent patients are limited in their QoL as a result of EVT. The Gastrointestinal Quality of Life Index (GIQLI) has been designed to assess specifically the health-related QoL outcome in patients with GI disorders.²² The aim of the present study was to evaluate health-related QoL after EVT of upper GI leaks using the GIQLI. We report, to our knowledge, the first prospective survey of QoL assessment after EVT for substantial esophageal wall defects in the upper GI tract in the largest patient cohort to date.

Materials and Methods

Study Design

A prospective monocentric survey on long-term QoL of patients consecutively treated by EVT for anastomotic leakages, iatrogenic esophageal perforations, or Boerhaave syndrome accompanied with no prior or post-therapeutic modalities at the Department of General and Visceral Surgery of the University Hospital Muenster between 12/2011 and 12/2015 was carried out. Data recording with standardized and prospective data collection including the documentation of all complications and adverse events occurring during the in-hospital stay and within 90 days of surgery was done. Postoperative complications were defined according to the Clavien-Dindo classification and the recommendations of the Esophagectomy Complications Consensus Group (ECCG).^{23,24}

Fifty-two patients were treated by EVT as previously reported and described in detail by our group for anastomotic insufficiency secondary to esophagectomy or gastrectomy ($n = 40$), iatrogenic esophageal perforation ($n = 8$), and Boerhaave syndrome ($n = 4$) (Fig. 1).⁶ Twenty-one patients with anastomotic leakage post-esophagectomy or gastrectomy

treated by prior stent therapy ($n = 11$) or prior surgery ($n = 10$) were excluded from this study. Due to the limited number of patients with alternative treatment options for leakage of the upper GI tract at our institution, the control group consisted of patients treated by esophagectomy or gastrectomy without anastomotic leakage or severe post-operative complications during the same time period. Of 221 patients without anastomotic leakage, an age-matched patient cohort of 63 patients consecutively treated by thoraco-abdominal or transhiatal esophagectomy between 12/2011 and 12/2015 was characterized by no major post-operative complications like anastomotic leak, conduit necrosis, chyle leak, respiratory failure, cardiac arrest or dysrhythmia, and renal failure nor adverse events like reintubation, reoperation, readmission, and death within 90 days of surgery. Sixty-nine of 132 patients without anastomotic leakage did not meet these requirements and were therefore excluded. Twenty of 52 patients with EVT and 89 of 221 patients w/o EVT had already died at the time of the survey in 11/2016.

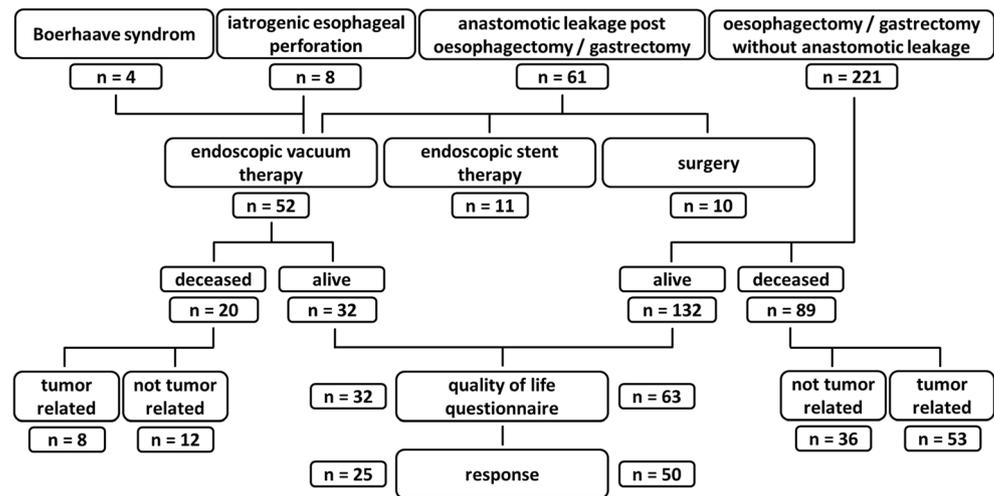
In the light of these inclusion and exclusion criteria, QoL questionnaires were sent by mail after initial telephone contact to 63 patients w/o EVT and 32 patients with EVT who completed post-operative or post-interventional follow-up with a minimum of 12 months. Health-related QoL was assessed prospectively with the Gastrointestinal Quality of Life Index (GIQLI), consisting of 36 items covering five domains: gastrointestinal symptoms (19 questions), physical function (7 questions), social function (4 questions), emotional function (5 questions), and one question about subjective treatment assessment.²² Every item was scored from 0 as least desirable option to 4 as most desirable option. Summing the points, the GIQLI score theoretically could range from 0 to 144.

Further potential cofactors influencing QoL as age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, histological dignity, (neo-) adjuvant therapy, type of operation/intervention, length of hospital stay, and tumor recurrence were analyzed using our follow-up database (Table 1). Apart from age, no further clinical variables were matched. Ethical approval for postoperative QoL survey was obtained (Ethics committee, University Muenster, Az: 2016-687-f-S) and all patients provided written informed consent.

Statistical Analysis

All returned questionnaires were collected by the Department of General and Visceral Surgery of the University Hospital Muenster. Statistical data analysis was performed in cooperation with the Institute of Biostatistics and Clinical Research of the University of Muenster using SPSS® Statistics Version 22 (IBM Corp. Armonk, NY) for Windows®. Data were expressed as median with standard deviation (SD). Statistical

Fig. 1 Study design. Selection criteria of patients for the quality of life survey without and after successful endoscopic vacuum therapy (EVT) of defects in the upper gastrointestinal tract. The response rate was 78.95% (75/95) including 25 survey respondents who were treated with EVT and 50 respondents with complication-free esophagectomy without EVT



significance was determined by using the two-tailed Student's *t* test to compare two data sets of absolute numbers of patients. Box-and-whisker plots demonstrating the median (middle quartile) were used to show the GIQLI scores in the different therapy groups. The middle half of a data set falls within the interquartile range represented by the width of the box. The whiskers indicate variability outside the upper and lower quartiles. The grand mean representing the overall mean of all data combined is displayed as a horizontal line across the entire graph. Comparison between GIQLI scores and categorical variables was conducted using the nonparametric Mann-Whitney *U* test or the Kruskal-Wallis test to test more than two groups. To test the correlation between the GIQLI index and cofactors of live quality, the Fisher's two-tailed exact test or the Chi² test were applied. All variables were dichotomized. We used the non-parametric Spearman's Rho test to determine the degree of correlation between the GIQLI index and cofactors of live quality. GIQLI scores and their percentage of improvement at follow-up were assessed for possible correlation by measuring Spearman's rank correlation coefficient (*r*), which was evaluated for significance within the 95% confidence interval. Values for $P < 0.05$ were considered to be statistically significant.

Results

Study Groups

EVT was performed in 52 patients (37 men and 15 women) with a median age of 65 years (range 41–94) for anastomotic insufficiency secondary to esophagectomy ($n = 30$) or gastrectomy ($n = 9$), iatrogenic esophageal perforation ($n = 9$), and Boerhaave syndrome ($n = 4$) between 2012 and 2015. Successful healing of the defects in the upper GI tract was achieved by EVT as previously reported and described in

detail by our group in 49 of 52 patients (94.2%) (Fig. 1).⁶ Twenty-one patients with anastomotic insufficiency treated in the same period by prior stent therapy ($n = 11$) or prior surgery ($n = 10$) were excluded from this study.

In 11/2016, a total of 32 EVT patients (27 men and 5 women) with a median age of 65 years (range 43–87) with a follow-up of 19.5 months (range 15.2–52.0 months) were surveyed about their current QoL. At the time of the survey, the remaining 20 EVT patients (38.46%) have already died due to cardiovascular failure ($n = 12$) or tumor recurrence ($n = 8$) with a median overall survival of 48 months postoperatively (range 12–48 months). Sixty-three patients (44 men and 19 women) with a median age of 65 years (range 36–92) w/o EVT after esophagectomy and with a follow-up of 21 months (range 11.1–47 months) were surveyed as complication-free control group during their hospital stay. Analyses of clinicopathological parameters revealed no differences in age, gender or BMI, and tumor stage between the two study groups. Patients with EVT showed significant higher ASA scores ($p = 0.000$), more benign pathologies ($p = 0.000$), less (neo-) adjuvant therapy ($p = 0.004$), and longer length of hospital stay ($p = 0.000$) (Table 1).

Ninety-day mortality was 0% in both study groups. The median follow-up was 19.5 months (range 15.2 to 52 months) for patients with EVT and 21 months (range 11.1 to 47 months) for patients w/o EVT. Follow-up analyses until 11/2016 revealed oral nutrition, no stenosis, and no fistula in the study group w/o EVT. A total of four patients (12.5%) required endoscopic dilation of moderate anastomotic strictures after completion of EVT. However, it remains unclear if manifestation of strictures in these cases could be ascribed to EVT. No recurrence of fistulas and leaks after completion of EVT occurred in the EVT patients. During follow-up, postoperative tumor recurrence was identified in one EVT patient (3.1%, 14 to 48 months) and five patients w/o EVT (7.9%, 15 to 48 months) ($p = 0.365$).

Table 1 Clinicopathologic characteristics and follow-up data of patients with endoscopic vacuum therapy (EVT) vs. without endoscopic vacuum therapy (w/o EVT)

	Total (n = 95)	Upper GI surgery		P
		EVT I (n = 32)	w/o EVT II (n = 63)	
Age (years)				
≤ 65	45	16	29	0.716
> 65	50	16	34	
Gender				
Female	24	5	19	0.241
Male	71	27	44	
BMI				
< 18.5	7	3	4	0.316
≥ 18.5 ≤ 30.0	68	24	44	
> 30.0	20	5	15	
ASA				
I–II	61	10	51	0.000
III–IV	34	22	12	
Dignity				
Benign	15	12	3	0.000
Malign	80	20	60	
(Neo-) adjuvant therapy				
Yes	58	13	45	0.004
No	37	19	18	
Length of hospital stay				
≤ 21 days	50	2	48	0.000
> 21 days	45	30	15	
Follow-up (median in months, range)		19.5 (15.2–52.0)	21 (11.1–47.0)	
Nutrition post hospital stay				
Oral	95	32	63	1
Parenteral	0	0	0	
Stricture post hospital stay				
No	91	28	63	0.004
Yes	4	4	0	
Tumor recurrence				
No	89	31	58	0.365
Yes	6	1	5	

Significant higher ASA scores ($p = 0.000$), more benign pathologies ($p = 0.000$), less (neo-) adjuvant therapy ($p = 0.004$), longer length of hospital stay ($p = 0.000$), and moderate anastomotic strictures ($p = 0.004$) were detected in patients with EVT. $P < 0.05$ indicates significance

BMI body mass index, ASA American Society of Anesthesiologists score

Gastrointestinal Quality of Life Index Survey

A total of 75 of 95 GIQLI questionnaires were completed and returned. This corresponds to an overall survey's response rate of 78.95% consisting of 78.13% in the study group with EVT (25/32) and 79.37% w/o EVT (50/63) (Fig. 1). The EVT group consisted of 16 patients (64%) with malignant diagnosis and 9 patients (26%) with benign diagnosis treated by thoraco-abdominal esophagectomy in 13 cases (52%),

transhiatal esophagectomy in 2 cases (8%), gastrectomy in 3 cases (12%), and without surgery in 7 cases (28%). The study group w/o EVT consisted of 47 patients (94%) with malignant diagnosis and 3 patients (6%) with benign diagnosis treated by thoraco-abdominal esophagectomy in 37 cases (74%) and transhiatal esophagectomy in 13 cases (26%).

Analyzing the different GIQLI items, patients with EVT expressed a significant worse “coping with daily activities” ($p = 0.006$), higher “sexual life impairment by illness”, and

Table 2 Total Gastrointestinal Quality of Life Index (GIQLI) and domain scores of patients with endoscopic vacuum therapy (EVT) vs. without endoscopic vacuum therapy (w/o EVT)

Content	Score EVT	Score w/o EVT	<i>P</i> value
Gastrointestinal symptoms	52 (31–76)	55 (23–73)	0.660
Physical function	12 (2–23)	14 (2–27)	0.132
Social function and subjective treatment assessment	12 (3–20)	15.5 (5–20)	0.009
Emotional function	12 (2–20)	15 (1–20)	0.085
Total GIQLI score	83 (42–131)	96.5 (43–134)	0.185

Except for a worse social function for patients with EVT ($p = 0.009$), the other GIQLI categories did not differ significantly between both study groups resulting in a total median GIQLI score of 83 in EVT vs. 96.5 in patients w/o EVT ($p = 0.185$). Data are given as median and range. $P < 0.05$ indicates significance

“frustration about illness” (each $p = 0.048$) comparing to patients w/o EVT (Table 2 and supplementary Table 1). Patients with EVT complain less “happiness with life in general” ($p = 0.054$), “feeling unfit” ($p = 0.056$), and more “sadness about illness” ($p = 0.062$) without reaching significance versus the control group w/o EVT. Regurgitation, difficulty to swallow food, or trouble with digestion was expressed in both study groups without significant differences (Supplementary Table 1). Overall, patients with EVT express a worse “social function” ($p = 0.009$) (Table 2, Figs. 2 and 3). However, in the GIQLI categories “symptoms”, “emotions”, “physical functions”, and “medical treatment”, the median GIQLI score was equally high for both study groups without significant differences resulting in a total median GIQLI score of 83 (range 42–131) in EVT versus 96.5 (range 43–134) in patients w/o EVT ($p = 0.185$) (Figs. 2 and 4). Spearman Rho analysis revealed that a high GIQLI score correlated with a low ASA score ($r = -0.530$; $p = 0.000$), a benign pathology ($r = 0.374$, $p = 0.001$), and a hospital stay less than 21 days ($r = -0.648$, $p = 0.000$) but not with age, gender, or body mass index.

Discussion

The aim of this study was to assess long-term QoL in patients after EVT for esophageal leakages and to potentially identify risk factors for impaired QoL. When compared with control subjects, who underwent thoraco-abdominal esophagectomy or transhiatal esophagectomy followed by an uncomplicated postoperative course, we observed impaired generic and health-related QoL concerning daily activities, sexual life, and coping with illness in patients treated by EVT. A high GIQLI score correlated with a low ASA score, a benign pathology, and a hospital stay less than 21 days but not with age, gender, or body mass index.

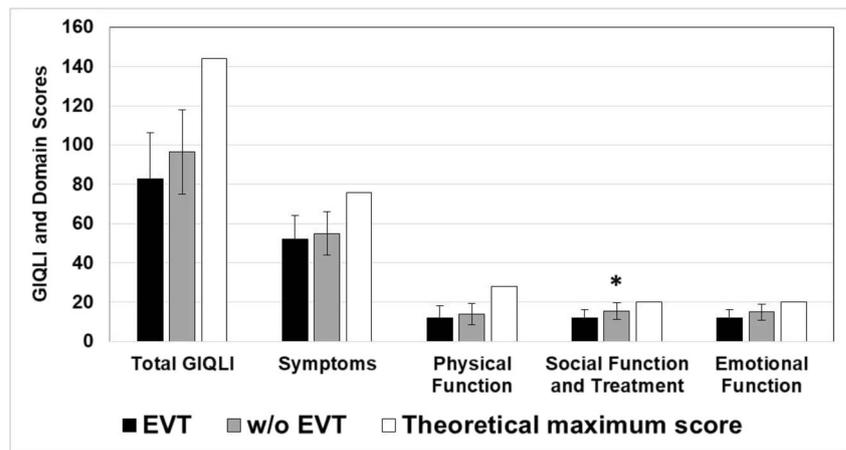
Comparative studies between different treatment modalities in the management of postoperative surgical complications in the upper GI tract are rare, resulting in lack of clinical evidence for directing treatment modalities.²⁵ Therefore,

therapy still differs depending on institution and primary attending discipline. Recently, we discussed that EVT in the upper GI tract seems to be not only feasible but superior to previous therapeutic procedures such as surgical revision and stent placement for esophageal defects.^{18,26} We could reaffirm the role of EVT as a minimally invasive endoscopic option for leaks of the upper GI tract with an extraordinary success rate in a prospective single-center study containing patients with spontaneous, iatrogenic, or postoperative leaks in the upper GI tract.⁶

There is increasing evidence suggesting that the change of therapeutic paradigm in the form of endoscopic therapy is associated with improved outcome, better QoL, and shortened length of hospital stay. Therefore, recent European guidelines on endoscopic management of leakages of the upper GI tract have strengthened the role of endoscopy in the management of conditions where there is a breach in the continuity of the GI wall.²⁷

However, no studies dealing with long-term QoL assessment after endoscopic vacuum therapy of defects in the upper gastrointestinal tract are available to date. The question remaining is to what extent patients are limited in their QoL as a result of EVT. Remarkably, in the major GIQLI categories “symptoms”, “emotions”, “physical functions”, and “medical treatment”, the median GIQLI score was equally high for both study groups without significant differences. Moreover, EVT was well tolerated by patients in critical clinical conditions. This new life saving therapy seems to have no major impact on the overall QoL emphasizing the significance of this therapeutic tool. There is evidence that QoL is reduced in patients treated by esophagectomy with stomach tube compared to extended gastrectomy with Roux-en-Y reconstruction mainly due to increased pulmonary and reflux-related complications.²⁸ The proportion of patients with gastrectomy is 12% in this study, whereas 60% of EVT study patients were treated by esophagectomy with stomach tube reconstruction. Although the course of therapy is prolonged by EVT with multiple endoscopic procedures every 3 to 4 days, its advantages with regard to previous treatment options remain the

Fig. 2 Gastrointestinal Quality of Life Index (GIQLI) of patients with endoscopic vacuum therapy (EVT) vs. without endoscopic vacuum therapy (w/o EVT) vs. theoretical maximum score. Except for a worse social function for patients with EVT ($p = 0.009$), no differences were detected for the other GIQLI items. Data are given as median with standard deviation. Asterisks indicate to a significant difference of $p < 0.05$



regular visualization of the wound cavity and optimal drainage provided by the vacuum system. This leads to effective sepsis control and final closure of the defect without major impact on the long-term QoL assessment of the treated patients in this study.

We are aware of the limitations of this study because of the retrospective design, the small size of our cohort, heterogeneity in indications for EVT, and lack of alternative treatment modalities. However, comparative retrospective studies demonstrated that EVT in the upper GI tract was superior to previous therapeutic procedures such as surgical revision with high mortality rates and stent placement in managing esophageal leaks, especially in septic patients with severe leakage and mediastinal abscess. Even in dedicated centers, procedure-related complications like hemorrhage, migration, and perforation have been reported after placement or removal of endoscopic stents with mortality rates of up to 13% and

failure rates of anastomotic healing of 15–20%.^{29,30} Concerning health economic aspects, stent therapy seems to be more profitable which in contrast does not compensate for the superior clinical outcome of EVT. Therefore, EVT has replaced stent therapy as gold standard for the treatment of esophageal anastomotic leaks in recent years. Together with other experienced centers of upper GI surgery and endoscopy, we implemented EVT as first-line procedure in the treatment of esophageal leakage. A retrospective analysis, comparing the QoL of leakage treatment by surgical revision or stenting was not possible because of the limited number of patients with these leakage treatment options at our institution. So far, there is a lack of literature concerning long-term QoL of patients treated for anastomotic leakages or perforations of the upper GI by stent therapy, surgical revision, or EVT. A multicenter prospective and randomized study design comparing EVT with alternative treatment modalities is needed to confirm the results of this study. However, ethically it would be critical to potentially promote a treatment modality, which is inferior concerning the outcome comparing literature data from independent studies of alternative treatment modalities with EVT.

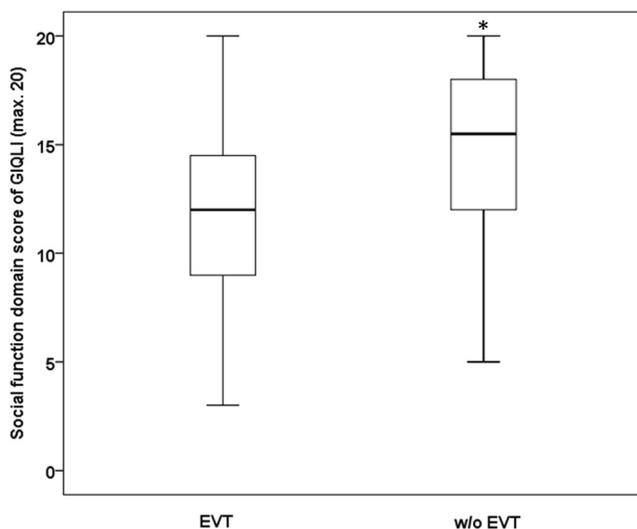


Fig. 3 Social function domain scores of the Gastrointestinal Quality of Life Index (GIQLI) of patients with endoscopic vacuum therapy (EVT) vs. without endoscopic vacuum therapy (w/o EVT). Patients with EVT express a worse social function ($p = 0.009$). Asterisks indicate to a significant difference of $p < 0.05$

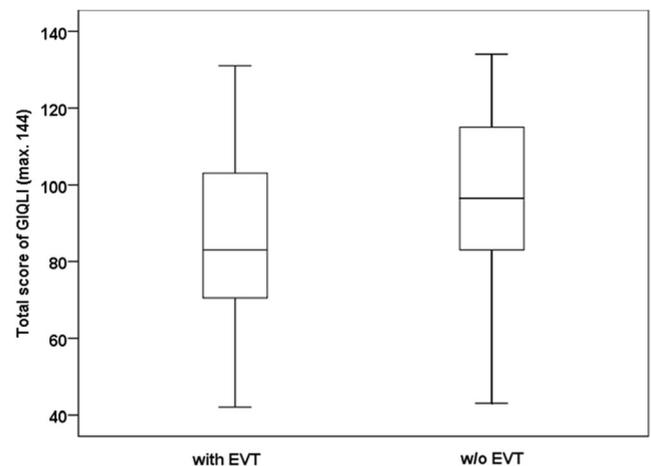


Fig. 4 Total scores of the Gastrointestinal Quality of Life Index (GIQLI) of patients with endoscopic vacuum therapy (EVT) vs. without endoscopic vacuum therapy (w/o EVT) without a significant difference

In conclusion, EVT is feasible, safe, and effective with good short-term and long-term clinical outcomes in the damage control of upper GI tract leaks of different etiology without influencing negatively the patients' QoL.

Acknowledgements The authors thank our study secretary Ms. Ulrike Thoben for her support and expert technical assistance.

Authors' Contribution SAD and MGL designed the study. All authors contributed substantially to the conception and acquisition of the study. All authors collected all data and SAD, RS, and MGL analyzed all data. Further, all authors performed critical revision for important intellectual content and gave final approval of the version to be published. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with Ethical Standards

Ethical approval for postoperative QoL survey was obtained (Ethics committee, University Muenster, Az: 2016-687-f-S) and all patients provided written informed consent.

This analysis was approved by the local institutional review board and was performed in accordance with the Helsinki Declaration of 1975, as revised in 1983.

Conflict of Interests M.G. Laukoetter is a member of the expert panel of negative pressure wound therapy of the Paul Hartmann (AG) holding company. He received fees for invited speeches on endoscopic vacuum therapy. All other authors declare that they have no conflicts of interest or financial ties to disclose.

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