Endoscopic Endoluminal Vacuum Therapy in Esophageal Perforation

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**Background.** Esophageal perforation is a serious disease with a high morbidity and mortality rate. Endoscopic vacuum therapy (EVT) is a new endoscopic treatment option, which is used to treat anastomotic leakages after rectal and esophageal resections. We report on 10 patients treated with EVT for esophageal perforation.

**Methods.** Clinical and therapy-related data such as age, sex, duration of intensive care stay, length of hospital stay, reasons for perforation, EVT-associated complications, mortality, need for alternative treatment options, and course of infectious variables were analyzed.

**Results.** Ten patients were treated with 54 vacuum sponges that were placed in upper gastrointestinal defects. Causes for perforation were iatrogenic, spontaneous, or foreign body-associated. Mean number of sponge insertions was 5.4 (range, 2 to 12) with a mean period of 19 ± 14.26 days. Successful therapy was achieved in 9 of 10 patients. After successful primary treatment, 1 patient died during therapy as a result of general failure of the cardiovascular system. In 1 patient, surgical resection was necessary after repeated Mallory-Weiss lesions and minor perforations during the course of immunosuppressive therapy. In a third patient an endoscopic stent was inserted in the clean wound cavity after primary EVT.

**Conclusions.** In this small trial EVT has been shown to be a safe and feasible therapy option for perforations of the upper gastrointestinal tract. If necessary, EVT can be combined with operative revision for better control of the local septic focus or used as a bridging procedure for wound conditioning before aggressive surgical treatment.

Kiel of those treated with EVT after a perforation of the esophagus. After a positive vote of the local ethical review committee we analyzed clinical data and length of intensive care unit (ICU) and hospital stay, and specified the perforation and treatment strategies (treatment begin, length, number of sponges used, and complications). Complications were categorized with reference to the modified Clavien-Dindo classification [20]. Complications deemed to be of clinical relevance were grouped into infections, respiratory insufficiency, esophageal strictures, and others. Hospital mortality was defined as the death of the patient up to 4 weeks after discharge from the hospital. Sepsis was defined according to the consensus definition of sepsis of the American College of Chest Physicians and Society of Critical Care Medicine (ACCP-SCCM Consensus Conference) [21]. Procalcitonin was chosen as an inflammatory marker for the monitoring of inflammatory response. For all patients procalcitonin was measured daily during the first 3 days of EVT to monitor mediastinitis and sepsis. For patients requiring intensive care treatment, further measurements of procalcitonin were taken daily for the length of their stay on the ICU or intermediate care unit (IMC).

Patients were monitored after discharge from the hospital for a median of 9 ± 6.4 months.

The perforation was detected either by the ingestion of contrast dye followed by a computed tomography (CT) scan of the thorax or by primary endoscopy in cases of suspected esophagus perforation. In all cases the extent and location of the perforation was verified with the use of an endoscopy and a CT scan of the thorax, which was performed to detect possible pleural effusions, mediastinal abscess, or pneumothorax (Fig 1). In patients with a detected pneumothorax, mediastinal emphysema, or pleural empyema, an additional pleural drainage was placed or the pleural cavity was cleaned by means of the thoroscopic approach. Before endoscopic positioning of the sponge, the wound cavity was washed with the implementation of an endoscopic jet lavage.

In all patients an Endo-Sponge system (B. Braun, Melsungen, Germany) was used. The endoscope was used to appraise the size of the wound cavity, and the polyurethane sponge was trimmed to the cavity size (Fig 1). In cases of a large cavity a second sponge was placed to fully seal and better drain the cavity. An overtube was placed over the endoscope, and the cavity was intubated again. Using the endoscope as a guide, the overtube was placed under vision in the cavity (Fig 2). The endoscope was then withdrawn, and the trimmed sponge was pushed through the overtube into the cavity using the pusher device. In cases in which the wound cavity was deeper than the length of the overtube, the trimmed sponge was pushed into the esophagus and placed under vision with endoscopic hook-mouth forceps. After placing the sponge in the wound cavity, the overtube was withdrawn, and the correct placement of the sponge was confirmed by endoscopy (Fig 3). The sponge was connected to the drainage tube, which was diverted through the nose and connected to a vacuum pump or redon bottle that provided a continuous negative pressure of 75 to 200 mm Hg [14]. In the first week of therapy, sponges were replaced every second day. If the wound cavity was free from pus and clean and granulation tissue was detectable, the sponge was replaced twice a week. Longer intervals have shown to be a risk for ingrowth and device integration of the sponge [22]. The use of EVT was terminated when the remaining wound cavity was smaller than approximately 1 cm in radius and 2 cm in depth. Patients had weekly endoscopic follow-up examinations until the cavity had completely healed. Complete healing was defined as the macroscopic reestablishment of the mucosal lining and the absence of granulation tissue (Fig 4). To detect long-term complications patients were interviewed during the long-term follow-up.

Data were analyzed using SPSS for Macintosh (version 21.0) software (IBM Corp, Armonk, NY). All metric variables are expressed as total numbers (%) or mean ± standard deviation. All distribution and frequencies of medical data were compared by Fisher’s exact test. The one-way Student’s t test was used for assessment of whether variables differed significantly. A probability value of less than 0.05 was considered statistically significant.

Results

Study Population

Between 2008 and 2012, 10 (5 male, 5 female) patients were treated owing to a benign cause of esophageal perforation. During this period, all patients were treated with EVT regardless of clinical presentation. The mean age was 66 ± 10.7 years. On admission 8 patients presented a septic clinical condition. Five patients required artificial ventilation. In 4 of these 8 patients the implementation of EVT came after more than 24 hours after diagnosis. Comorbidities of the patients are shown in Table 1.

On admission, all patients with a cervical perforation (n = 3) presented in a septic clinical condition with a mediastinal abscess (n = 3) and pleural empyema (n = 1), and needed to be admitted to the ICU or IMC. Artificial ventilation was needed for 2 of the 3 patients. For all patients with cervical perforations, the start of EVT was longer than 24 hours after diagnosis. An aggressive endoscopic lavage of the mediastinal abscess was needed in all 3 patients, and an additional thoroscopic lavage and decortication of the pleural cavity was carried out in 1 patient.

Clinical Data

The perforation was localized in the cervical esophagus in 30% (n = 3) and thoracic esophagus in 70% (n = 7). Four patients (40%) experienced an iatrogenic injury. 1 patient (10%) had a foreign body ingestion, and 5 patients (50%) had Boerhaave’s syndrome. Of the 10 patients, 2 were fed by gastric tube, 3 by a percutaneous endoscopic gastrostomy tube, and 9 by total parenteral nutrition during EVT. The mean diameter of the
The perforated cavity was 4.2 ± 2.5 cm (range, 1 to 10 cm). In 3 patients the diameter of the perforated cavity was greater than 5 cm. In 5 patients an additional drainage of the pleural cavity was needed by placement of a chest drain (Table 1).

**Endoluminal Vacuum Therapy**

In most of the cases (60%, n = 6), EVT started within 24 hours after diagnosis of the perforation. In 4 patients (40%), the start of EVT was longer than 24 hours after diagnosis. These 4 patients were transferred to our center from other hospitals. The length of EVT (p = 0.003) and hospital stay (p = 0.001) was significantly longer for patients with an interval of more than 24 hours before the start of EVT (Fig 5). The average number of EVT sessions was 5.4 ± 3.4. In 80% of patients (n = 8) one sponge was used, and in 20% (n = 2) two sponges were placed into the cavity. After 12 days of EVT, a decrease of 93% was monitored for the systemic inflammatory laboratory marker procalcitonin (Fig 6). Alternative therapy options had to be initiated in 2 patients (20%). In 1 patient surgical resection was performed after conditioning the wound cavity because of repeated Mallory-Weiss lesions and minor perforations under immunosuppressive therapy after renal transplantation. An attempt to accelerate the healing process was undertaken in a second patient with the insertion of an endoscopic stent because of the good clinical status. Complete healing of the wound cavity was achieved in 90% (n = 9) of the patients (Table 2). During EVT treatment, antibiotic and antifungal treatment was undertaken in 9 of 10 patients after microbiological results of antibiotic and antifungal sensitivity screenings. Length of antibiotic treatment was 19.5 days ± 25.8. On the day of discharge all of the 9 remaining patients declared no symptoms of dysphagia.

**Complications**

Endoluminal vacuum therapy–associated complications occurred in 70% (n = 7) of the patients. Complications occurred as mediastinal emphysema in 7 patients detected by CT. Every patient received a CT scan after the first endoscopy. For initial endoscopy and insertion of the sponge, artificial respiration was provided. In stable patients the change of EVT sponges was performed under sedation. Perforation-associated complications related to the modified Clavien-Dindo classification were IIIa in Table 1. Patient Characteristics of the Study Group

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Cause of Perforation</th>
<th>Comorbidity</th>
<th>Localization of Perforation</th>
<th>Hospital Stay (days)</th>
<th>Intensive Care (days)</th>
<th>Complications Associated to MCDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>73</td>
<td>Iatrogenic</td>
<td>Arterial hypertension; cervical esophageal diverticula</td>
<td>Cervical</td>
<td>97</td>
<td>50</td>
<td>4b</td>
</tr>
<tr>
<td>42</td>
<td>Foreign body</td>
<td>...</td>
<td>Thoracic</td>
<td>9</td>
<td>1</td>
<td>4a</td>
</tr>
<tr>
<td>66</td>
<td>Spontaneous</td>
<td>Squamous cell carcinoma of the tongue; low-grade non-Hodgkin lymphoma; Insulin-dependent diabetes mellitus</td>
<td>Cervical</td>
<td>46</td>
<td>0</td>
<td>3a</td>
</tr>
<tr>
<td>44</td>
<td>Spontaneous</td>
<td>Bronchial asthma; immune suppression; COPD</td>
<td>Thoracic</td>
<td>31</td>
<td>2</td>
<td>4a</td>
</tr>
<tr>
<td>61</td>
<td>Spontaneous</td>
<td>Pancycopenia after bone-marrow transplantation</td>
<td>Thoracic</td>
<td>...</td>
<td>0</td>
<td>3a</td>
</tr>
<tr>
<td>86</td>
<td>Spontaneous</td>
<td>Crohn's disease; arterial hypertension</td>
<td>Thoracic</td>
<td>20</td>
<td>4</td>
<td>3a</td>
</tr>
<tr>
<td>75</td>
<td>Iatrogenic</td>
<td>Arterial hypertension; aneurysm of the infrarenal aorta; heart insufficiency</td>
<td>Thoracic</td>
<td>8</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>61</td>
<td>Iatrogenic</td>
<td>Obesity; depression</td>
<td>Thoracic</td>
<td>36</td>
<td>15</td>
<td>4a</td>
</tr>
<tr>
<td>68</td>
<td>Spontaneous</td>
<td>Obesity; arterial hypertension; hyperthyreosis</td>
<td>Thoracic</td>
<td>74</td>
<td>65</td>
<td>4b</td>
</tr>
<tr>
<td>63</td>
<td>Iatrogenic</td>
<td>Coronary heart disease; diabetes mellitus II; osteoporosis</td>
<td>Cervical</td>
<td>74</td>
<td>37</td>
<td>3a</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; MCDC = modified Clavien-Dindo classification.

Fig 1. Patient with perforation of the thoracic esophagus of 4 cm before endovacuum insertion (white arrow = perforation cavity).
Complications were mediastinitis (70%, n = 7), pleural empyema (30%, n = 3), sepsis (40%, n = 4), acute renal failure (30%, n = 3), respiratory insufficiency (30%, n = 3), and septic encephalopathy (10%, n = 1; Fig 7). Of the patients, 8 required IMC or ICU therapy. In these patients the mean ICU or IMC stay was 22 ± 21 days (range, 1 to 59 days). Five patients needed artificial ventilation. The mean length of artificial ventilation was 9.3 ± 15.9 days (range, 2 to 39 days). There were 2 patients who needed continuous venovenous hemofiltration for a period of 13 and 42 days. The mean hospital stay of all patients was 48 ± 30 days (range, 9 to 97 days; Table 2).

Survival
Hospital mortality was 10% (n = 1). This patient most probably died as a result of general failure of the cardiovascular system caused by a known heart insufficiency, which occurred after the successful primary treatment during intermediate care without any signs of systemic inflammation. In the long-term follow-up, another patient died of pneumonia after readmission to the hospital 97 days after the completion of EVT and 8 weeks after being discharged. An endoscopy was used to rule out a fistula in the wound cavity. A third patient died 535 days after discharge owing to progressive disease of a squamous cell carcinoma of the tongue. The mean follow-up of all patients was 336.2 ± 220.4 days.

Comment
Perforation of the esophagus is a serious disease with a mortality rate of up to 20% [1, 2]. One disadvantage of the aggressive surgical approach is the invasiveness, which
poses the risk of sepsis in stable patients. One major variable that influences the outcome of all therapy options is the time between perforation and the start of therapy. It is well known that an interval of less than 24 hours has a major impact on the development of the disease [23, 24].

Because of the high morbidity rate after surgical treatment, other less-invasive therapy options have been established, e.g., different endoscopic approaches, minimal invasive surgical approaches, or conservative treatment methods [2, 4–11]. Disadvantages of the conservative treatment approach are that no cleaning or draining of the perforation cavity can be performed.

Endoscopic stent insertion mortality rates of 0% to 33% and successful healing of the wound cavity are shown in 13% to 69% [9–11, 25, 26]. However, disadvantages of stent therapy are stent dislocation, migration into the esophagus and an associated risk of greater lesions of the esophageal mucosa after stent removal, and false placement of the stent [27]. A few studies reported successful treatment of esophageal perforations with endoscopic clips in a small number of patients [28–30]. Disadvantages of this technique are that no draining of the infected perforation cavity and closure of bigger cavities can take place. A further difficulty posed is the ability to grip the fragile and inflamed cavity margin. Advantages of EVT are the minimally invasive and minor traumatic approach, the possibility of an aggressive endoscopic lavage, and the active drainage of the cavity with the stimulus for granulation and wound healing. As others found, we have reported encouraging EVT results in patients with anastomotic leakages after recent esophageal resections [14–17]. Therefore, we applied EVT also to patients with esophageal perforation regardless of the reason of perforation. There was no selection of the treatment modality—every patient with an esophageal perforation was treated with EVT. In our trial, hospital mortality of just 1% after EVT of esophageal perforations was noted. The patient who died was on the regular unit after successful treatment in intensive care on the IMC. The death was unexpected and was most probably the result of cardiac failure owing to advanced cardiovascular disease. This can be assumed as the patient had no elevated inflammation variables and was clinically robust. The second patient who died during the long-term follow-up experienced a new severe pneumonia after being discharged in good health. The pneumonia does not appear to have arisen as a result of EVT treatment as neither endoscopy nor radiology showed any evidence for a mediastinal abscess or fistula to the trachea or mediastinum. Complete healing of the wound cavity was seen in 89% of patients. There were only 2 cases in which a change in therapy was deemed necessary. In both patients EVT was used to stabilize the patient with an early stage of sepsis and to control and treat the inflammation of the wound cavity.

Schorsch and associates [17] already presented encouraging results concerning the use of EVT after esophageal perforation in 7 patients. However, the data gained are difficult to make comparisons with because the authors do not report on data about the clinical condition, the start of therapy after perforation, ICU stay, and inflammatory response. The patients had an iatrogenic perforation, and EVT may have begun early after diagnosis of the perforation. This might explain the longer duration of EVT in our study (17 days versus

Table 2. Endoluminal Vacuum Therapy Associated Therapy Characteristics

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>EVT Sessions</th>
<th>Placed Endosponges</th>
<th>Start of EVT &lt; 24 h</th>
<th>Chest Drain</th>
<th>Conversion to Alternative Therapy</th>
<th>Healing of Wound Cavity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>1</td>
<td>No</td>
<td>Yes</td>
<td>...</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>...</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>1</td>
<td>No</td>
<td>Yes</td>
<td>...</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>Esophageal resection</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>...</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>...</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>...</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>2</td>
<td>No</td>
<td>Yes</td>
<td>Stent insertion</td>
<td>Yes</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>10</td>
<td>11</td>
<td>1</td>
<td>No</td>
<td>No</td>
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</tr>
</tbody>
</table>

EVT = endoluminal vacuum therapy.
after every diagnosis of the perforation, we noted a significantly shorter hospital stay and duration of EVT treatment. Our results confirm those of previous studies, in which a significantly better outcome was achieved when therapy was undertaken within 24 hours after diagnosis of the perforation [23, 24].

Our experience with EVT of esophageal perforations has shown that a CT scan of the thorax should be done after every endoscopic placement of the sponge to exclude the need of external drainage of a pneumothorax, mediastinal emphysema, pleural empyema, or mediastinal abscess. Moreover, an aggressive endoscopic approach is needed with an optional jet lavage and dilation of the perforation cavity before aggressive surgery in patients with extensive perforations or to achieve healing of the wound cavity without surgical intervention. On the day of discharge all 9 patients showed no symptoms of dysphagia. With regard to these good results, EVT appears to be a good alternative treatment option to stabilize patients and the wound cavity in extensive perforations or to achieve healing of the wound cavity without surgical intervention. However, further studies are required to verify these encouraging results owing to the small numbers of patients treated using EVT and a lack of studies analyzing this promising new therapeutic approach for esophageal perforations.

Endoluminal vacuum therapy is a promising and safe minimally invasive therapy option in esophageal perforations. If surgery is needed, EVT can also be successfully used to gain control of an inflammatory response, stabilize the patient, and improve edematous tissue in the wound cavity. Decisive for the rate of success using EVT therapy is the interdisciplinary work between thoracic surgery, radiology, endoscopy, and intensive care medicine departments in an experienced center, as well as the prompt aggressive endoscopic treatment and drainage of the inflammatory wound cavity after perforation.

References


Fig 7. Perforation-associated complications.

7 days). In 3 patients therapy was commenced more than 24 hours after perforation as these patients were transferred from other hospitals to our center in a severe clinical condition. Furthermore, 7 patients needed temporary ICU or IMC treatment. Nevertheless, hospital mortality was just 11% and healing was achieved in 78% of patients using EVT treatment. In patients who were treated with EVT within 24 hours after diagnosis of the perforation, we noted a significantly shorter hospital stay and duration of EVT treatment. Our results confirm those of previous studies, in which a significantly better outcome was achieved when therapy was undertaken within 24 hours after diagnosis of the perforation [23, 24].
INVITED COMMENTARY

This article from Heits and colleagues [1] looks at 10 patients who were treated after acquiring a perforated esophagus through placement of a polyurethane sponge into the cavity and transnasal application of an external vacuum connected to the sponge (EVT). Half of the patients required pleural drainage with a chest tube, and only 1 patient required a video-assisted thoracic operation. With this strategy, they reported successful healing in 9 of the 10 patients using this novel device. Although 2 patients had their treatments switched to esophagectomy (n = 1) and stenting (n = 1), these alternatives were not undertaken because of failure of the device.

These results provide promising evidence of a new alternative that can be added to the armamentarium for treating esophageal perforation. Not that long ago, the only options were open repair with buttress and drainage or esophageal diversion with or without resection if primary repair failed. Contemporary series using fully covered self-expanding esophageal stents, often combined with video-assisted thoracic operations or percutaneous chest tube drainage, have achieved healing and avoided operation in 60% to 94% of patients. However, these studies contain a mixture of esophageal leaks and perforations and fail to fully describe the extent of the defect, the degree of mediastinal contamination, and patient illness.

Despite the advancements in endoscopic therapy, I think there is still a tendency toward surgical treatment in patients with larger cavities, sepsis, and perhaps older (> 24 hours) perforations in many practices. EVT is a potentially attractive option for these patients, because this series included patients who were septic at presentation, had larger cavities these patients, because this series included patients


