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REVIEW

Endoscopic Vacuum Therapy (EVT) for the Treatment of Post-Bariatric Surgery Leaks and Fistulas: a Systematic Review and Meta-analysis

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Abstract

Bariatric surgery remains the most effective treatment for morbid obesity and its comorbidities. However, post-surgical leaks and fistulas can occur in about 1–5% of patients, with challenging treatment approaches. Endoscopic vacuum therapy (EVT) has emerged as a promising tool due to its satisfactory results and accessibility. In this first systematic review and meta-analysis on the subject, EVT revealed rates of 87.2% clinical success, 6% moderate adverse events, and 12.5% system dislodgements, requiring 6.47 EVT system exchanges every 4.39 days, with a dwell time of 25.67 days and a total length of hospitalization of 44.43 days. Although our results show that EVT is a safe and effective therapy for post-surgical leaks and fistulas, they should be interpreted with caution due to the paucity of available data.

Keyword Endoscopic vacuum therapy; Obesity; Endoscopy; Leaks; Fistulas; Bariatric surgery

Key Points

- Endoscopic vacuum therapy (EVT) showed high clinical success rates in the treatment of post-bariatric surgery leaks and fistulas.
- However, EVT may be associated with multiple endoscopic sessions and a long length of hospital stay.
- Adjunctive therapies could be performed during EVT when needed.
- Incidents such as EVT system dislodgment may occur in around 12.5% of cases. Moderate AEs occurred in 6% of the patients but no mortality or severe adverse events (AEs) related to the EVT were reported.
- Although this systematic review and meta-analysis, the first of its kind on the subject, showed that EVT is a safe and effective therapy, our results should be interpreted with caution due to the paucity of available data.

Introduction

The pandemic of obesity is now recognized as one of the most important public health challenges the world is facing today, with an estimated global prevalence, showing that 1 billion adults will be affected by it in 2025. Bariatric surgery continues to be the most efficient therapy in treating morbid obesity and its comorbidities [1, 2], but despite its satisfactory clinical results, the number of adverse events (AEs) has increased due to the broad adoption of the procedures [3, 4]. The most common severe adverse events (SAEs)

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post-bariatric surgery (PBS) are staple line leaks, showing prevalence rates varying from 0.4 to 5.6% after Roux-en-Y Gastric Bypass (RYGB), and 0.4 to 2.3% after laparoscopic sleeve gastrectomy (LSG), with increasing rates after revision surgeries [5].

Although reoperation is frequently performed to treat PBS leaks and fistulas, closure of the defect itself is technically difficult and is associated with high morbidity [6].

Therefore, less-invasive therapies, such as endoscopic approaches for the management of PBS leaks and fistulas, have been explored, including closing, covering, and draining techniques, transforming endoscopy into a first-line minimally invasive approach for the treatment of these conditions. Closing and covering endoscopic therapies include clips (through-the-scope [TTS] and over-the-scope clips [OTSC]), esophageal and customized self-expandable metal stents (SEMS), glues, and tissue sealants, cardiac septal defect occluders (CSDO), and endoscopic suturing. Endoscopic internal drainage therapies include the use of double plastic pigtail stents (DPPS), septotomy, and endoscopic vacuum therapy (EVT).

Endoscopic techniques attempting to only close or occlude the leak or fistulous orifice might not be the ideal treatment strategy, as drainage is one of the main principles for treating such defects. Consequently, based on this pivotal principle, EVT may be the most appropriate technique for the management of these conditions considering its mechanisms of action which promotes defect closure via multiple approaches such as promoting macro/micro deformation, changes in perfusion (stimulation of angiogenesis), exudate control, and bacterial clearance [14, 15].

EVT is performed by placing a sponge (open-pore polyurethane sponge (OPS) or open-pore film (OPF) on the distal portion of a nasogastric tube (NGT), which is then positioned in the peri gastric collection (intracavitary) or into the lumen of the gastrointestinal (GI) tract (intraluminal) when intracavitary placement is not feasible. This is followed by connecting the NGT to a vacuum system with continuous negative pressure (between 125 and 175 mmHg).

Some case series and observational studies have reported a high efficacy and low SAEs rates of EVT in the management of PBS complications. Nonetheless, EVT demands multiple endoscopic procedures that should be performed every 3 to 7 days to exchange the EVT system. This has been considered a limitation by some centers due to the associated prolonged use of an NGT and potentially increased costs [16].

Therefore, to better understand the role of the EVT in the management of leaks and fistulas after bariatric surgery, we aimed to perform a systematic review and meta-analysis evaluating the efficacy, safety, and unique aspects of this treatment modality until now.

Materials and Methods

Protocol and Registration

The study protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the file number CRD42022300958 and was previously approved by the Ethics Committee of Hospital das Clínicas, Faculty of Medicine at The University of São Paulo. This systematic review and meta-analysis were performed in conformity with the recommendations from the Cochrane Handbook of Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines (PRISMA) [17].

Data Sources and Study Selection

Individualized searches of multiple electronic databases (MEDLINE, Embase, Cochrane, LILACS, and gray literature) were performed based upon a standardized protocol from their inception through January 2022. Data search was made without language or publication date limitations following this search strategy in all databases: (leak OR leakage OR sleeve OR surgery OR postoperative complications OR transmural OR fistula OR perforation) AND (negative pressure OR vacuum OR EVT OR evac OR SEMS) AND (endoscopy OR endoscopic OR endoluminal).

Two researchers independently conducted the eligibility screening. From the initial search results, duplicate articles were excluded, and then the titles and abstracts of all potentially relevant studies were evaluated for eligibility. Any disagreements were settled by consensus or by consulting a third reviewer.

Relevant published abstracts and full text of randomized controlled trials, cohorts, and case series that report the use of EVT for the treatment of PBS leaks or fistulas, regardless of either year of publication or language, were considered eligible. Exclusion criteria included a nonexplicit study design, studies with insufficient data, and studies from the same authors that had been updated in which only the actualized ones were selected for analysis. For comparative studies, only data regarding the use of EVT was included.

Included patients were those diagnosed with PBS leaks or fistulas regardless of the time of the defect (acute, early, late, and chronic) treated with EVT, independently of the device used (open-pore film or open-pore polyurethane sponge).

Outcomes and Data Extraction

The main outcomes assessed were clinical success, defined as defect closure, and safety profile. This last outcome included incidents secondary to system dislodgment and adverse events

related to the EVT graded according to the 2010 American Society for Gastrointestinal Endoscopy (ASGE) lexicon for endoscopic adverse events [18]. Other outcomes evaluated included the number of EVT system exchanges, the interval between EVT system exchanges (days), EVT system dwell time, adjunctive therapy performed during EVT, EVT system dislodgment, and length of hospital stay (measured in days).

An Excel spreadsheet was used to organize relevant data extracted from the selected articles, which consisted of the name of the first author, year of publication, type of study, number of patients included, number of patients treated with EVT, and data related to the outcomes.

Risk of Bias in Individual Studies and Quality of Evidence

The risk of bias was assessed by the Joanna Briggs Institute (JBI) Critical Appraisal Tool, a specific tool for bias evaluation in case series [19]. The quality of evidence was assessed using the objective criteria from Grading Recommendations Assessment, Development, and Evaluation (GRADE) guidelines for each of the pre-specified results and outcomes using the GRADEpro—Guideline Development Tool software (McMaster University, 2015; Evidence Prime, Inc., Ontario, Canada [20].

Statistical Analysis

For results that did not present standard deviation, the estimation of a sample's mean and variance were estimated using its median and range utilizing the Hozo test [21]. For dichotomous variables, the risk difference (RD) was calculated using the Mantel–Haenszel method, with a corresponding 95% confidence interval (CI). For continuous variables, mean difference (MD) was calculated with inverse variance and a 95% CI.

We used the Comprehensive Meta-Analysis V3 software to carry out the data analysis, generate forest plots, and calculate confidence intervals. Absolute values, means, and standard deviations were used in the data analysis. All calculated p-values were 2-sided, and p-values < 0.05 were considered statistically significant.

Data heterogeneity was assessed and quantified according to the Higgins method (I^2). If the I^2 value was greater than 50%, the heterogeneity was considered high, and a random-effects model was used to evaluate this data. A fixed-effects model was preferred when I^2 values were lower than 50%. To assess for publication bias, a funnel plot was created and visually inspected for asymmetry and quantitatively using the Egger's regression test [22].

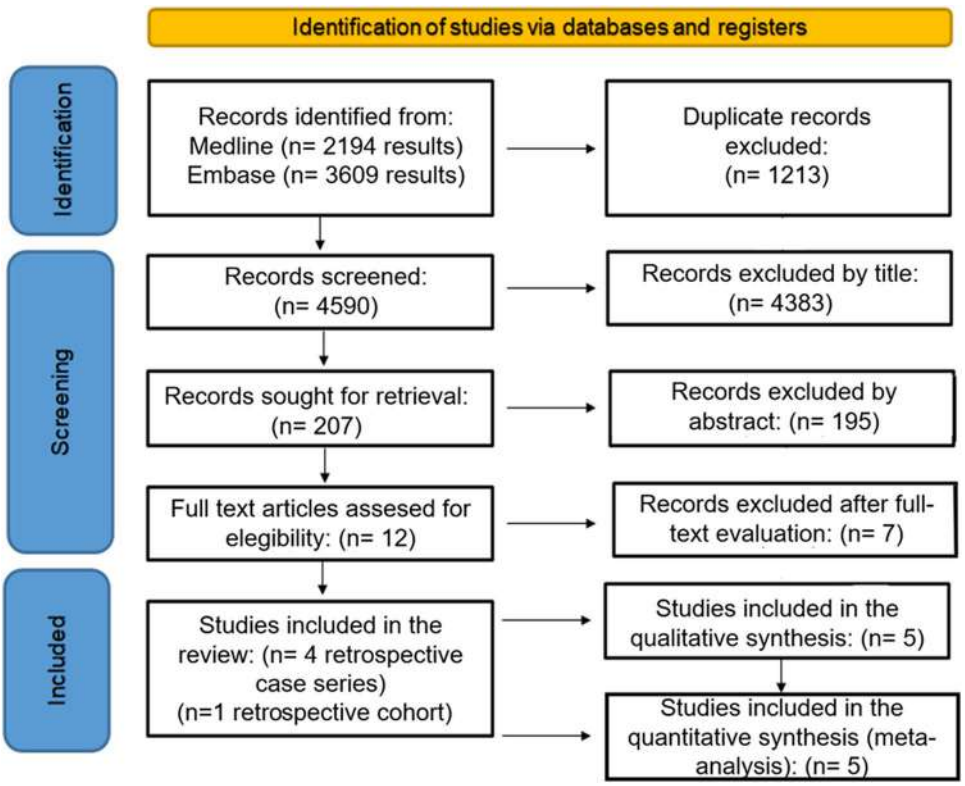

Fig. 1 PRISMA diagram flow

Results

Study Selection

The initial search identified a total of 5803 studies. After evaluation, 207 studies were considered for abstract review. After removal of duplicates, and evaluation of titles and abstracts, 12 studies were eligible for full text assessment, of which 7 were excluded because they were previous studies of the same authors that were updated. Therefore, five studies (4 retrospective case series and 1 retrospective cohort) were selected for qualitative synthesis and meta-analysis [23–27] (Fig. 1).

Table 1 Characteristics of included studies and outcomes

Author	Publication year	Country	Study type	Patients included in the analysis (n)	Outcomes
Morell B	2019	Switzerland	Retrospective case series	6	- Clinical success; - Number of EVT system exchanges; - Interval between EVT system exchanges (days); - Duration of EVT system dwell time (days); - Additional interventional therapy during EVT; - Length of hospital stay (days); - Adverse events
Christogianni V	2018	Germany	Retrospective case series	21	- Clinical success; - Duration of EVT system in place (days); - Need for stent placement after EVT; - EVT system dislodgment; - Adverse events
Archid R	2021	Germany	Retrospective cohort	14	- Clinical success; - Number of EVT device exchanges; - Duration of EVT system dwell time (days); - Additional interventional therapy during EVT; - Need for SEMS placement after EVT; - Length of hospital stay (days); - EVT system dislodgment; - Adverse events; - Death
Leeds SG	2016	United States of America	Retrospective case series	8	- Clinical success; - Number of EVT system exchanges; - Interval between EVT system exchanges (days); - Duration of EVT system dwell time (days); - Length of hospital stay (days); - Adverse events; - Death
Zaveri H	2017	United States of America	Retrospective case series	6	- Clinical success; - Number of EVT device exchanges; - Duration of EVT system dwell time (days); - Need for SEMS placement after EVT; - Length of hospital stay (days); - Adverse events

Table 2 Characteristics of patients, defects, and treatments

Author	Female n (%)	Age, mean and SD (years)	BMI, mean and SD	Type of bariatric surgery	Type of defect	PO days until diagnosis of leakage, mean and SD (days)	Days from diagnosis of leakage until EVT, mean and SD (days)	Type of first-line treatment, if any	Number of EVT system exchanges (= number of EGD), mean and SD (days)	Interval between EVT system exchanges, mean and SD (days)	Duration of EVT system in place, mean and SD (days)	Additional interventional therapy performed	Length of hospitalization, mean and SD (days)	Clinical success	Dislocation of the EVT system	Adverse events
Morell B (2019)	4 (66.66)	47 ± 8.9	45 ± 2.4	LSG (2/6) RYGB (4/6)	LSG: Staple line leak (2/6) RYGB: Anastomotic leakage (4/6)	4.75 ± 1.9	3 ± 1.7	Surgical repair (3/6) None (2/6) Laparoscopic lavage and drainage (1/6)	11 ± 6.6	4 ± 0.3	40 ± 23.6	*SEMS (do not mention when they were used) (5/6) *Laparoscopic lavage during EVT (1/6)	43 ± 14.1	(6/6)	NR	(0/6)
Christogianni V. (2018)	NR	NR	NR	Sleeve gastrectomy (21/21)	Staple line leak (21/21)	Up to 10 days	2–10 p.o. day	Repeat laparoscopy, lavage, and drainage of the abdominal cavity (21/21)	2–10 changes	2–7 days	23.7 ± 10.7	DPPS drainage post EVT (3/21)	NR	(18/21)	(04/21)	(0/21)

Table 2 (continued)

Author	Female n (%)	Age, mean and SD (years)	BMI, mean and SD	Type of bariatric surgery	Type of defect	PO days until diagnosis of leakage, mean and SD (days)	Days from diagnosis of leakage until EVT, mean and SD (days)	Type of first-line treatment, if any	Number of EVT system exchanges (=number of EGD), mean and SD (days)	Interval between EVT system exchanges, mean and SD (days)	Duration of EVT system in place, mean and SD (days)	Additional interventional therapy performed	Length of hospitalization, mean and SD (days)	Clinical success	Dislocation of the EVT system	Adverse events
Archid R. (2021)	10 (71.4%)	44.98 ± 16.74	51.51 ± 10.57	Sleeve gastrectomy (14/14)	Staple line leak (14/14)	25.50 ± 22.67	0.7 ± 0.27	EVT or SEMS combined with laparoscopic drainage (3/14) EVT or SEMS combined with CT drainage (1/14)	3.75 ± 2.6	NR	7.29 ± 7.43	*EVT followed by SEMS (1/14) *Laparoscopy during EVT (6/14) *Intrapyloric Botox injection performed (do not mentioned when were used) (4/14) *Pneumatic dilatation of pylorus performed (1/14)	22.71 ± 24.48	(12/14)	(0/14)	(2/14)

Table 2 (continued)

Author	Female n (%)	Age, mean and SD (years)	BMI, mean and SD	Type of bariatric surgery	Type of defect	PO days until diagnosis of leakage, mean and SD (days)	Days from diagnosis of leakage until EVT, mean and SD (days)	Type of first-line treatment, if any	Number of EVT system exchanges (=number of EGD), mean and SD (days)	Interval between EVT system exchanges, mean and SD (days)	Duration of EVT system in place, mean and SD (days)	Additional interventional therapy performed	Length of hospitalization, mean and SD (days)	Clinical success	Dislocation of the EVT system	Adverse events
Leeds SG. (2016)	7 (77.77%)	48.61 ± 13.2	45.3 ± 8.2	LSG (8/9) 1 patient not for bariatric surgery. Incarcerated/strangulated stomach from an intrathoracic stomach	Staple line leak (8/9)	NR	NR	Laparoscopic exploration attempts at closure or with drain placement (6/9)	10.25 ± 4.6	4.8 ± 0.5	47.35 ± 23	*SEMS (5/9) * OTSC (5/9) *Percutaneous drainage (1/9) *Laparotomy (1/9) (does not mention when they were performed)	81.3 ± 378	(9/9)	NR	(1/9)
Zaveri H. (2017)	NR	NR	NR	Sleeve gastrectomy (4) RYGB (1) Hernia hiatal repair and SG surgery (1)	Staple line leak (3/6) Perforated RYGB ulcer (1) Gastroesophageal leak (2)	153 ± 132.5	NR	None (3/6) Surgical drainage (1/6) Surgical drainage + esophageal stent (1/6) Esophageal stent + Fibrin glue (1/6)	4.6 ± 1.1	NR	22.5 ± 5.2	1 patient had the failure of resolution with EVT and then was changed to stent based therapy	31.4 ± 9.2	(5/6)	NR	(0/6)

SD standard deviation, *BMI* body mass index, *PO* post-operative, *LSG* laparoscopic sleeve gastrectomy, *RYGB* Roux-en-Y gastric bypass, *EVT* endoscopic vacuum therapy, *EGD* esophagogastroduodenoscopy, *OTSC* over the scope clips, *NR* not reported

Study Characteristics

Five studies with a total of 55 patients filled all the inclusion criteria of this systematic review and meta-analysis. A summary of each study is described below and summarized in Tables 1 and 2.

- Morell B, et al. [23]: Swiss study that assessed six patients treated with EVT using the Eso-SPONGE® (B. Braun Melsungen AG, Melsungen, Germany) device alone or in combination with a stent (if the transmural defect was considered too large), with the technique named Stent Over Sponge (SOS), for early postoperative leakages after laparoscopic sleeve gastrectomy (LSG) and Roux-en-Y gastric bypass (RYGB). Two patients were primarily treated with EVT and four initiated EVT as a secondary therapy after prior treatment failure. All patients achieved clinical success with no AEs.
- Christogianni V. et al. [24]: German abstract including 21 patients with early postoperative (up to 10 days) proximal staple line leaks after sleeve gastrectomy (SG), diagnosed with oral contrast-enhanced computerized tomography (CT) scan or after repeat laparoscopy. The EVT was initiated in all cases after a previous laparoscopy, lavage, and drainage of the abdominal cavity. Clinical success was achieved in all cases, 18 with the EVT alone, and in 3 cases, a persistent fistula was treated with endoscopic internal drainage with a double plastic pigtail stent (DPPS). Dislodgment of the EVT system was reported in four patients.
- Archid R, et al. [25]: German retrospective cohort study that assessed 27 patients to compare the outcomes of EVT versus self-expandable metal stents (SEMS) for the treatment of acute and chronic (3–62 days) staple line leaks following LSG. The use of two EVT devices was described, the Eso-SPONGE® (B. Braun Melsungen AG, Melsungen, Germany) was used for intracavitary placement and the open-pore film (OPF) was used for intraluminal therapy. The EVT was selected as a first-line therapy in 10 cases and as a secondary therapy in 4 cases after interventional radiology or surgical drainage. Clinical success was achieved in 12/14 (85.7%) patients, one of them requiring the use of SEMS post EVT. One death due to uncontrolled sepsis was reported in a patient who suffered from multiple severe comorbidities (dilated cardiomyopathy, idiopathic lung fibrosis, and pulmonary hypertension).
- Leeds SG, et al. [26]: American retrospective case series from who underwent EVT with a self-manufactured open-pore polyurethane sponge device for the treatment of staple line leaks after LSG. Nine patients, with acute and chronic leaks, met the criteria for inclusion; with 3 of them undergoing EVT as first-line therapy. Eight patients achieved clinical success, with 5 requiring the use of SEMS at some point during their hospital stay. One patient presented with persistent pancreatitis which was classified by the authors as an EVT-associated moderate AE. One death was reported due to multisystem organ failure not related to the EVT.
- Zaveri H, et al. [27]: An American abstract, consisted of a retrospective case series that summarized the experience of 2 bariatric centers using EVT with the open-pore polyurethane sponge device for patients with upper GI leaks. This study included 6 patients with acute and chronic (1–460 days) staple line leaks after LSG, 3 of them treated with EVT as a first-line therapy. Five of the 6 patients achieved clinical success, while 1 patient needed additional treatment with a SEMS. No deaths were reported in this study.

Risk of Bias and Quality of Evidence

The risk of bias in most studies as assessed by the JBI risk tool was low (Table 3). The quality of evidence of all outcomes was considered "low" evaluated by the JBI risk tool (Table 4) and by the GRADE guidelines (Table 5).

Meta-analysis

Clinical Success

All studies [23–27] reported clinical success rates (fistula/leak closure) as their primary outcome. The EVT showed a rate of successful closure of 87.2% (95% CI 75.4–93.8%; $I^2 = 0\%$; $P = 0.000$) (Fig. 2).

Number of EVT System Exchanges

Four studies [23, 25–27] assessed this outcome. The meta-analysis resulted in a mean of 6.47 EVT system exchanges (95% CI 4.00–8.94; $I^2 = 85.30\%$; $P = 0.000$) (Fig. 3).

Interval Between EVT System Exchanges

Two studies [23, 26] assessed the interval time between each EVT system exchange. The mean interval was 4.39 days (95% CI 3.60–5.17; $I^2 = 93.31\%$; $P = 0.000$) (Fig. 4).

Table 3 JBI risk tool for bias assessment

	Bernhard Morell et al. (2019)	Christogianni V. et al. (2018)	Rami Archid et al. (2021)	Steven G. Leeds et al. (2016)	Zaveri H. et al. (2017)
Clear criteria for inclusion	⊕	⊕	⊕	⊕	⊕
Condition measured in a standard, reliable way	⊕	⊕	⊕	⊕	⊕
Valid methods used for identification of the condition	⊕	⊕	⊕	⊕	⊕
Consecutive inclusion of participants	⊕	?	⊕	⊕	⊖
Complete inclusion of participants	⊕	?	⊕	⊕	⊕
Clear reporting of the demographics of the participants	⊕	⊖	⊕	⊕	⊖
Clear reporting of clinical information of the participants	⊕	⊖	⊕	⊕	⊕
Outcomes clearly reported	⊕	⊕	⊕	⊕	⊕
Clear reporting of the presenting site(s)/clinic(s) demographic information	⊕	⊖	⊕	⊕	⊕
Appropriate statistical analysis	⊕	⊕	⊕	⊕	⊕
OVERALL	✓	✓	✓	✓	✓

Judgement	
Yes	⊕
No	⊖
Unclear	?
Include	✓

Table 4 JBI risk tool for bias assessment (percentage)

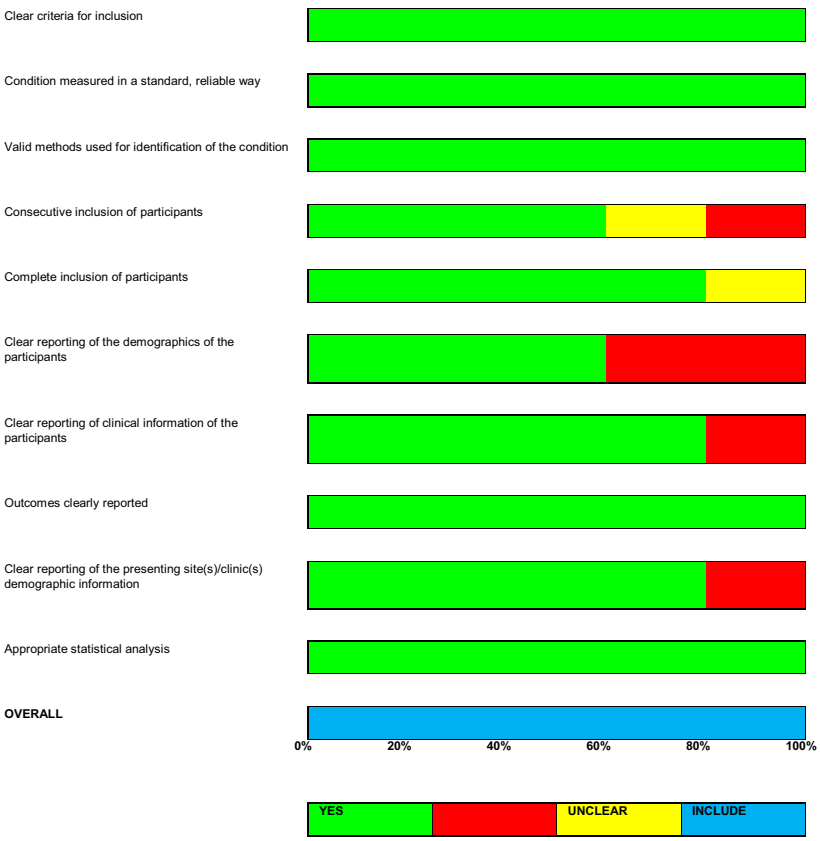

Table 5 Quality of evidence by Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines

Certainty assessment						№ of patients	Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Endoscopic vacuum therapy	Relative (95% CI)	Absolute (95% CI)	
Clinical success (assessed with: %)									
5	Observational studies	Not serious	Not serious	Not serious	Not serious	50/55 (90.9%)	RR 87.2 (75.4 to 93.8)	87 fewer per 100 (From 94 to 75 fewer)	⨁⨁◯◯ Low
Number of EVT system exchanges (assessed with: sessions; scale from: 1 to 24)									
4	Observational studies	Not serious	Not serious	Not serious	Not serious	34	-	Mean 6.47 higher (4 higher to 8.94 higher)	⨁⨁◯◯ Low
Interval between EVT system exchanges (days) (assessed with: days; scale from: 3 to 5,75)									
2	Observational studies	Not serious	Not serious	Not serious	Not serious	15	-	Mean 4.39 higher (3.608 higher to 5.176 higher)	⨁⨁◯◯ Low
Duration of EVT system dwell time (days); (assessed with: days; scale from: 4 to 84)									
5	Observational studies	Not serious	Not serious	Not serious	Not serious	55	-	Mean 25.67 higher (15.16 higher to 36.18 higher)	⨁⨁◯◯ Low
Adjunctive therapy during EVT (assessed with: patients that required)									
2	Observational studies	Not serious	Not serious	Not serious	Not serious	7/20 (35.0%)	RR 35.3 (15.3 to 62.3)	35 fewer per 100 (From 62 to 15 fewer)	⨁⨁◯◯ Low
Length of hospital stay during EVT (days) (assessed with: days; Scale from: 16 to 97)									
4	Observational studies	Not serious	Not serious	Not serious	Not serious	34	-	Mean 44.43 higher (30.01 higher to 58.84 higher)	⨁⨁◯◯ Low
EVT system dislodgment (assessed with: %)									
2	Observational studies	Not serious	Not serious	Not serious	Not serious	4/35 (11.4%)	RR 12.5 (2.7 to 42.7)	13 fewer per 100 (From 43 to 3 fewer)	⨁⨁◯◯ Low
Adverse events (assessed with: %)									
5	Observational studies	Not serious	Not serious	Not serious	Not serious	1/55 (1.8%)	RR 6.0 (1.9 to 17.0)	6 fewer per 100 (From 17 to 2 fewer)	⨁⨁◯◯ Low

CI confidence interval, *RR* risk ratio

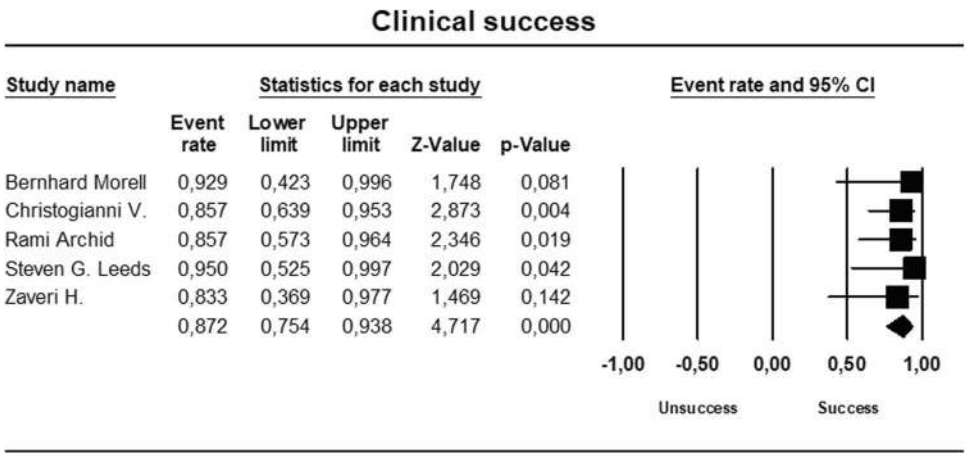

Fig. 2 Forest plot for rate of clinical success, using the fixed-effects model. CI, confidence interval

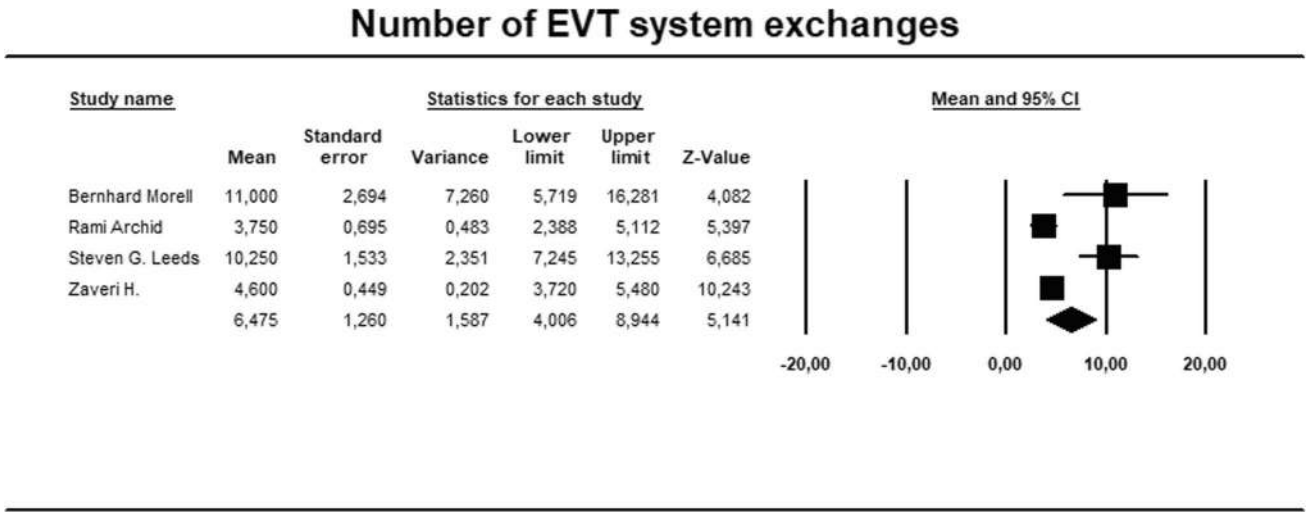

Fig. 3 Forest plot for the number of EVT system exchanges, using the random-effects model. CI, confidence interval

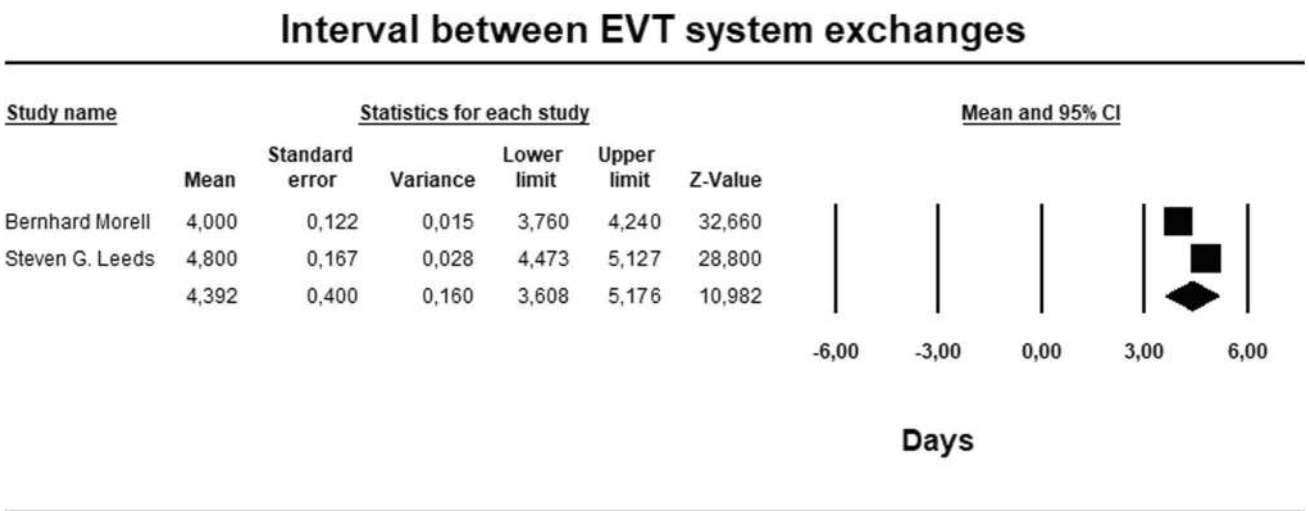

Fig. 4 Forest plot for duration of interval time between EVT system exchanges, using the random-effects model. CI, confidence interval

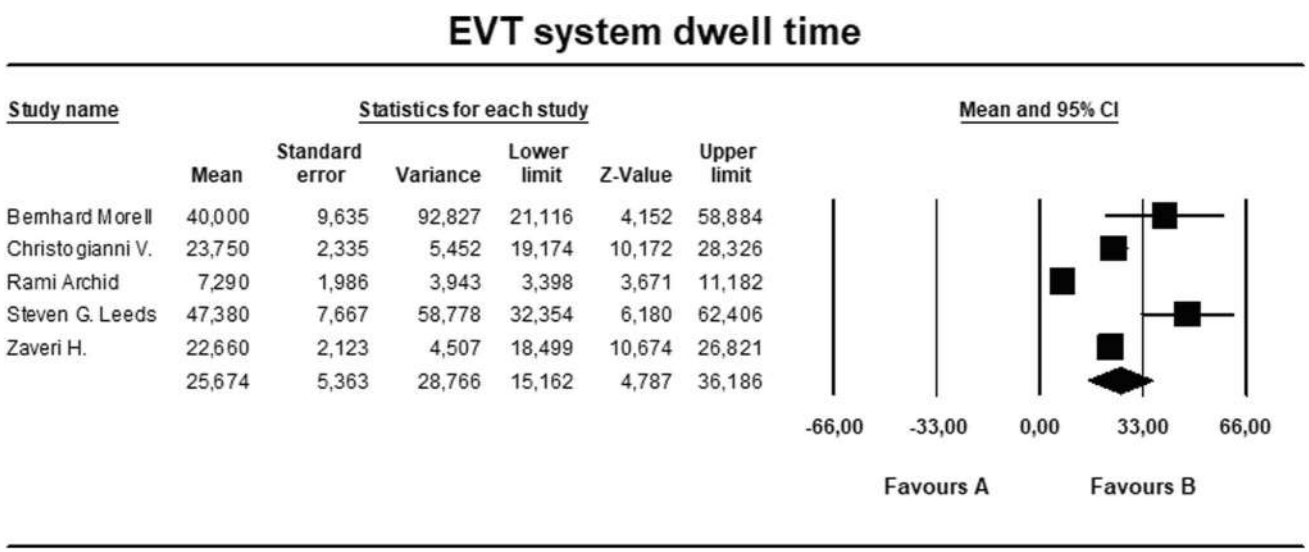

Fig. 5 Forest plot for duration of EVT system dwell time, using the random-effects model. CI, confidence interval

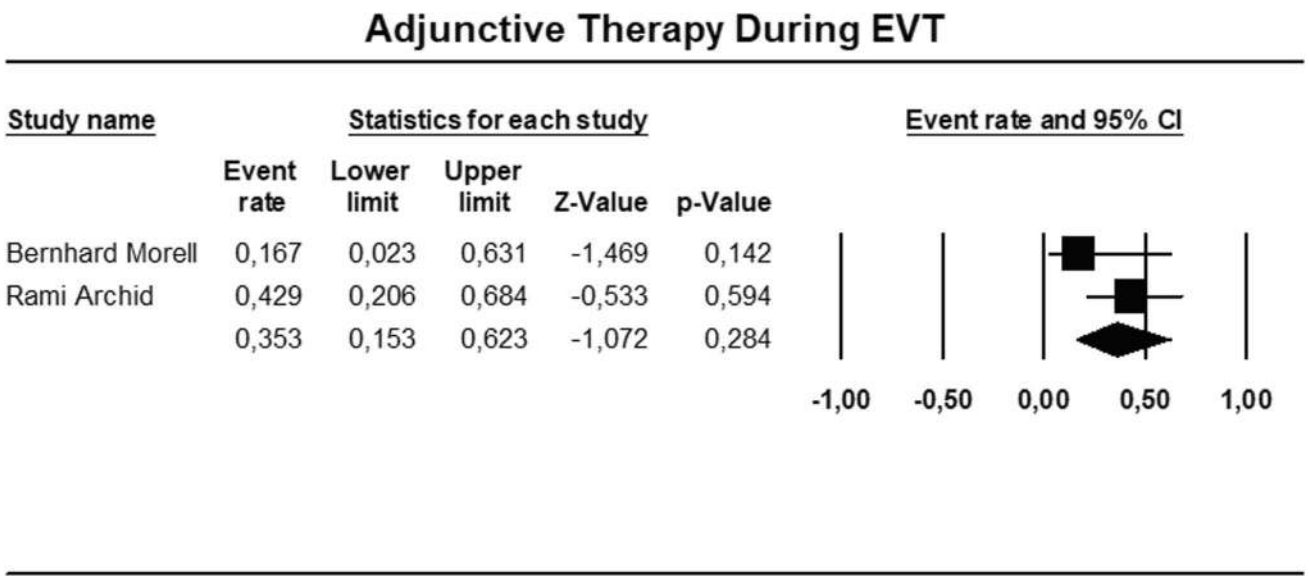

Fig. 6 Forest plot for patients that received adjunctive therapy during EVT, using the random-effects model. CI, confidence interval

Duration of EVT System Dwell Time

All studies [23–27] assessed the duration of the EVT system dwell time reported in days, resulting in a mean of 25.67 days (95% CI 15.16–36.18; $I^2 = 93.31\%$; $P = 0.000$) (Fig. 5).

Adjunctive Therapy During EVT

Two studies [23, 25] reported the rate of patients receiving adjunctive therapy during EVT (both of them reported laparoscopic intervention), resulting in a mean rate of 35.3% of patients that received adjunctive therapy during EVT treatment (95% CI 19.3–75.2; $I^2 = 14.617\%$; $P = 0.284$) (Fig. 6).

Length of Hospital Stay

Four studies [23, 25–27] assessed the length of hospital stay during the EVT treatment reported in days, resulting in a mean of 44.43 days (95% CI 30.01–58.84 days; $I^2 = 80.82\%$; $P = 0.000$) (Fig. 7).

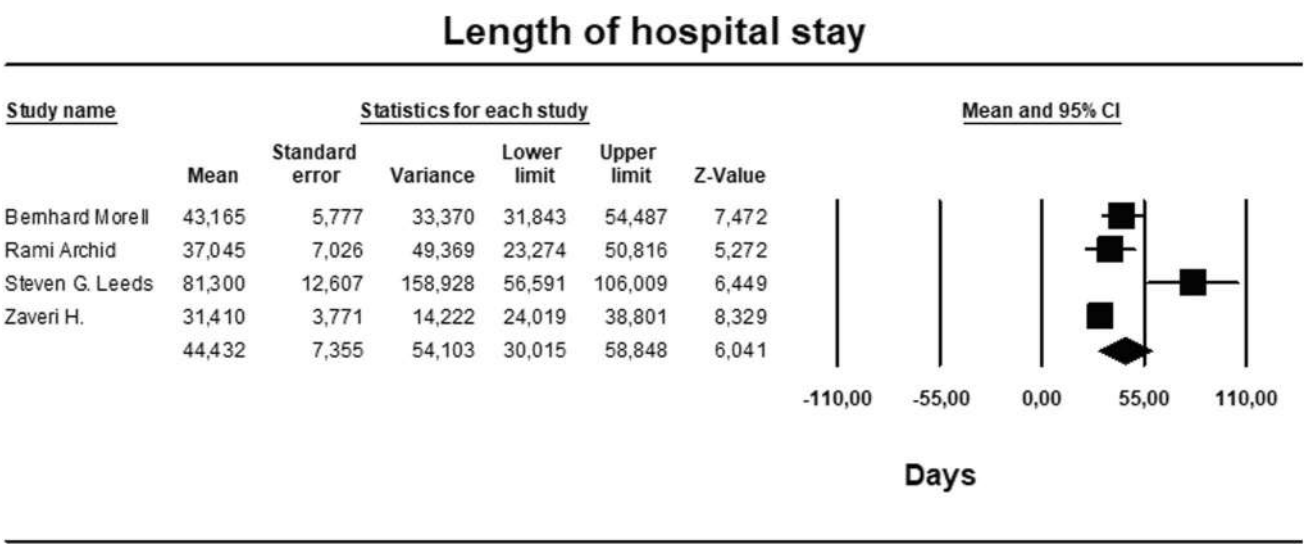

Fig. 7 Forest plot for length of hospital stay, using the random-effects model. CI, confidence interval

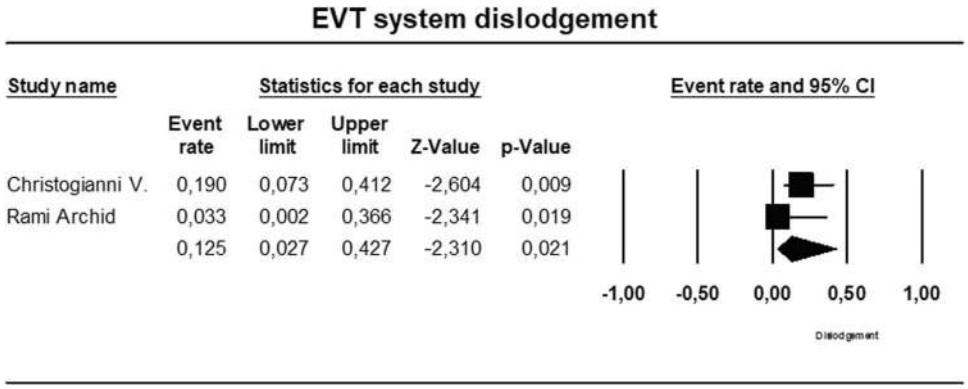

Fig. 8 Forest plot for EVT system dislodgment, using the random-effects model. CI, confidence interval

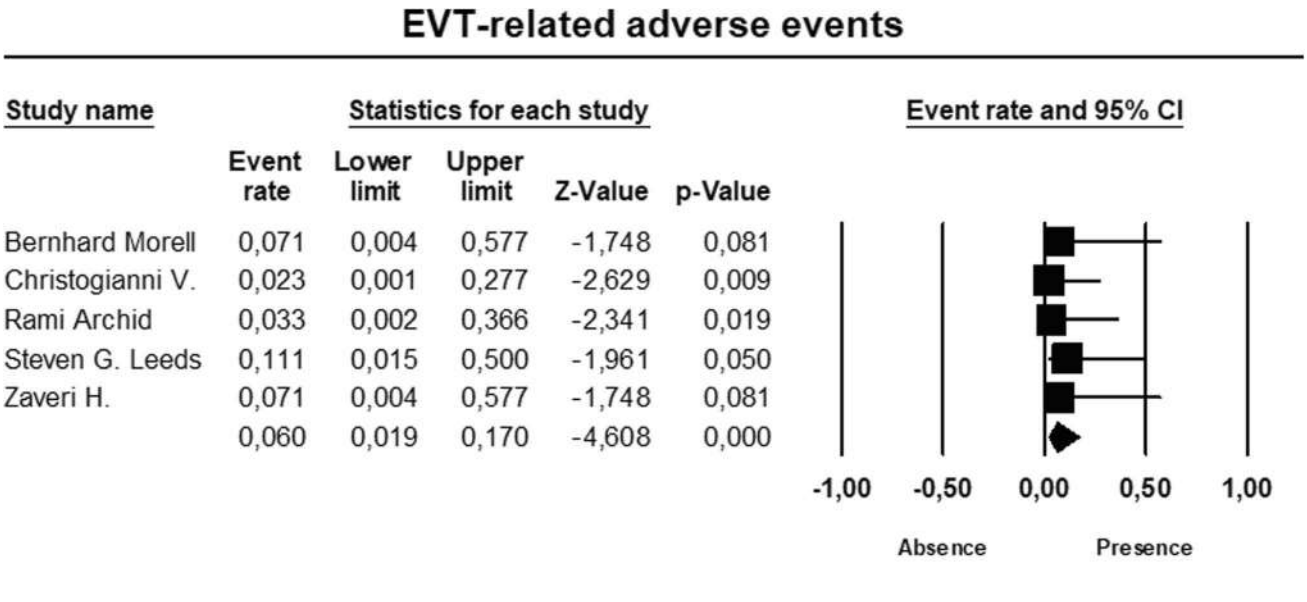

Fig. 9 Forest plot for moderate adverse events during EVT, using the fixed-effects model. CI, confidence interval

EVT System Dislodgment

Two studies [24, 25] reported the rate of the EVT system dislodgment, resulting in a mean rate of 12.5% (95% CI 2.7–42.7; $I^2 = 35.52\%$; $P = 0.021$) (Fig. 8).

Adverse Events

All studies [23–27] reported the rate of AEs related to the use of the EVT. All AEs were graded as moderate, resulting in a mean rate of 6% of moderate AEs (95% CI 1.9%–17%; $I^2 = 0\%$; $P = 0.000$) (Fig. 9).

Mortality

From all included studies [23–27], two deaths were reported. One of the patients suffered from multiple severe comorbidities (dilated cardiomyopathy, idiopathic lung fibrosis, and pulmonary hypertension) and died from uncontrolled sepsis [25]. The death of the other patient occurred within the 30-day period after the removal of the EVT. This was an elderly patient with several comorbidities who died due to multisystem organ failure [26]. Both reported deaths were not related to the EVT, and thus mortality was not meta-analyzed.

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis evaluating the use of EVT on PBS leaks and fistulas, showing that EVT is safe and effective in the treatment of these challenging conditions, with clinical success rates of 87.2%. However, this technique requires multiple system exchanges (approximately 6.47 sessions) with a mean of 4.39 days between exchanges. Additionally, it has a dwell time of 25.67 days, and a long hospitalization length of 44.43 days.

It is important to note that in the studies included in this meta-analysis, EVT was used as first-line therapy in only 32.72% of the cases (18 of 55 patients). As it is well-known, chronic defects are more challenging to treat than acute defects, in which EVT could achieve a higher clinical success rate [28–30], but even with the limitations mentioned below, EVT showed a high rate of clinical success, proving to be effective in late and chronic defects as well [31]. Unfortunately, we could not meta-analyze the efficacy of EVT in acute and chronic defects separately due to the lack of available data in the included studies.

A mean of 6.47 endoscopy sessions were performed for EVT system exchanges. In most studies, this high number of EVT exchanges was associated with the use of the open-pore polyurethane sponge system [23, 24, 26, 27]. The traditional sponge used for this particular device is associated with tissue ingrowth and obstruction, requiring a shorter interval between EVT exchanges. Despite the use of the traditional sponge system, Archid R, et al. [25], also used the OPF, resulting in a low number of EGD sessions due to the characteristics of the material which is not associated with tissue ingrowth and obstruction due to the slippery surface and the several fenestrations alongside the device. Unfortunately, the data available does not allow a meta-analysis comparing these devices. Considering these peculiarities, other EVT devices are being explored showing similar benefits of the OPF compared to the traditional system, such as the cost-effective modified EVT. The OPF and the cost-effective EVT systems present several advantages compared to the OPS, such as easy placement (insertion through the nares) and lower procedural time [32–35]. Recently developed systems such as the triple-lumen tube (TLT) allow drainage and nutrition with a single tube through the nares, which, in our experience, has shown to improve tolerability since it prevents the placement of two tubes through the nares thus minimizing discomfort. Thus, these novel EVTs systems may have the potential to spread the use of the EVT worldwide [36].

The mean EVT dwell time was of 25.67 days (95% CI 15.16–36.18; $I^2 = 93.31\%$; $P = 0.000$), with a mean length of hospital stay of 44.43 days (95% CI 30.01–58.84 days; $I^2 = 80.82\%$; $P = 0.000$), both results showing relevant statistical differences between all the included studies. These results can be associated with the differences between the studies population, inclusion of acute to chronic defects, defects with and without an associated collection, and the use of adjunctive therapies. Additionally, personal and local experience may also interfere with the results, as well as the type of the device. Leeds SG, et al. [26], presented a mean of 81.30 days (95% CI 56.59 to 106.00 $P = 0.000$) with the use of the OPS in all cases while Archid R et al. [25] reported a mean of 37.04 days (95% CI 23.27 to 50.81 $P = 0.000$) using the OFD in some cases.

Regarding AEs, moderate AEs were reported in 6% of the cases, including one case of bleeding [25] and one case of acute pancreatitis [26]. No serious AEs or deaths related to the EVT were reported.

Despite this being the first systematic review and meta-analysis evaluating the role of EVT in the management of PBS leaks and fistulas, our study has some limitations. The major limitation is the small number of studies and patients included in the analysis due to the paucity of available literature. As a quite new technique, no randomized clinical trials, as well as cohort studies, are available, which contributes to the high risk of bias in all the included studies in this analysis. Second, the lack of standardization of clinical conditions can directly affect the results. Relevant data such as time of the defect, defect size, presence of an associated collection, EVT devices used, negative pressure regimens, and clinical management was not reported or standardized in the evaluated studies, which

precludes a more detailed analysis. Despite these limitations, the high clinical success and adequate safety profile found in our study suggest that EVT is a promising therapeutic option for the management of PBS leaks and fistulas.

Given the established efficacy and safety profile of the EVT in the management of transmural GI defects, including PBS complications as demonstrated in this meta-analysis, novel indications are currently being explored, including preemptive EVT after surgery and treatment of GI hemorrhages [37–41]. The use of prophylactic EVT presented satisfactory results in several series [37–39]. Loske et al. [39] successfully used the OPF in a TLT as a prophylactic EVT after an Ivor-Lewis esophagectomy allowing for early nutrition and healing with a mean treatment duration of 8 days. In our experience, prophylactic EVT can also be used after high-risk surgeries such as revisional bariatric surgery, pancreaticoduodenectomy, and colorectal anastomosis after radiotherapy [40]. Recently, we described its use for diffuse duodenal hemorrhage in critically ill patients with severe inflammatory states, with 100% technical and clinical success. Our approach was based on the mechanisms of action of the EVT which include improving local inflammation by micro/macro deformation, reduction in intraluminal pressure, clearance of gastric and biliopancreatic secretions, and changes in tissue perfusion [41].

In summary, this systematic review and meta-analysis showed that the use of the EVT as a first or second-line therapy, alone or associated with an adjunctive therapy, is a safe, and effective approach for the management of PBS leaks and fistulas. Notwithstanding, it is critical to understand that the treatment of patients with PBS transmural defects is challenging and an individualized approach is required to decide what treatment is the most appropriate for each situation. Until now, there has been a relative lack of data to support any technique as a gold standard method, and often more than one intervention is required. Personal and local expertise, resource availability, potential advantages, and disadvantages of each therapy, and patient preferences should be considered when choosing the best treatment strategy. Ultimately, a multidisciplinary approach is essential [42–47].

Future, ideally randomized clinical trials, providing more high-quality data regarding the use of EVT for the treatment of leaks and fistulas PBS, are warranted to confirm our findings.

Conclusion

Endoscopic vacuum therapy (EVT) appears to be a safe and effective approach for the management of post-bariatric surgery leaks and fistulas. However, its use may be associated with multiple endoscopic sessions and a longer length of hospital stay. The low quality of data available must be considered when interpreting our findings.

Author Contribution Vera Intriago JM: acquisition of data, analysis, interpretation of data, drafting the article, revising the article, final approval; de Moura DTH: analysis and interpretation of data, revising the article; Proença IM and Monteiro Junior ES: acquisition of data, analysis, interpretation of data, drafting the article, revising the article, final approval; Ribeiro IB: drafting the article, revising the article, final approval; Sánchez-Luna SA: drafting the article, linguistic correction, revising the article, final approval; Bernardo WM: analysis and interpretation of data, drafting the article, final approval; de Moura EGH: analysis and interpretation of data, drafting the article, revising the article, final approval.

Declarations

Ethics Approval The study was approved by the Research Ethics Committee. For this type of study, formal consent is not required.

Conflict of Interest Dr. Diogo Turiani Hourneaux De Moura: BariaTek—Advisory Board Member (Consulting fees). Dr. Sergio A. Sanchéz-Luna: Recipient of the 2021 American Society for Gastrointestinal Endoscopy (ASGE) Endoscopic Training Award by the ASGE and Fujifilm. This was not relevant to this study. Dr. Eduardo Guimaraes Hourneaux De Moura: Olympus—Consultant (Consulting fees), Boston Scientific—Consultant (Consulting fees). They were not relevant to this study.

References

1. O'Brien PE, Hindle A, Brennan L, et al. Long-term outcomes after bariatric surgery: a systematic review and meta-analysis of weight loss at 10 or more years for all bariatric procedures and a single-centre review of 20-year outcomes after adjustable gastric banding. Obes Surg Internet. 2019;29:3–14 Available from: http://www.ncbi.nlm.nih.gov/pubmed/30293134.
2. Colquitt JL, Pickett K, Loveman E, et al. Surgery for weight loss in adults. Cochrane Database Syst Rev [Internet]. 2014;CD003641. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25105982
3. Schulman AR, Thompson CC. Complications of bariatric surgery: what you can expect to see in your GI practice. Am J Gastroenterol Internet. 2017;112:1640–55 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/28809386).
4. Moura D, Oliveira J, De Moura EGH, et al. Effectiveness of intragastric balloon for obesity: a systematic review and meta-analysis based on randomized control trials. Surg Obes Relat Dis Internet. 2016;12:420–9 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/26968503).
5. Zellmer JD, Mathiason MA, Kallies KJ, et al. Is laparoscopic sleeve gastrectomy a lower risk bariatric procedure compared with laparoscopic Roux-en-Y gastric bypass? A meta-analysis. Am J Surg Internet. 2014;208:903–10 (discussion 909-10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25435298).
6. Cariani S, Nottola D, Grani S, et al. Complications after gastroplasty and gastric bypass as a primary operation and as a reoperation. Obes Surg Internet. 2001;11:487–90 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/11501361).
7. Haito-Chavez Y, Kumbhari V, Ngamruengphong S, et al. Septotomy: an adjunct endoscopic treatment for post-sleeve gastrectomy

fistulas. Gastrointest Endosc Internet. 2016;83:456–7 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/26358326).
8. Haito-Chavez Y, Law JK, Kratt T, et al. International multicenter experience with an over-the-scope clipping device for endoscopic management of GI defects (with video). Gastrointest Endosc Internet. 2014;80:610–22 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/24908191).
9. Lippert E, Klebl FH, Schweller F, et al. Fibrin glue in the endoscopic treatment of fistulae and anastomotic leakages of the gastrointestinal tract. Int J Colorectal Dis Internet. 2011;26:303–11 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/21190028).
10. Mukewar S, Kumar N, Catalano M, et al. Safety and efficacy of fistula closure by endoscopic suturing: a multi-center study. Endoscopy Internet. 2016;48:1023–8 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/27576179).
11. Schmidt F, Mennigen R, Vowinkel T, et al. Endoscopic vacuum therapy (EVT)-a new concept for complication management in bariatric surgery. Obes Surg Internet. 2017;27:2499–505 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/28695459).
12. Okazaki O, Bernardo WM, Brunaldi VO, et al. Efficacy and safety of stents in the treatment of fistula after bariatric surgery: a systematic review and meta-analysis. Obes Surg Internet. 2018;28:1788–96 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/29654447).
13. Gonzalez JM, Lorenzo D, Guilbaud T, et al. Internal endoscopic drainage as first line or second line treatment in case of postsleeve gastrectomy fistulas. Endosc Int open Internet. 2018;6:E745–50 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/29876512).
14. Kumbhari V, Cummings DE, Kalloo AN, et al. AGA Clinical practice update on evaluation and management of early complications after bariatric/metabolic surgery: expert review. Clin Gastroenterol Hepatol Internet. 2021;19:1531–7 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/33741500).
15. Vargas EJ, Abu Dayyeh BK. Keep calm under pressure: a paradigm shift in managing postsurgical leaks. Gastrointest Endosc Internet. 2018;87:438–41 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/29406928).
16. de Moura DTH, de Moura BFBH, Manfredi MA, et al. Role of endoscopic vacuum therapy in the management of gastrointestinal transmural defects. World J Gastrointest Endosc Internet. 2019;11:329–44.
17. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev Internet. 2015;4:1 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/25554246).
18. Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc Internet. 2010;71:446–54 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/20189503).
19. Munn Z, Barker TH, Moola S, et al. Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. JBI Evid Synth Internet. 2020;18:2127–33 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/33038125).
20. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ Internet. 2008;336:924–6 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/18436948).
21. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol Internet. 2005;5:13 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/15840177).
22. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. Br Med J. 1997.
23. Morell B, Murray F, Vetter D, et al. Endoscopic vacuum therapy (EVT) for early infradiaphragmal leakage after bariatric surgery—outcomes of six consecutive cases in a single institution. Langenbeck's Arch Surg Internet. 2019;404:115–21 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/30645682).
24. Christogianni V, Bemponis P, Buesing M, et al. O-068: The endoscopic-vacuum assisted closure-technique in the treatment of staple line leaks after sleeve gastrectomy. Obes Surg Internet. 2018;28:1–130 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/29693216).
25. Archid R, Bazerbachi F, Abu Dayyeh BK, et al. Endoscopic negative pressure therapy (ENPT) is superior to stent therapy for staple line leak after sleeve gastrectomy: a single-center cohort study. Obes Surg Internet. 2021;31:2511–9 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/33650088).
26. Leeds SG, Burdick JS. Management of gastric leaks after sleeve gastrectomy with endoluminal vacuum (E-Vac) therapy. Surg Obes Relat Dis Internet. 2016;12:1278–85 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/27178614).
27. Zaveri H, Surve A, Cottam D, Richards C, et al. A142 - Management of upper gastro-intestinal leaks with endoscopic vaccum-assisted closure system (E- VAC): two center experience. 34th Annu Meet Am Soc Metab Bariatr Surg [Internet]. 2017; Available from: https://asmbs.org/app/uploads/2018/03/ASMBS-2017-Abstract-Book-1.pdf
28. Donatelli G, Dumont J-L, Cereatti F, et al. Endoscopic internal drainage as first-line treatment for fistula following gastrointestinal surgery: a case series. Endosc Int Open Internet. 2016;04:E647–51 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/27556072).
29. Willingham FF, Buscaglia JM. Endoscopic management of gastrointestinal leaks and fistulae. Clin Gastroenterol Hepatol Internet. 2015;13:1714–21 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/25697628).
30. Newton NJ, Sharrock A, Rickard R, et al.. Systematic review of the use of endo-luminal topical negative pressure in oesophageal leaks and perforations. Dis esophagus Off J Int Soc Dis Esophagus Internet. 2017;30:1–5 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/27628015).
31. Rached AA. Gastric leaks post sleeve gastrectomy: review of its prevention and management. World J Gastroenterol Internet. 2014;20:13904 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/25320526).
32. de Moura DTH, Hirsch BS, Do Monte Junior ES, et al. Cost-effective modified endoscopic vacuum therapy for the treatment of gastrointestinal transmural defects: step-by-step process of manufacturing and its advantages. VideoGIE Internet. 2021;6:523–8 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/34917860).
33. de Moura DTH, do Monte Junior ES, Hathorn KE, et al. The use of novel modified endoscopic vacuum therapies in the management of a transmural rectal wall defect. Endoscopy [Internet]. 2020. Available from: http://www.thieme-connect.de/DOI/DOI?10.1055/a-1173-7727
34. de Moura DTH, do Monte Junior ES, Hathorn KE, et al. Modified endoscopic vacuum therapy in the management of a duodenal transmural defect. Endoscopy [Internet]. 2020; Available from: http://www.thieme-connect.de/DOI/DOI?https://doi.org/10.1055/a-1173-7282
35. Kuehn F, Loske G, Schiffmann L, et al. Endoscopic vacuum therapy for various defects of the upper gastrointestinal tract. Surg Endosc Internet. 2017;31:3449–58 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/28078463).
36. de Moura DTH, Hirsch BS, Boghossian MB, et al. Low-cost modified endoscopic vacuum therapy using a triple-lumen tube allows nutrition and drainage for treatment of an early post–bariatric surgery leak. Endoscopy [Internet]. 2021; Available from: http://www.ncbi.nlm.nih.gov/pubmed/34374043
37. Neumann P-A, Mennigen R, Palmes D, et al. Pre-emptive endoscopic vacuum therapy for treatment of anastomotic ischemia after esophageal resections. Endoscopy Internet. 2017;49:498–503.

38. Gubler C, Vetter D, Schmidt HM, et al. Preemptive endoluminal vacuum therapy to reduce anastomotic leakage after esophagectomy: a game-changing approach? Dis Esophagus [Internet]. 2019;32. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30596963
39. Loske G, Müller J, Schulze W, et al. Pre-emptive active drainage of reflux (PARD) in Ivor-Lewis oesophagectomy with negative pressure and simultaneous enteral nutrition using a double-lumen open-pore film drain (dOFD). Surg Endosc Internet. 2022;36:2208–16 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/34973079).
40. de Medeiros FS, do Junior ESM, de França RL, et al. Preemptive endoluminal vacuum therapy after pancreaticoduodenectomy: a case report. World J Gastrointest Endosc Internet. 2020;12:493–9.
41. de Moura DTH, de Moura EGH, Hirsch BS, et al. Endoscopic vacuum therapy for duodenal hemorrhage in critically ill patients with COVID-19. Am J Gastroenterol Internet. 2022;117:688–688 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/35137700).
42. de Moura EGH, Silva GLR, de Moura ETH, et al. Esophageal perforation after epicardial ablation: an endoscopic approach. Endoscopy Internet. 2015;47(Suppl 1):E592–3 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/26671539).
43. Sachdev AH, Iqbal S, Ribeiro IB, et al. Use of omental patch and endoscopic closure technique as an alternative to surgery after endoscopic full thickness resection of gastric intestinal stromal tumors: a series of cases. World J Clin Cases Internet. 2020;8:120–5 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/31970177).
44. Barrichello Junior SA, Ribeiro IB, Fittipaldi-Fernandez RJ, et al. Exclusively endoscopic approach to treating gastric perforation caused by an intragastric balloon: case series and literature review. Endosc Int Open Internet. 2018;06:E1322–9.
45. Cereatti F, Grassia R, Drago A, et al. Endoscopic management of gastrointestinal leaks and fistulae: what option do we have? World J Gastroenterol Internet. 2020;26:4198–217 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/32848329).
46. de Moura DTH, Boghossian MB, Hirsch BS, et al. Long-term endoscopic follow-up after closure of a post-bariatric surgery fistula with a cardiac septal defect occluder. Endoscopy Internet. 2022;54:E127–8 (Available from: http://www.ncbi.nlm.nih.gov/pubmed/33862651).
47. Boghossian MB, Funari MP, do Monte Junior ES, et al. Endoscopic septotomy for fistula after bariatric surgery. Endoscopy Internet. 2022;54:E38–9 Available from:http://www.ncbi.nlm.nih.gov/pubmed/33607658.