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Endoscopic Treatment of Non-malignant Esophageal Perforation: Time to Go Vacuum?

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Abstract

Purpose of review This article provides a comprehensive review of the endoscopic treatment of non-malignant esophageal perforation (NMEP), highlighting endoscopic vacuum therapy

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(EVT) and its benefits compared to other therapies based on the available data and in our experience in the management of this condition.

Recent findings The treatment of NMEP is challenging, often being a life-threatening situation. Historically, the management was always performed surgically, although associated with significant morbidity and mortality. Less invasive approaches such as endoscopic therapies are now preferred for clinically stable patients. There is no data to state a gold standard approach; thus, treatment needs to be individualized. EVT use is increasing worldwide due to its unique mechanism of action and satisfactory outcomes.

Summary EVT should be considered the best approach for NMEP, except for clinically unstable patients with uncontained collection. EVT has an adequate safety profile and presents a higher clinical success rate than any other endoscopic therapies for NMEP as a primary or rescue therapy, as an individual or adjunctive therapy, in defect with or without associated collection, regardless of defect location or duration. Thus, we are positive that it is time to go vacuum for NMEP!

Introduction

Non-malignant esophageal perforations (NMEP) are associated with high morbidity and a non-negligible mortality, especially in larger defects. Rapid diagnosis and management are crucial for successful treatment. Late intervention is associated with worse outcomes, including sepsis, repeated interventions, prolonged hospital stay, and substantial healthcare costs [1, 2, 3••, 4].

Although surgical management was traditionally performed to treat NMEP, surgical defect closure is technically difficult, raising complication rates [1]. Therefore, less-invasive approaches are now preferable, mainly for clinically stable patients. Endoscopic techniques are highly effective in reducing morbidity and mortality in the management of NMEP including closure, covering, and drainage techniques. When determining the appropriate endoscopic approach for closing NMEP, certain fundamental principles should be considered, including systemic treatment, drainage, management of related factors, and defect closure [5, 6••, 7, 8••, 9••].

The purpose of this review is to discuss the role of endoscopic therapies in the management of NMEP, highlighting endoscopic vacuum therapy (EVT) and its benefits compared to other therapies, including mechanisms of action, types of EVT systems, technical aspects along with tips and tricks, patients' management during treatment, outcomes, and future perspectives based on the available literature and on our large experience.

Definitions and Etiology

Perforation is defined as an acute rupture of the esophageal wall. Etiologies for esophageal perforation (EP) include iatrogenic (surgical and endoscopic complications) and non-iatrogenic causes (trauma, active ulceration, infection diseases, eosinophilic esophagitis, foreign body impaction, corrosive agents' ingestion, and Boerhaave syndrome [9••, 10].

Leaks are defined as communication between the intraluminal and extraluminal compartments, usually due to a non-treated perforation or after surgical anastomosis dehiscence. Most leaks are associated with an infected collection. Long-term undrained associated collections may spontaneously drain to another organ, turning into a fistula, which is defined as an abnormal communication between two epithelialized surfaces [3••, 5].

The three recognized narrowing topographies of the esophageal lumen often correlate with the etiology of the NMEP. Iatrogenic perforations often occur in the cricopharyngeal. Foreign body ingestion-related NMEP happens mainly in the broncho-aortic constriction and barotrauma after vomiting usually occurs at esophagogastric junction [9••].

Clinical Presentation and Diagnosis

NMEP diagnosis is based on clinical history, physical examination, and supplementary exams, including laboratory tests and imaging.

Clinical manifestation, symptoms, and signs depend on NMEP cause, location, size, and timing. Cervical NMEP is generally less severe than a thoracic or abdominal NMEP, which are usually associated with rapid deterioration, including sepsis and systemic shock [11, 12].

Esophagogastroduodenoscopy (EGD) is key as it allows for diagnosis and management. Fluoroscopy assistance during EGD is very helpful and should be used, especially for iatrogenic defect closure confirmation, evaluation of leaks associated with collections, and fistulous tract. Additionally, when an external drain is present, it can be used for injection of water-soluble contrast, methylene blue, or air/water to perform a bubble test [3••, 12].

Except for iatrogenic perforations during EGD, diagnosis is usually confirmed with imaging exams, notably computed tomography (CT) scan with oral and intravenous (IV) contrast. CT scan allows the evaluation of associated collections, pneumoperitoneum, free fluid, indirect signs of the source of the defect, and provides a broad evaluation of other organs [3••, 7].

Upper gastrointestinal (GI) series (UGIS) is helpful to identify if there is extraluminal extravasation, providing information regarding defect characteristics. Additionally, it is useful after treatment to confirm successful closure. Barium is not recommended due to the risk of barium-induced chemical mediastinitis [3••, 13].

Management

Management depends on several factors, including patient's clinical condition, etiology, timing, location, and degree of infection. Early treatment is associated with a high clinical success rate [5, 6••, 7].

For iatrogenic perforations identified during EGD, immediate treatment is essential. Experienced staff, device availability, standardized protocols, and adequate endoscopic closure are key to success. It is recommended to keep the area around the defect clean and avoid extravasation of fluids [5, 7].

For patients with NMEP related-infection, initial management is similar to other transmural gastrointestinal defect (TGID), including systemic treatment for clinical stabilization (NPO, IV antibiotics, fluid resuscitation, gastric acid suppression, and definition of nutritional route), and drainage (surgical, radiological, or endoscopic). After these pivotal steps, endoscopic management should be performed, mainly for clinically stable patients [3••, 4, 5, 6••, 14].

Patients with hemodynamic instability and/or uncontained collections demand surgical intervention in most cases. The goal of surgery is to drain associated collections. Surgical defect closure depends on its size, location, degree of contamination, and presence of necrotic tissue on its edges. Endoscopic therapies are recommended when defect closure attempt is not performed or also as an adjunctive therapy [3••, 15].

Endoscopic Therapies

Endoscopic therapies utilize several mechanisms of action and can be classified into closure (glues/tissue sealants, clips, and endoscopic suturing (ES)) cover (self-expandable metal stents (SEMS) and cardiac septal defect occluder (CSDO)), and draining techniques (septotomy, endoscopic internal drainage with double pigtail stents (EID-DPS), and EVT). Table 1 summarizes all therapies used for the management of NMEP [3••, 4, 5, 6••, 7, 8••, 9••, 16, 17•, 18–26, 27•, 28–32].

Endoscopic Vacuum Therapy

Endoscopic vacuum therapy (EVT), also known as endoscopic negative pressure therapy, was developed based on negative pressure wound therapy and consists in submitting GI tract tissue to a continuous negative pressure (usually between −125 and −175 mmHg) through a device assembled to a nasogastric tube connected to a vacuum machine [33••, 34••].

Since its first description in 2003 [35], EVT has been shown to be highly effective and safe for several TGID [3••, 5, 6••, 20, 36••, 37, 38••, 39, 40••, 41, 42•, 43, 44]. In particular for NMEP, the results are impressive, with several meta-analyses proving its satisfactory outcomes in different scenarios [8••, 45, 46•, 47].

A recent meta-analysis with 18 studies including all types of NMEP reported a pooled clinical success of 89.4% with 13.6% adverse events (AEs), and overall mortality of 7.1%. The reported AEs should be interpreted with caution because most of the AEs were not serious, as device dislocation and minor bleeding (that occurs especially during system exchanges) [45]. However, there is still a concern regarding major bleeding based on previous reports, especially when the device is placed close to large blood vessels [48–50].

EVT allows continuous drainage of GI fluids, preventing fluid accumulation, reducing local edema, increasing local perfusion, and thus promoting healing through an unique multifactorial mechanism of action [6••, 33••, 34••, 37, 38••, 40••, 41, 51, 52•, 53••, 54••], as summarized in Table 2.

Table 1. Endoscopic devices/therapies for NMEP

Endoscopic technique	Device / characteristics	Mechanism of action	Indication	NMEP characteristics for success	Advantages	Disadvantages	Efficacy	Safety
GLUES/TISSUE SEALANTS	Includes fibrin glue, acellular matrix biomaterial, and cyanoacrylate	Closure Fibrin glue induces a cellular response, extracellular matrix formation and neovascularization Acellular matrix biomaterial induces fibroblast proliferation	Esophago-cutaneous fistula with thin tract Always used as an adjunctive therapy	Location: anywhere Size: thin tract Margins/Tissue: epithelialized surface	Available in most centers Easy application	Limited for larger and/or acute and/or infected defects	Perf: ↓↓↓ Leak: ↓↓↓ Fistula: ↑	Perf: ↑ Leak:↑↑ Fistula: ↑↑↑
TTSC	Used for hemostasis and defect closure Different characteristics and functional profiles: opening width, jaw length, clip length, tail length, material, rotatability, overshoot, open/close precision, and tensile/closure length	Closure Tissue approximation	Acute Perforation (endoscopic iatrogenic perforation)	Location: anywhere below 1 cm from the cricopharyngeal Size: <1–2 cm or multiples TTSC placed in a "zipper" configuration, preferably starting at the distal limit of the defect Margins: non-everted Tissue: healthy	Widely available Low cost Easy application	Limited for small perforations with healthy surrounding tissue and regular margins	Perf: ↑↑↑ Leak: ↓↓ Fistula: ↓↓↓	Perf: ↑↑↑ Leak: ↑↑ Fistula: ↑↑↑

Table 1. (continued)

Endoscopic technique	Device / characteristics	Mechanism of action	Indication	NMEP characteristics for success	Advantages	Disadvantages	Efficacy	Safety
OTSC	Larger clip placed at the tip of the endoscope and deployed similar to a band ligation Has stronger closuring force and captures larger amounts of tissue compared to TTSC	Closure Allows full-thickness closure	Acute/early or late/chronic small defects (perforation, leaks, or fistulas) without narrowed lumen Better results when combined with other therapies	Location: anywhere below 1 cm from the cricopharyngeal Size: < 2 cm Margins: non-everted or everted Tissue: healthy or unhealthy	Easy application Can be used for SEMS and CSDO fixation	Low availability in some countries Challenging application in restricted spaces Better results for non-everted margins and health surrounding tissue Challenging removal	Perf: ↑↑↑ Leak: ↑ Fistula: ↑	Perf: ↑↑ Leak: ↑↑ Fistula: ↑↑
SUTURING	Suturing machine allowing full-thickness suture Interrupted or continuous suture	Closure Allows for full-thickness closure	Iatrogenic perforation closure, especially large defects	Location: anywhere below 5 cm from the cricopharyngeal due to technical issues Size: small to large defects Margins: non-everted Tissue: healthy	Very useful for iatrogenic perforation Can be used for SEMS and CSDO fixation	Need previous experience with the device Challenging application in restricted spaces High cost Poor long-term success for chronic defects	Perf: ↑↑↑ Leak: ↑ Fistula: ↓	Perf: ↑↑ Leak: ↑↑ Fistula: ↑↑

Table 1. (continued)

Endoscopic technique	Device / characteristics	Mechanism of action	Indication	NMEP characteristics for success	Advantages	Disadvantages	Efficacy	Safety
CARDIAC SEPTAL DEFECT OCCLUDER (CSDO)	Self-expanding, double-disc device with shape-memory and high expansion force Developed for cardiac defects closure	Covering Placed into the defect orifice or into the fistula tract like a plug	Chronic epithelialized fistulas refractory to conventional therapies No associated collection	Location: anywhere Size: any size. The size must be selected according to the defect size Margins/Tissue: epithelialized surface	Rescue therapy for refractory cases	High cost Off-label use	Perf: ↓↓↓ Leak: ↓↓↓ Fistula: ↑↑↑	Perf: ↓↓↓ Leak: ↓↓↓ Fistula: ↑
ESOPHAGEAL STENTS	SEMS made of nitinol that conform to the organ and maintain continuous radial force Can be either fully covered or partially covered Available in multiple lengths and diameters	Covering SEMS cover the defect and divert GI contents, avoiding contamination and promoting healing	Acute perforations (if too large for closure with TTSC) Acute and early leaks preferably at the intra-thoracic esophagus	Location: avoid cervical esophagus Size: any size that stent can cover (better results for < 3 cm) Margins: non-everted Tissue: healthy or unhealthy	Easy placement Widely available Early oral intake Low number of repeated procedures PCSEMS: better seal, no leakage around the stent Downstream stenosis concomitant treatment	Need for external drainage if associated collection Symptoms related to the stent (worse if cervical position) High migration rates (FCSEMS > PCSEMS), mainly if non associated stenosis Tissue ingrowth and challenging removal (PCSEMS > FCSEMS)	Perf: ↑↑ Leak: ↑↑ Fistula: ↓↓↓	Perf: ↑ Leak: ↑ Fistula: ↓↓

Table 1. (continued)

Endoscopic technique	Device / characteristics	Mechanism of action	Indication	NMEP characteristics for success	Advantages	Disadvantages	Efficacy	Safety
SEPTOTOMY	Endoscopic technique that consists in sectioning the septum between the lumen and the defect associated collection	Drainage Section of the septum enlarges the communication between the defect and the lumen, thus, matching the pressure between the intraluminal and extraluminal compartments, facilitating drainage	Whenever a septum is identified, septotomy must be performed	Location: anywhere Size: any size Margins: non-everted or everted Tissue: healthy or unhealthy	High efficacy for refractory leaks or fistulas Outpatient procedure	Usually more than one session is required Bleeding: electrosurgical knives > APC	Perf: ↓↓↓ Leak: ↑↑↑ Fistula: ↑↑	Perf: ↓↓↓ Leak: ↑↑ Fistula: ↑↑
EID with DOUBLE PIGTAIL STENTS	Endoscopic internal drainage of defect associated collections using pigtails plastic stents	Drainage The lower pressure of the intraluminal compartment compared to the associated collection facilitates the drainage flow and promotes the progressive reduction of the cavity	Acute or Chronic defects with contained associated collection Ureteral pigtail stents: very low AEs rates (softer and more flexible)	Location: anywhere – need of an associated contained collection Size: any size Margins: non-everted or everted Tissue: healthy or unhealthy	Easy to perform Low cost Allows early oral intake No need for external drainage Short hospital stay	Need of an associated contained collection Usually more than one session is required Few data for NMEP Long time for defect closure	Perf: ↓↓↓ Leak: ↑↑ Fistula: ↑	Perf: ↓↓↓ Leak: ↑ Fistula: ↑

Table 1. (continued)

Endoscopic technique	Device / characteristics	Mechanism of action	Indication	NMEP characteristics for success	Advantages	Disadvantages	Efficacy	Safety
EVT	Consists in the placement of a sponge at the tip of a nasogastric tube connected to a continuous negative pressure machine (-125 to -175 mmHg) The EVT system can be placed in intraluminal or intracavitary position (if associated collection > 3 cm)	Drainage Multiple mechanisms of action: microdeformation, macrodeformation, changes in perfusion, exudate control, and bacterial clearance	Very high efficacy for acute and early NMEP with associated infected collections Adjunctive therapy after closure of acute perforation	Location: anywhere Size: any size Margins: non-everted or everted Tissue: healthy or unhealthy	High efficacy and very few AEs Effective in catastrophic scenarios with no other endoscopic treatment options No need for external drainage	Discomfort related to the device (nasogastric tube) Need for multiple exchanges Possible prolonged hospital stay Not indicated for esophagocutaneous and/or esophagorespiratory fistulas – need to achieve negative pressure to be effective	Perf: ↑↑↑ Leak: ↑↑↑ Fistula: ↑↑	Perf: ↑↑↑ Leak: ↑↑↑ Fistula: ↑↑↑

NMEP, non-malignant esophageal perforation; *Perf*, perforation; *TTSC*, through-the-scope clips; *OTSC*, over-the-scope clips; *SEMS*, self-expandable metal stent; *CSDO*, cardiac septal defect occluder; *GI*, gastrointestinal; *FCSEMS*, fully covered self-expandable metal stent; *PCSEMS*, partially covered self-expandable metal stent; *EID*, endoscopic internal drainage; *AE*, adverse event; *EVT*, endoscopic vacuum therapy. The number of arrows correspond to the level of efficacy and safety (1 arrow = lower—3 arrows = higher) and the direction of the arrows if it is satisfactory or not (↑ = satisfactory and ↓ = unsatisfactory)

Table 2. Mechanism of action of endoscopic vacuum therapy

Multiple mechanisms	Mechanism of action
Macroderformation and Microdeformation	Both occur when suction is applied, resulting in deformational forces exerted on the defect edges, drawing the boundaries together Deformation of the cytoskeleton initiates signaling cascades, promoting cell proliferation and migration, increasing the expression of elements necessary for healing Factors known to affect the efficiency of this mechanism include the level of suction, consistency of the sponge, as well as the type and deformability of tissue being treated
Angioneogenesis	Adequate blood flow is essential for healing, delivering oxygen and vital nutrients to the tissue and removing waste products Vacuum therapy causes temporary hypoperfusion, resulting in localized hypoxia-inducible factor 1α and simultaneous modulation of vascular endothelial growth factor expression, leading to increased angiogenesis A negative pressure of 125 mmHg considerably increases blood vessel density (up to 4 × more than before treatment)
Exudate control	The accumulation of fluid in extracellular space inhibits healing which, associated with tissue edema, compresses local cells and tissues By removing fluids, a reduction in the compression forces occurs, acting on the microvasculature, which allows increased blood flow and perfusion of the tissue
Bacterial clearance	A high bacterial load may interfere with the defect-healing process. By decreasing the bacterial load, infection control and faster healing are expected

In the management of NMEP, the EVT device can be placed at intraluminal (esophageal lumen) or intracavitary position (into an associated collection). It is essential to notice that if there is an undrained collection larger than 2–3 cm associated with the defect, the priority is to place the EVT into the cavity. In many situations, it is recommended to perform a combined approach with two EVT devices (intraluminal and intracavitary). The simultaneous use of intracavitary and intraluminal EVT allows optimal drainage, lumen (anastomosis) remodeling, and enteral nutrition [3••, 40••, 53••]. In our experience, we use simultaneous intracavitary and intraluminal EVT in cases of extensive transmural defects with associated collection. The intracavitary EVT treats the associated (infected) cavity and the intraluminal EVT repairs the transmural wall defect (remodel), allowing enteral nutrition with the triple lumen tube (TLT)-EVT.

For adequate drainage with EVT, the system needs to function. EVT system blockage must be rapidly recognized and adjusted. Remember that a non-working EVT system may be hazardous. Therefore, all staff needs to be carefully trained for managing these patients. The ability to achieve negative pressure is critically important. Thus, some conditions such as tracheal-esophageal fistula (TEF), esophageal-cutaneous fistula without skin orifice occlusion, and pleurostomy should be considered a contraindication for EVT. Additionally, external drains connected to a similar cavity need to be capped or removed [20, 40••].

EVT is traditionally performed using an open pore polyurethane sponge (OPPS) connected to the distal tip of a nasogastric tube. However, this device is associated with challenging placement and removal, prolonged procedures due to the sponge's large diameter, which hinders endoscopic placement through the hypopharynx, and the need for multiple exchanges due to tissue ingrowth, which may increase costs and the risk for AEs [6••, 34••]. These characteristics are considered a limitation for the spread of the technique in some countries [6••, 40••]. More recently, different EVT devices addressed these limitations, demonstrating easier placement through the nares, longer indwelling period (with the need for fewer exchanges), and lower procedural time and AEs rates, as summarized in Table 3 [6••, 33••, 34••, 36••, 40••, 41, 44, 48, 52•, 53••, 54••, 55–60]. In our personal experience with one of these new EVT devices, named homemade-EVT (H-EVT), overall clinical success was 92.86% with no severe AEs [40••].

Endoscopic Treatment

Endoscopic evaluation must be performed under CO2 insufflation or underwater, to reduce the risk of pneumoperitoneum or pneumomediastinum and to avoid wall rupture of a contained collection, especially when there is no external drainage [3••, 5, 40••]. As perforations, leaks, and fistulas are different entities, requiring individual approaches, in this topic, all NMEP are discussed separately.

Esophageal Perforation

For closing small (< 10 mm) iatrogenic perforations, through-the-scope clips (TTSC) are recommended [21, 61]. TTSC can also be used for larger (> 2 cm) iatrogenic perforations in a "zipper" fashion placement or combined with endoloop [5, 40••]. For larger EPs (> 10 mm but < 20/25 mm), over-the-scope clips (OTSC) are preferable due to their higher clinical success rate, as 85.3% reported in a systematic review [23]. Failures usually occur in defect > 2 cm and/or late (> 72 h) treatment [21]. Stenosis in the proximal esophagus, especially after cervical radiation may preclude OTSC (cap mounted clip) use as it increases the scope tip diameter [61]. ES is also an option, especially if endoscopic closure failed with clips. ES allows full-thickness closure and has the advantage to close extensive defects without size limitation. In a randomized controlled trial comparing clip closure, suturing, and thorascopic repair in porcine models, all approaches performed similarly [62].

SEMS are reserved for cases where primary closure is not possible, such as no adequate visibility due to bleeding. Additionally, for EP related to esophageal stenosis, SEMS is a good option as it treats both EP and stenosis. SEMS covers the defect and diverts GI contents, avoiding contamination, and thus improving healing. Both fully covered (FCSEMS) and partially covered SEMS (PCSEMS) can be used with similar clinical success (> 80%) [63, 64]. SEMS-related AEs are well known including ulcerations, post-stent stricture, bleeding, tissue ingrowth, SEMS-related symptoms (pain, nausea, and reflux), and

Table 3. Summary of different EVT devices

Types of EVT	Characteristics of the device	Advantages	Disadvantages	Our experience
"Traditional sponge" system (OPPS) 	- OPPS connected at the tip of a NGT - Sponge system adapted from the wound vacuum therapy	- Not off-label - Faster healing (more granulation tissue) - Commercially available	- Larger diameter: difficult placement and removal - Tissue ingrowth: shorter interval between exchanges - More AEs - High cost	- Challenging placement, increasing procedure time - Need for endotracheal intubation - Best and faster than other systems in promoting tissue ingrowth - High cost (no insurance covering)
Open-pore film (OPF) 	- OPF connected to the tip of a NGT - Permeable film	- Shorter diameter: easy placement and removal - Longer time between exchanges - High permeability: allows for more fluid aspiration then OPPS - Fewer AEs (bleeding)	- High cost - Small diameter: less adherence, more risk for device dislocation - Not available in some countries	- No experience as it is very similar to the homemade-EVT with higher cost - High cost (no insurance covering)
Homemade EVT (H-EVT) 	- Modification of the OPF manufactured with widely available materials: - Half gauze placed around the tip of a NGT, covered by a surgical drape and fixed with sutures. Then, multiple punctures are made at the covered portion of the device	- Low cost - Widely available material - Slippery surface - Easy placement and removal - Longer interval between exchanges - More fluid aspiration - Fewer AEs	- Off-label - Small diameter: less adherence, more risk for device dislocation	- Preferable for large cavities with high volume of fluid - Very easy placement through the nares, no need for endotracheal intubation after the first sessions - To reduce costs of the vacuum machine, we use wall suction. After connected the NGT to the suction tube, a 20G IV catheter is connected to the tube to maintain a pressure between –75 and –150 mmHg - Preferable for scarce resources centers
Tube-in-tube 	- Aspiration device using a 12Fr Levin tube within a 20Fr Levin tube. The vacuum pump is attached to the inner tube, and the outer tube functioned to prevent aspiration biopsies or clogging	- Low cost - Widely available material - Slippery surface - Easy placement and removal - Longer interval between exchanges - More fluid aspiration - Fewer AEs - Allows rinsing of the cavity with cleansing liquids	Off-label - No sponge or modified sponge systems is used - Less granulation tissue - Not useful for intraluminal placement	- Less effective to stimulate granulation tissue - Useful for large cavities with high volume of fluid - Useful for thin fistulous tract - Very easy placement through the nares, no need for endotracheal intubation after the first sessions - Less effective for intraluminal placement - Useful for scarce resources centers
Triple-lumen tube	- EVT system is connected at the gastric/aspiration portion of the TLT	- Allows simultaneous intraluminal drainage and	- Allows only intraluminal placement	- Reduces patient's discomfort.

Table 3. (continued)

(TLT) 	placed in intraluminal position and the enteral portion is placed in the jejunum	enteral nutrition with only one tube through the nares	- Not available in some countries - Enteral feeding tube has a very small diameter with high risk for obstruction	- Enteral nutrition reduces the need of parenteral nutrition and intestinal bacteria translocation - We use this approach for all NMEPs treated with EVT in defects with (simultaneous intracavitary and intraluminal EVT) or without associated cavity (intraluminal EVT) - We recommend guide-wire placement, as distal as possible, using a ultraslim gastroscope through the nares for TLT-EVT placement
Stent-over-Sponge (SOS)	- OPPS combined with FCSEMS - Allows intraluminal and extraluminal placement of OPPS	- SEMS keeps the GI lumen open after EVT sponge insertion, allowing oral intake - SEMS seals the sponge and secures it in position - SEMS isolates the sponge from saliva and other GI secretions - Commercially available	- High cost, particularly if multiple device exchanges are needed - Not available in some countries	- No personal/local experience as this device is not available in South America - We do not think it will change paradigms as stent related AEs are expected - May be useful for some cases such as large cavities with downstream stenosis
Vac Stent	- OPPS combined with FCSEMS - Allows only placement of OPPS due the cylindrical shape of the sponge	- SEMS seals the sponge and secures it in position - Commercially available	- High cost, particularly if multiple device exchanges are needed - Not available in some countries	- No personal/local experience as this device is not available in South America - We do not think it will change paradigms as stent related AEs are expected - May be useful for some cases such as defects without associated collections, especially large defects and/or downstream stenosis

EVT, endoscopic vacuum therapy; *NGT*, nasogastric tube; *AE*, adverse event; *IV*, intravenous; *OPPS*, open-pore polyurethane sponge; *Fr*, French; *OPF*, open-pore film; *TLT*, triple lumen tube; *SOS*, stent-over-sponge; *GI*, gastrointestinal; *FCSEMS*, fully covered self-expandable metal stent migration. Migration has higher incidences in FCSEMS (26%) compared to PCSEMS (12%) [63–66]. Stent fixation with suturing or OTSC reduces stent migration rates [24, 65]. We only use SEMS when there is an associated stenosis, reducing the risk of migration and treating both NMEP and stenosis. We prefer PCSEMS as it is associated with more tissue ingrowth, providing better sealing, avoiding fluids extravasation around the stent, and reducing the risk of migration. On the other hand, removal is challenging, thus it should be performed between 14–21 days. In some cases, endoscopic mucosal resection and/or argon plasma coagulation (APC) is needed. Stent-in-stent technique is rarely necessary.

EVT can be used for large EPs as an individual therapy or adjunctive therapy [3••, 38••, 39, 40••]. We usually use EVT for EP as an adjunctive therapy after endoscopic closure, especially for large defects. TLT-EVT for 3–10 days is our preferred approach allowing drainage and nutrition with one tube through the nares [3••, 53••]. Although challenging in achieving negative pressure and more EVT device-related symptoms, it can be performed for hypopharynx and proximal EPs with similar efficacy when used in distal EPs [3••, 40••, 44].

Esophageal Leak

Several endoscopic approaches can be used for managing esophageal leaks (ELs). To achieve clinical success and successful defect closure, associated collections must be drained, either surgically, percutaneously, or endoscopically [3••, 40••].

As closure techniques present better results when used to close defects with non-everted margins and healthy surrounded tissue, we prefer to use these techniques for EP, reserving their use for ELs for selected ELs few days after the operation and for stent fixation. Efficacy of closure techniques is not high and concomitant stent placement is suggested to increase clinical success [3••, 5, 61, 67]. SEMS is the most used technique worldwide for managing ELs. Despite its satisfactory efficacy, especially in acute/early scenarios, the migration rate is considerable, mainly if there is no related stenosis. PCSEMS is useful in some catastrophic scenarios such as complete dehiscence, allowing for GI lumen re-connection [68, 69]. We do not recommend SEMS for esophagogastric anastomotic leak (AL) as the distal end of the SEMS stays inside the stomach and cannot avoid gastric and biliopancreatic secretions reflux as the larger gastric lumen precludes sealing between the gastric wall and the SEMS, even when a PCSEMS is used. Although longer and larger SEMS are being used, we do not recommend their use for NMEP as there is no difference between the conventional esophageal SEMS and these novel customized bariatric SEMS [66, 70]. In our experience, this novel stent is associated with more severe AEs, including EP [41, 71].

Endoscopic drainage techniques are our preferred approach, as they provide drainage and healing without the need for external drainage.

Septotomy must be performed when a septum is identified. The principle is similar to the Zenker's diverticulotomy. The septum is sectioned to facilitate fluid drainage from the leak to the digestive tract, avoiding fluid accumulation. The procedure is effective and safe; usually more than one session is required [3••, 26, 72, 73]. In our practice, presence of a septum is a frequent cause of failure and/or prolonged treatment of ELs.

EID-DPS has been widely adopted with high clinical success rates for both acute and chronic leaks [3••, 17•, 27•, 74, 75]. The principle is based on the concept that when the pressure within the GI lumen is lower than that of the associated collection, the flow will be directed into the GI tract [28, 75]. To be effective, it must not be used for uncontained periesophageal collection, concomitant with external drain, and/or high intraluminal pressure due to downstream stenosis. With drainage, the associated collection will typically contract until it is obliterated, achieving successful closure. Although placement is easy as a 7Fr DPS can be placed with a gastroscope, fluoroscopic assistance is recommended, especially for small orifices [3••, 27•]. Besides long treatment period to achieve successful closure, it is not considered an issue as most patients are not hospitalized, present no symptoms, receive oral diet, and return to their daily activities [3••, 5, 17•, 27•]. AEs are uncommon, reported in about 4.5% of patients, including stent migration, perforation, and bleeding [75]. To minimize these risks, we use ureteral DPS as they are more flexible and softer than biliary DPS, avoiding damage to tissue and vessels [29]. We indicate EID-DPS for ELs with associated contained collections without signs of infection. In most cases, we use intracavitary EVT until granulation tissue is observed, then we exchange EVT to EID-DPS to allow early hospital discharge [3••, 40••].

EVT is now considered the best approach for ELs with an associated contained collection [3••, 6••, 8••, 30, 31, 38••]. A meta-analysis evaluating EVT for AL after esophagectomy and total gastrectomy reported a successful closure rate of 81.6% and a 10% lower risk of mortality favoring EVT compared to stents [31]. When comparing EVT and stents for intra-thoracic AL after esophagectomy, EVT was significantly associated with higher healing (OR 2.47) and shorter treatment duration (MD - 11.57 days) with no difference in terms of hospitalization, in-hospital mortality rate, and rate of major and treatment-related complication [46•]. For postoperative esophageal-enteric AL EVT was also significantly associated with a higher rate of leak closure (OR 3.14), shorter treatment duration, and lower mortality rate (OR 0.39) but with the need of more devices exchange (MD 3.09) [47]. The simultaneous use of intracavitary and intraluminal EVT is our preferred approach as it allows optimal drainage, lumen (anastomosis) remodeling, and enteral nutrition. In a recent study simultaneous intracavitary and intraluminal EVT was considered a predictor of clinical success and shorter time to defect resolution [40••]. As we are confident using EVT, we are not afraid to perform aggressive dilation of leak orifice to access the associated cavity and/or downstream stenosis, which is also a benefit of EVT.

Esophageal Fistula

Spontaneous esophageal fistula (EF) closure is rare and due to the formation of an epithelial path, definitive repair is typically challenging [3••, 5, 9••]. Traditionally, it is done with surgical techniques, but with the technical evolution of endoscopy, different strategies are being used, both for temporary support and definitive treatment [25, 76, 77].

TEF and bronchoesophageal fistulas might be treated with most endoscopic therapies; however, complete fistula closure and long-term clinical success are rarely acquired. A systematic review reported a success rate of 84% with a recurrence rate of 63% for TEFs [78]. SEMS are limited by high rate of migration and poor long-term outcomes [9••]. OTSC has been used for small esophageal-respiratory fistulas. If clipping is unsuccessful, suturing is another reasonable option [79, 80]. Prior de-epithelization using thermal (APC/Bugbee electrocautery) and/or mechanical abrasion (cytology brushing) are performed in most cases, increasing successful closure [81]. Comparing ablation alone to ablation with glues/tissue sealants, reported success rates are 67% and 86%, respectively [32]. Due to the impossibility of maintaining negative pressure, EVT should not be used alone [40••]. Off-label use of the CSDO seems to be the best endoscopic option for TEF and bronchopleural, with excellent technical and clinical success rates and few AEs [25]. In our experience, we perform de-epithelization with APC, followed by glue injection into the fistula tract as an adjunctive therapy before orifice closure with OTSC or suturing. SEMS are only used as a temporary adjunctive therapy after endoscopic closure approaches. We consider CSDO the gold-standard endoscopic approach for esophageal-respiratory fistulas. However, due to its off-label use and high cost, we use it after conventional approaches fail. We do not perform de-epithelization prior to its placement and if contrast extravasation is observed after placement, we inject cyanoacrylate into the device [3••, 4, 25, 82–84].

EF to blood vessels or to the heart is a life-threatening condition, whose treatment is always challenging. Endoscopic therapies include SEMS, OTSC, and EVT. SEMS can be used temporarily until the cardiovascular defect is fixed and also as a primary therapy. Additionally, for hematemesis, SEMS and Sengstaken-Blakemore tube can be used to tamponade bleeding before referring the patient for emergency surgery.

Atrioesophageal fistula is among the most serious and lethal complication after atrial fibrillation ablation diagnosed within 2 months after the procedure [21]. Overall, mortality is 55%, with significantly reduced mortality in patients undergoing surgical repair (33%) compared with endoscopic treatment (65%) and conservative management (97%). Therefore, surgery is considered the gold standard treatment and endoscopic therapy, such as SEMS and OTSC, should be reserved for patients unfit for surgery [21]. However, in our experience, endoscopic clipping is a good option for small early ENMP after atrial fibrillation ablation [22]. In our center, all patients undergo EGD 24 h after atrial fibrillation ablation. If an ulcer is diagnosed, TTSCs are used for repair as OTSC is used for EP. For aortoesophageal fistula, esophageal repair is always combined with endovascular treatment or surgery (aortic defect repair) [85]. Thoracic endovascular aortic repair is preferred over surgery due to its minimal invasiveness and certified hemostasis. Although esophagectomy is commonly performed for esophageal lesions to remove the infectious source, endoscopic therapies should be considered as a less invasive approach [85, 86]. In our practice, in patients unfit for surgery, H-EVT (OPPS is avoided in this scenario) is performed after thoracic endovascular aortic repair, with good outcomes. Care must be taken to avoid contact between the EVT device and the aortic wall. Thus, when possible, closure or tissue approximation with TTSC or suturing prior to H-EVT placement is recommended.

Future Directions

Given the established efficacy and safety profile of the EVT for TGID, novel indications are being explored, including pre-emptive EVT (pEVT) and treatment of GI hemorrhage, with promising results [51, 52•, 87, 88, 89••, 90],

Pre-Emptive Endoscopic Vacuum Therapy

To date there is still no consensus on whether pEVT reduces the incidence of post-surgical EL and which group of patients is most likely to benefit from this approach. Recent studies demonstrated positive outcomes of the pEVT with low incidence of AL after esophagectomy when EVT was placed intraoperatively or after anastomotic ischemia detection through an early postoperative EGD [87, 88]. In a series including 8 patients, 75% had complete mucosal recovery after pEVT, and the 25% who developed leaks were successfully treated with ongoing EVT [87]. Although a study including post-revisional esophagectomy patients did not demonstrate reduction in AL incidence, the pEVT was effective in infection control and thus improved clinical condition [91]. Recently, a systematic review showed potential benefit of pEVT to prevent AL after GI surgery, especially in high-risk patients [89••]. We do perform pEVT in high-risk anastomosis after GI surgery. In our opinion, pEVT should be indicated when the surgeon is not confident with the quality of the anastomosis. Although nasoenteral feeding tube (NFT) placement is the traditional approach after a high-risk upper GI surgery, we strongly believe that in this cases, TLT H-EVT should be used as the patient will have a tube through his nares anyway, providing not only enteral nutrition but also reducing the risk for AL and infection.

Endoscopic Vacuum Therapy for GI Hemorrhage

Recently, we described the use of the TLT H-EVT device for diffuse duodenal hemorrhage in critically ill patients and for a large bleeding eroded artery in a giant ulcer, with 100% technical and clinical success, and no AEs [51, 52•, 90]. We trust that its efficacy is related to the treatment of local severe inflammation which is the cause of bleeding. Additionally, TLT H-EVT allows enteral nutrition, which is important as most patients with GI hemorrhage do not receive oral diet. This approach is useful for refractory bleeding from erosive esophagitis. This strategy appears to be safe and effective and can be considered an option when conventional therapies fail. Nevertheless, further studies are necessary to confirm our findings.

Expert Commentary

As endoscopic therapies for TGID evolve with advancements in skills, tools, and techniques, endoscopists are now able to treat NEMP, especially in clinically stable patients (Fig. 1).

There are several endoscopic approaches to manage NEMP and to date there is no data to state a gold-standard method or a precise algorithm to treat this condition. Individualized approach considering personal and local experience and follow-up with multidisciplinary team is critical.

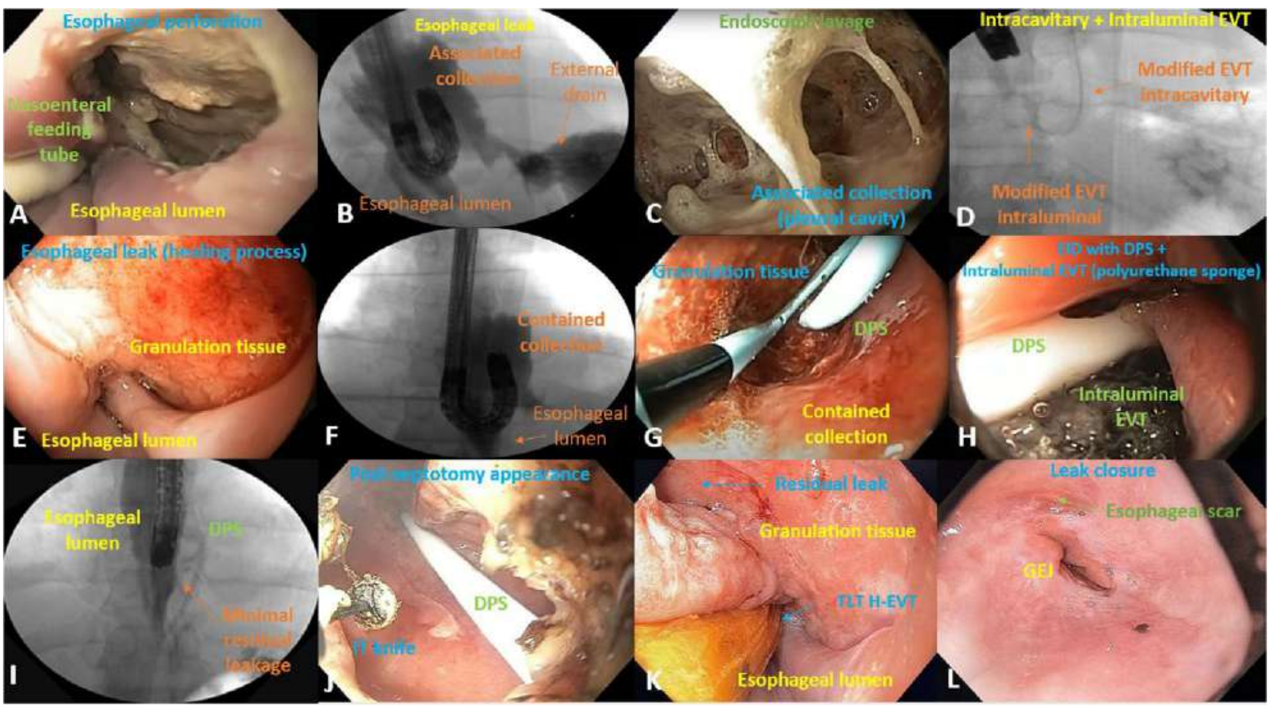

Fig. 1 Endoscopic treatment of Boerhaave syndrome in a patient with eosinophilic esophagitis. **A** Large esophageal perforation with non-everted margins and unhealthy surrounding tissue diagnosed 3 days after initial symptoms. **B** Fluoroscopic image of the esophageal leak with an associated intrathoracic contained collection with the gastroscope inside the collection in a retroflex position and contrast extravasation to the external chest drain. **C** Endoscopic image of the associated infected collection during lavage. **D** Fluoroscopic image after external drain removal and placement of two modified EVT systems (intraluminal and intracavitary). **E/F** Images of the 10th day after EVT treatment with clear improvement, no signs of infections, ongoing healing process with granulation tissue formation, and reduction of the associated collection without contrast extravasation to the skin. **G/H/I** EID-DPS associated with an intraluminal polyurethane sponge EVT system placement (bridge therapy). **J** Endoscopic appearance after septotomy performed to enlarge the communication between the esophageal lumen and the proximal portion of collection (see image **I**) to improve drainage. **K** Esophageal defect with granulation tissue and no more associated collection-intraluminal TLT/H-EVT to allow simultaneous drainage and nutrition. **L** Endoscopic evaluation 1 week after septotomy and intraluminal TLT/H-EVT showing successful closure

Besides there is no sufficient high-quality data to consider EVT as a gold-standard approach, different from recent guidelines [61, 92, 93], we consider EVT the best therapy for most clinically stable patients with NMEP due to its unique mechanism of action, efficacy, safety, and low-invasive profile. EVT can be employed for both acute or chronic NMEP as primary or rescue therapy, thus including a broad patient population. Its best indication is acute perforations (alone or as adjunctive therapy) or leaks with an associated collection as initial treatment. Although patient´s discomfort related to the tube through the nares and longer hospital stay are arguments against EVT use, these two drawbacks are easily overcome by the effectiveness of the EVT. To reduce hospital stay and avoid patient´s discontentment, when a large wound cavity presents granulation tissue and no more signs of infection, we move from intracavitary H-EVT to EID-DPS. Table 4 summarizes our approach in clinical practice, including tips and tricks for the management of NMEP with EVT.

The World Society of Emergency Surgery (WSES) guidelines [93] follow the criteria developed by Altorjay et al. [94] more than 20 years ago of non-operative indications for EP, including early (< 24 h) management, absence of symptoms and signs of sepsis, cervical or thoracic location of the EP, contained perforation by surrounding tissues, minimal peri-esophageal extravasation of contrast with intra-esophageal drainage, absence of massive pleural contamination, no pre-existent esophageal disease, possibility of close surveillance by expert esophageal team, and availability of round-the-clock surgical and radiological teams. In our practice [4, 36••, 40••], we only consider the following criteria against EVT: collection with no endoscopic access, unstable patients with massive extraluminal contamination, and uncontained collections. Although best indication for EVT is a contained collection in a clinically stable patient, EVT can also be used in non-contained perforations as it may organize the fluids, turning them into a contained collection in about 3–7 days. Furthermore, EVT may also be an option for unstable patients as it can be associated with rapid clinical improvement.

The ESGE guidelines for management of iatrogenic perforations [92] recommend first-step endoscopic treatment, as TTSC for defect < 10 mm, OTSC for > 10 mm, and SEMS for larger defects (> 20 mm). Although the guidelines cited two systematic reviews [95, 96] showing the benefits of EVT compared to SEMS, it does not recommend EVT.

The American Gastroenterological Association (AGA) [61] recommendation is similar to the ESGE [92] for defects < 2 cm. However, for > 2 cm, SEMS is reserved for cases where primary closure is not possible. EVT is also not recommended and was just reported as a novel technique to address large or persistent NMEP with high successful closure rates based on the results of a systematic review reporting a successful closure rate of 90% for AL and 96% for EP, with a median EVT use of 17 days [97].

In our practice, we prefer EVT over SEMS for NMEP due to its advantages as internal drainage, no risk of migration and perforation, fewer symptoms, and lower treatment time [8••, 41, 66, 70, 71]. SEMS presents a high risk of migration, especially if there is no associated stenosis. Additionally, SEMS cannot be placed in the very proximal esophagus due to intolerable symptoms. For distal NMEP, SEMS is not able to perform adequate sealing in its distal end due to the large size of the stomach. For infants, EVT is an option

Table 4. Tips and tricks for the management of NMEP with EVT

EVT for NMEP	Tips and tricks
Patient / family / surgeons approach	- Discuss all endoscopic therapies, explain in detail the options available, and your personal experience - Discuss "the good and the ugly" of EVT, including "tube through the nostril", median time for healing, need for hospital stay, efficacy and safety, costs, and obviously sign the consent form - A friendly relationship is needed!
Endoscopic examination	- Orotracheal intubation is preferred: airway protection, and more comfort for the patient, anesthesiologist, and endoscopist - Always perform EGD with orotracheal intubation in the 1st procedure. Following procedures may be performed without orotracheal intubation - Prefer underwater technique with very low CO2 insufflation, especially for acute and early NMEP - Be careful if there is an uncontained collection, especially if undrained. In these cases, insufflation and/or lavage should be avoided. The goal is to place the device as fast as possible to create a compartment
Imaging exams	- CT scan with water-soluble contrast before intervention is helpful for procedure plan - EGD + fluoroscopic assistance is preferred! - Always perform EGD with fluoroscopic assistance in the 1st procedure. Following procedures may be performed without fluoroscopic assistance if not available
Endoscopic procedures prior to EVT placement	- Small orifices with associated collection need to be dilated with hydrostatic balloon allowing intracavitary access - Extensive lavage of the associated collection with water + hydrogen peroxide + acetylcysteine (sachet) - Foreign body removal (external drains, surgical clips/sutures, and residual food content) - When intracavitary placement, nasoenteral feeding tube is placed as distal as possible
Placement	- We often place a 0.035-in. guidewire with an ultra-slim gastroscope through patients' nostrils to facilitate EVT placement. Then, after removing the ultra-slim scope, conventional gastroscope with or without a forceps is used to assist the correct EVT placement - Perforation without fluid extravasation: defect closure + intraluminal H-EVT/TLT as an adjunctive therapy - Perforation with fluids extravasation: tissue approximation (not complete closure) + intraluminal H-EVT/TLT - Leak with undrained contained collection: intracavitary placement – be cautious with insufflation, disruption of the collection may be catastrophic - Leak with drained contained collection: 0.035-in. guidewire placement through the external drain and capture with a forceps biopsy + external drain removal. With both guidewire tips in hands (mouth / cutaneous), intracavitary placement is easy. Always close the cutaneous orifice to allow negative pressure - Fistula: when there is no cavity between the two epithelized organs, EVT is not our preferred approach. It may be used to promote tissue granulation as a bridge therapy - Pediatric (< 3 yo) population: H-EVT (smaller than OPPS) through the mouth keeping the patient under orotracheal intubation or rendezvous if a PEG is placed
Negative pressure settings	- Intracavitary:—175 mmHg, continuous, maximum intensity - Intraluminal:—200 mmHg, continuous, maximum intensity - Wall suction: -75 to -150 mmHg, continuous
EVT types	- See Table 3
EVT position	- Intracavitary: associated cavity > 3 cm - Intraluminal: no associated cavity or cavity < 3 cm - Simultaneous intraluminal and intracavitary: anastomotic leak (dehiscence > 40% of the circumference) with associated cavity > 3 cm. An intraluminal TLT is preferable to promote improve drainage, remodeling of the anastomosis, and enteral nutrition
EVT exchange	- Intracavitary: OPPS: 5 to 10 days / H-EVT: 7 to 15 days - Intraluminal: 7 to 15 days - EVT system removal: 1. Disconnect the EVT tube from the vacuum machine; 2. flush 4 syringes (20 ml) of saline to facilitate removal. 3. Slowly pull the EVT tube (continuous traction). If unsuccessful removal: 1. Flush 2 syringes of hydrogen peroxide and 1 more of saline. 2. Slowly pull the EVT tube. If it continues impossible to remove, perform EGD with underwater technique and remove the device with foreign body forceps assistance - Challenging removal is due to tissue ingrowth. Thus, do not keep OPPS for more than 10 days - EVT exchange is based on patient's clinical condition, device functioning, and defect characteristics. Costs are also considered on timing for system exchange

Table 4. (continued)

EVT for NMEP	Tips and tricks
Adjunctive therapies	- Inaccessible/challenging placement associated collection: DPS + intraluminal EVT - Septotomy must be performed when a septum is identified - Downstream stenosis needs to be dilated prior to EVT placement
NPO X oral diet	- Clear liquid diet for patients' comfort - Intracavitary placement: no more than 500 cc/day
Nutrition	- Nutrition is essential to achieve clinical success. The nutrition via is selected after a multidisciplinary discussion - In most cases, we prefer enteral nutrition, especially for intraluminal placement using TLT-EVT system - We rarely indicate PEG tubes in these situations
Inpatients X outpatients	- For NMEP, hospital stay is required due to the high volume of fluids aspiration, needing canister exchange every 1 to 3 days
Time to stop EVT	- Cavity reduction with extensive granulation tissue and no signs of infection - For large cavities with extensive granulation tissue and no signs of infection, EVT can be changed for DPS - For cavity < 3 cm, intracavitary EVT needs to move for intraluminal position. In these cases, if the orifice is smaller than 10 mm, we recommend septotomy to improve EVT performance
Follow-up	- After achieving clinical success, EGD is scheduled after 15 and 45 days (post-EVT stenosis is rare but can occur) - If symptoms related to the NMEP, early EGD is performed
Costs-related issues	- In general, we prefer to use the H-EVT system to reduce costs - In most continents, EVT is not insurance covered, therefore, in private practice, we inform patients and family about all costs before starting the treatment - In the public hospital, commercially available devices are avoided due to the high cost, and the H-EVT is preferable

NMEP, non-malignant esophageal perforation; *EVT*, endoscopic vacuum therapy; *EGD*, esophagogastroduodenoscopy; *OPPS*, open-pore polyurethane sponge; *DPS*, double pigtail stents; *PEG*, percutaneous endoscopic gastrostomy; *H-EVT*, homemade endoscopic vacuum therapy; *TLT*, triple lumen tube

as there is no specific SEMS for this population [40••]. If clipping or suturing closure appears not effective, we use TLT-EVT as an adjunctive therapy, allowing for both drainage and early nutrition, as well as clear liquids oral intake. Table 5 summarizes our opinion regarding the management of NEMP based on patients' clinical condition and NEMP characteristics.

Despite the proven high clinical success rate, there are some concerns related to EVT use, such as safety, technical challenges, prolonged procedures, need for multiple exchanges, and high cost. However, most of these limitations are related to the traditional sponge system. OPPS is associated with more tissue ingrowth, increasing AEs risks, especially when kept for more than 7 days, such as EVT system obstruction. It is important to underscore that a non-working EVT system may be hazardous for patients. Thus, the entire staff needs to be well-trained. Additionally, OPPS is associated with challenging placement and removal, more prolonged procedures due to its large diameter, which hinders endoscopic placement through the hypopharynx. The risk of major bleeding is the most feared AE due to few reports of fistulas to large blood vessels [48]. Fortunately, several "modified" EVT systems were proposed to overcome these limitations. These novel low-cost devices are affordable and easily reproducible, presenting a smaller diameter and slippery surface with several fenestrations allowing for easier placement and removal through the nares, facilitating endoscopic manipulation and positioning, thus, reducing procedure time. Additionally, these smaller devices appear to

Table 5. Suggested recommendations for the management of NMEP

NMEP characteristics + patient clinical condition	Recommended (first line) approach	Possible (second line) approach
Iatrogenic endoscopic perforation without fluid extravasation to the extraluminal compartments	**< 3 cm:** Endoscopic closure technique (TTSCs / OTSC / Suturing) ± Intraluminal EVT (H-EVT/TLT) for 3 days **> 3 cm:** Endoscopic closure technique (TTSCs / Suturing) + Intraluminal EVT (H-EVT/TLT) for 5 days	Intraluminal EVT – "traditional" sponge system (single therapy) for 5 – 7 days **OR** SEMS (PCSEMS is preferable – better sealing)
Iatrogenic endoscopic perforation with fluid extravasation to the extraluminal compartments	Endoscopic partially closure (TTSCs / OTSCs / Suturing) – tissue approximation + Intraluminal EVT (H-EVT/TLT) for 5 – 7 days	Endoscopic closure (TTSCs / OTSCs / Suturing) + radiological external drainage **OR** SEMS (PCSEMS is preferable – better sealing) + radiological external drainage **OR** Intraluminal EVT – "traditional" sponge system (single therapy) for 7 – 10 days **OR** Surgical lavage + surgical drainage + endoscopic approach (TTSCs / OTSC / Suturing) ± Intraluminal EVT (H-EVT/TLT) for 3—5 days
Non-iatrogenic perforations with uncontained collections in unstable patients	Surgical approach (lavage + drainage + repair) + Intraluminal EVT (H-EVT/TLT) for 7 – 10 days	Surgical lavage + surgical drainage + endoscopic approach (TTSCs / OTSC / Suturing) ± Intraluminal EVT (H-EVT/TLT) for 3—5 days **OR** Surgical lavage + surgical drainage + endoscopic approach (SEMS [PCSEMS is preferable – better sealing]) **OR** Radiological external drainage + endoscopic approach (SEMS [PCSEMS is preferable – better sealing]) **OR** Endoscopic lavage + Intracavitary EVT ± Intraluminal EVT (H-EVT/TLT) **OR** Esophagectomy
Non-iatrogenic perforations/ thoracic or abdominal leaks with uncontained collections in stable patients	Surgical approach (lavage + drainage + repair) ± Intraluminal EVT (H-EVT/TLT) for 5—7 days	Surgical lavage + surgical drainage + endoscopic approach (TTSCs / OTSC / Suturing) ± Intraluminal EVT (H-EVT/TLT) for 3—5 days **OR** Surgical lavage + surgical drainage + endoscopic approach (SEMS [PCSEMS is preferable – better sealing]) **OR** Endoscopic lavage + Intracavitary EVT ± Intraluminal EVT (H-EVT/TLT) **OR** Radiological external drainage + endoscopic approach (SEMS [PCSEMS is preferable – better sealing])
Non-iatrogenic perforations/ thoracic or abdominal leaks with contained collections in stable patients	Endoscopic lavage + Intracavitary EVT ± Intraluminal EVT (H-EVT/TLT)	Endoscopic lavage + EID with DPS + Septotomy (if a septum is identified) ± Intraluminal EVT (H-EVT/TLT) **OR** Radiological external drainage + endoscopic approach (SEMS [PCSEMS is preferable – better sealing])

Table 5. (continued)

NMEP characteristics + patient clinical condition	Recommended (first line) approach	Possible (second line) approach
Esophageal leaks (cervical anastomosis – patients are usually stable)	Endoscopic lavage + endoscopic dilation + Intraluminal EVT (H-EVT/TLT)	Radiological external drainage + endoscopic dilation + nasoenteral feeding tube **OR** Surgical lavage + surgical drainage + endoscopic dilation ± Intraluminal EVT (H-EVT/TLT) for 3—5 days **OR** Surgical lavage + surgical drainage + endoscopic dilation + nasoenteral feeding tube
Esophageal-respiratory fistula	**< 3 cm:** Endoscopic techniques De-epithelization + endoscopic closure techniques (OTSC / Suturing) ± glue/tissue sealant **> 3 cm:** Surgery	**< 3 cm:** Cardiac septal defect occluder ± glues/tissue sealant

NMEP, non-malignant esophageal perforation; *TTSC*, through-the-scope clips; *OTSC*, over-the-scope clips; *SEMS*, self-expandable metal stent; *PCSEMS*, partially covered self-expandable metal stent; *TLT*, triple lumen tube; *H-EVT*, homemade endoscopic vacuum therapy; *EID*, endoscopic internal drainage; *DPS*, double pigtail stents; *EVT*, endoscopic vacuum therapy be more appropriate for pediatric patients. Furthermore, it reduces the system obstruction and the need for multiple EVT system exchanges, reducing the risk for AEs [40••]. Therefore, these novel devices have the potential to expand EVT use around the world.

Conclusions

Endoscopy is now considered the first-line therapy for most NMEP, except for clinically unstable patients with uncontained collections. Due to its unique mechanism of action, promoting tissue healing and infection control, EVT presents a high efficacy and adequate safety profile as a primary or rescue therapy, as an individual or adjunctive therapy, with or without associated collection, regardless of defect location or duration. Moreover, EVT presents a higher clinical success rate than any other endoscopic therapies for NMEP. Thus, we are positive that it is time to go vacuum for NMEP!

Declarations

Conflict of Interest
Dr. Turiani Hourneaux de Moura received personal fees as an Advisory Board member for BariaTek. Dr. Khashab is a consultant for Boston Scientific Corporation, Olympus, Pentax, Medtronic and Apollo, received research support from Boston Scientific, and receives royalties from UpToDate and Elsevier. Dr. Guimarães Hourneaux de Moura received personal fees as a consultant for Olympus and Boston Scientific. All other authors have nothing to disclosure.

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- • Of importance
- •• Of major importance

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