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Original article

Options in the management of esophageal perforation: analysis over a 12-year period

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SUMMARY. **Controversies exist about the management of esophageal perforation in order to eliminate the septic focus. The aim of this study was to assess the etiology, management, and outcome of esophageal perforation over a 12-year period, in order to characterize optimal treatment options in this severe disease. Between May 1996 and May 2008, 44 patients (30 men, 14 women; median age 67 years) with esophageal perforation were treated in our department. Etiology, diagnostic procedures, time interval between clinical presentation and treatment, therapeutic management, and outcome were analyzed retro- or prospectively for each patient. Iatrogenic injury was the most frequent cause of esophageal perforation ($n = 28$), followed by spontaneous ($n = 9$) and traumatic ($n = 4$) esophageal rupture (in three patients, the reasons were not determinable). Eight patients (18%) underwent conservative treatment with cessation of oral intake, antibiotics, and parenteral nutrition. Twelve (27%) patients received an endoscopic stent implantation. Surgical therapy was performed in 24 (55%) patients with suturing of the lesion in nine patients, esophagectomy with delayed reconstruction in 14 patients, and resection of the distal esophagus and gastrectomy in one patient. In case of iatrogenic perforation, conservative or interventional therapy was performed each in 50% of the patients; 89% of the patients with a Boerhaave syndrome underwent surgery. The hospital mortality rate was 6.8% (3 of 44 patients): one patient with an iatrogenic perforation after conservative treatment, and two patients after surgery (one with Boerhaave syndrome, one with iatrogenic rupture). No death occurred in the 25 patients with a diagnostic interval less than 24 hours, whereas the mortality rate in the group ($n = 16$ patients) with a diagnostic interval of more than 24 hours was 19% ($P = 0.053$). In three patients, the diagnostic interval was not determinable retrospectively. An individualized therapy depending on etiology, diagnostic delay, and septic status leads to a low mortality of esophageal perforation.**

KEY WORDS: **diagnostic procedures, esophageal perforation, therapy.**

INTRODUCTION

Despite improvements in detection, surgical techniques, and intensive care medicine, esophageal perforation remains a potentially fatal disease.[1–6] In fact, mortality rates of 10% up to 40% in patients with esophageal perforation have been reported.[7] Therefore, an effective therapeutic management is of great importance.

In the last years, several factors have been characterized that seem to influence the outcome of patients with esophageal perforation, including etiology, time interval between presentation, and initiation of therapy.[1–6] Several studies have demonstrated the prognostic impact of the etiology of perforation. In fact, the Boerhaave syndrome, a disease with a variable clinical manifestation leading to a delayed recognition and severe complications, often shows a higher mortality rate compared to an iatrogenic perforation which is usually less difficult to diagnose and manage.[1,8,9]

The time interval from perforation to initiation of treatment appears to be another important determinant in the outcome of patients with esophageal perforation.[3] For example, Eroglu *et al.* revealed in patients with this severe disease that survival was significantly influenced by a delay of more than 24 hours in the initiation of treatment.[3]

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Controversies remain about the optimal therapeutic approach of esophageal perforation in order to achieve the fundamental principles in the management of this disease: the elimination of the septic focus and supply of a sufficient drainage of the mediastinum. Traditionally, most surgeons prefer an aggressive surgical approach to this disorder, including mainly primary surgical repair or esophageal resection.[1–6] Indeed, results of a large review by Brinster *et al.* in 559 patients with esophageal perforation undergoing operative or nonoperative therapy suggest that the primary surgical repair is the most successful treatment option.[2] Quite the opposite was shown by Vogel *et al.*[10] demonstrating that a consequent conservative treatment of sepsis and control of esophageal leaks avoid major surgery in most patients with esophageal perforation.[10]

For that reason, the aim of this study was to assess the etiology, management, and outcome of esophageal perforation over a 12-year period, in order to characterize optimal treatment options in this severe disease.

PATIENTS AND METHODS

From May 1996 to May 2008, 44 consecutive patients with esophageal perforation were treated in the Department of General, Visceral and Cancer Surgery, University of Cologne. There were 14 women and 30 men with a median age of 67 years. Because our department is a center of esophageal surgery, 29 (66%) of the 44 study patients were transferred from regional hospitals to us. A retrospective/prospective analysis of these patients' clinicopathologic characteristics was performed and formed the basis of this study. This included the etiology and localization of perforation, diagnostic procedures, time interval between diagnosis and initiation of therapy (≤24 hours: early treatment group; >24 hours: late treatment group), therapeutic management, and outcome.

The local Institutional Review Board approved this retrospective study and indicated that individual consent could be waived because individual patients were not identified.

RESULTS

Etiology of esophageal perforation

Iatrogenic injury was the most frequent cause of esophageal perforation, followed by Boerhaave syndrome and traumatic perforation caused by accidentally swallowed foreign bodies. In three patients, the reasons were not determinable (Table 1).

Table 1 Etiology of esophageal perforation in 44 study patients

Etiology	Patient (*n*)	(%)
Iatrogenic	28	64
Diagnostic upper endoscopy	11	–
Interventional upper endoscopy	9	–
Implantation of an aortic stent/allograft	2	–
Surgical therapy of an upper gastrointestinal bleeding	2	–
Osteosynthesis of the cervical spine	1	–
ERCP	1	–
Transesophageal echocardiography	1	–
Antireflux operation	1	–
Boerhaave syndrome	9	20.5
Traumatic	4	9.0
Accidentally swallowed denture	2	–
Accidentally swallowed bone	2	–
Undeterminable	3	6.5

ERCP, endoscopic retrograde cholangiopancreatography.

Location and size of esophageal perforation, and its correlation to the etiology

The cervical esophagus was perforated in seven (16%) patients, the middle thoracic in 16 (36%), and the distal thoracic or abdominal esophagus in 19 (43%) patients. In two patients, the site of perforation was not clearly documented.

Because the documentation of the size of esophageal perforation was often lacking or without specific measurement, we could not analyze this parameter in more detail.

In patients with an iatrogenic perforation, the location of esophageal rupture was mainly located in the middle or distal third. Eight of the nine patients with a Boerhaave syndrome had a distal esophageal perforation. All traumatic perforations were located in the cervical esophagus (Table 2).

Diagnostic procedures

Diagnostic procedures comprised endoscopy in 26 (59%) cases, computed tomography (CT) in 19 (43%), and a gastrografin esophagography in 16 (36%) cases.

Therapy and its correlation to the etiology and location of esophageal perforation

Eight patients (18%) underwent conservative treatment with cessation of oral intake, broad-spectrum

Table 2 Correlation between the location of perforation and etiology

Location of perforation	Etiology of esophageal perforation			
	Iatrogenic	Boerhaave	Traumatic	Others
Cervical	3	–	4	–
Middle	15	1	–	–
Distal	10	8	–	1

In two patients, the site of perforation was not clearly documented.

Table 3 Therapeutic procedures in 44 study patients

Therapeutic procedure	Patients (*n*)	(%)
Conservative	8	18
Stent implantation	12	27
Operative	24	55
Local closure	9	21
Esophagectomy (without reconstruction [*n* = 13]; with reconstruction [*n* = 1])	14	32
Transhiatal resection of the distal esophagus with gastrectomy and esophagojejunostomy	1	2

antibiotics, and parenteral nutritional support Table 3. As shown in Table 5, six of the eight patients had an iatrogenic rupture.

An endoscopic stent implantation (self-expanding metal stent [SEMS]; Ultraflex stent, Microvasive, Boston Scientific, Boston, MA) was performed in 12 (27%) patients, of which 67% also had an iatrogenic esophageal perforation (Table 5). Nine of the 12 patients were scheduled for stent removal within 6 weeks after implantation. In just one patient, a stent migration occurred.

Surgical therapy was performed in 24 (55%) patients with local closure in nine patients including four patients with additional coverage by fundoplication or pleural patch in one patient. A transhiatal resection of the distal esophagus with total gastrectomy was conducted in one patient with perforation of a cardia carcinoma during bougienage. Esophagectomy was performed in 14 patients (transhiatal: *n* = 11; transthoracic: *n* = 3) (Table 3). Of these patients, one underwent primary repair by gastric pull-up with intrathoracic anastomosis, while in 13 patients initially a cervical esophagostoma and closure of the upper stomach were constructed. A reconstruction of the esophagus was done in nine patients with colon interposition (*n* = 8) or gastric pull-up (*n* = 1) after a median of 7 months. In four patients, the cervical stoma remained because of poor cardiopulmonary conditions (*n* = 2) or hospital death (*n* = 2).

In case of iatrogenic perforation, conservative or interventional therapy was performed in 50% of the patients, while the other 50% underwent surgical therapy. Quite the opposite was found for patients with a Boerhaave syndrome: eight of nine (89%) patients received surgery, while just one patient was treated by endoscopic stent implantation (Table 5).

In terms of the location of esophageal perforation, conservative treatment was performed in four cervical and four distal perforations. An endoscopic stent implantation was mainly done in middle esophageal perforations (*n* = 8), while a local closure was evenly distributed at each height of the esophagus. In five middle and nine distal esophageal perforations, an esophagectomy was carried out (Table 4).

Morbidity and mortality rate

With a mean length of hospital stay of 21 days (2–60 days), the most common complications were pneumothorax (16%), mediastinitis (14%), and pleural effusion (11%). The hospital mortality rate was 6.8% (3 of 44 patients). One patient with iatrogenic perforation died undergoing conservative treatment, and two patients, one with Boerhaave syndrome and the other with an iatrogenic rupture, were undergoing esophageal resection. In the first case, a 75-year-old patient underwent an acute endovascular stent graft implantation because of a symptomatic aneurysm of the thoracic aorta with compression of the heart and the esophagus. At first, the patient had an uneventful postoperative course. However, subsequently, there was a need for reintubation because of sepsis. The following upper endoscopy showed a large thoracic esophageal perforation without options of interventional treatment. Because the patient was in a reduced cardiopulmonal condition, a surgical treatment was also impossible, so that the patient died under conservative treatment.

The second 75-year-old patient with esophageal cancer of the distal esophagus had an iatrogenic perforation during a pretherapeutic transesophageal echocardiography. The rupture was detected approximately 28 hours after the examination. Surgical therapy with esophagectomy and cervical esophagostoma was performed. However, after a prolonged and complicated postoperative course, the patient died from septic complications.

The last 62-year-old patient with a Boerhaave syndrome initially underwent a surgical therapy with local closure and coverage fundoplication from

Table 4 Correlation between the therapeutic procedure and the location of perforation

	Therapy				
Location of perforation	Conservative	Stent implantation	Local closure	Esophagectomy	Transhiatal resection of the distal esophagus with gastrectomy
Cervical	4	–	3	–	–
Middle	–	8	3	5	–
Distal	4	2	3	9	1

In two patients, the site of perforation was not clearly documented.

Table 5 Correlation between the therapeutic procedure and the etiology of esophageal perforation

Therapy	Etiology of esophageal perforation			
	Iatrogenic	Boerhaave	Traumatic	Others
Conservative	6	–	1	1
Stent implantation	8	1	1	2
Local closure	7	1	1	–
Esophagectomy	6	7	1	–
Transhiatal resection of the distal esophagus with gastrectomy	1	–	–	–

a transabdominal approach. As the postoperative course remained complicated, a reoperation was performed finally showing an uncovered leakage of the distal esophagus. Consequently, an esophagectomy was tried to perform. As this procedure was technically not feasible from a transhiatal approach, a right-sided thoracotomy was conducted which led to severe bleedings in the mediastinum. Finally, a cardiopulmonary reanimation was necessary, but the patient ultimately died intraoperatively.

Diagnostic interval

In 41 patients, the interval between clinical presentation and initiation of treatment was assessable. Twenty-five patients (57%) were treated within 24 hours sustaining the esophageal injury, and 16 (37%) after 24 hours. No death occurred in the early-treatment group; all three fatal outcomes were observed in the late-treatment group ($P = 0.053$; Fisher's exact test; Table 6).

DISCUSSION

In our retrospective study, iatrogenic injury was the most frequent cause of esophageal perforation, followed by spontaneous rupture (Boerhaave syndrome). Similar data were reported by Brinster *et al.* in a large review of 726 patients with esophageal perforation: 59% of all patients showed an iatrogenic injury to the esophagus, while spontaneous perforations accounted for 15% of all patients.[2] Thereby, the most common reason of iatrogenic perforation was diagnostic and interventional upper endoscopy, as shown in our study. However, in contrast to other studies, we were not able to show a major correlation between the etiology of perforation and mortality. This is because the mortality rate was low, and of the three patients that died in the hospital, two had an iatrogenic and just one a spontaneous rupture.

The diagnosis of esophageal perforation can be complicated as its presentation is frequently unspecific and is simply confused with other disorders.[3,6] In this study, upper endoscopy, CT, and gastrografin esophagography were the most common diagnostic procedures for the detection of an esophageal perforation. In the literature, gastrografin esophagography is the study of choice of suspected esophageal perforation, although it has an overall false negative rate of 10%.[2,11] Moreover, in patients with critical illness, there is a great risk of gastrografin aspiration that can cause severe, necrotizing pneumonitis because of its hypertonicity.[12] In patients with a negative esophagography, as well as in patients with untypical symptoms, we therefore prefer a chest CT to confirm the diagnosis of esophageal perforation. Although upper endoscopy is not recommended as the primary diagnostic procedure for the detection of esophageal perforation, it is highly valuable for the direct visualization and measurement of the size of perforation, as well as the viability of the surrounding epithelium, and therefore it is important for planning the appropriate therapy. In fact, Horwitz *et al.* showed in 13 patients with penetrating esophageal injury that esophagoscopy had a sensitivity of 100% and a specificity of 83% in the assessment of an esophageal perforation.[13] Nevertheless, argument against upper endoscopy as a primary diagnostic tool in this disease is the potential risk to convert a small rupture into a large perforation during air insufflation. Finally, the diagnostic procedures used for initial investigations in patients with esophageal perforation should be adjusted to the etiology of perforation. In patients with iatrogenic perforations, especially the ones caused and directly detected by endoscopy, mainly do not need further investigations but rather can undergo a defined therapeutic approach. In contrast, especially patients with a spontaneous rupture should receive a CT scan to ensure a complete assessment of the mediastinum.

The fundamental principles in the management of esophageal perforation include the elimination of the septic focus in order to prevent multiple organ

Table 6 Mortality and diagnostic interval

	≤24 hours	>24 hours
Patients (%)	25 (57%)	16 (37%)
Mortality (%)	0	3 (19%)

$P = 0.053$; Fisher's exact test.

Table 7 Series of esophageal perforation between 2001 and 2006

Author/Year	Patients (*n*)	Etiology of esophageal perforation				Mortality (%)		
		Iatrogenic	Boerhaave syndrome	Traumatic	Others	Total	Treatment delay; ≤24 hours	Treatment delay; >24 hours
Vogel *et al.* 2005[10]	47	25	14	3	3	4.2	–	–
Kiernan *et al.* 2006[4]	48	30	13	–	5	12.5	8	17.4
Tomaselli *et al.* 2002[15]	38	38	–	–	–	15.8	–	–
Brinster *et al.* 2004[2]	559	330	84	117	28	18	14	27
Chao *et al.* 2005[16]	28	11	8	9	–	10	0	13.6
Hinojar *et al.* 2003[17]	7	1	–	6	–	0	–	–
Gupta and Kaman 2004[18]	57	44	6	7	–	14	–	–
Port *et al.* 2003[19]	26	20	2	–	4	3.8	0	8.3
Richardson 2005[20]	69	34	18	9	–	1.5	–	–
Eroglu *et al.* 2004[3]	36	23	2	11	–	13.9	3.7	44.4
D'Journo *et al.* 2006[21]	18	–	18	–	–	16.6	–	–
Ökten *et al.* 2001[22]	31	25	2	2	2	29	–	–
Current series	44	28	9	4	3	6.8	0	19
Total	1004	609	176	168	42	13.8 (median)	1.85 (median)	18.2 (median)

failure which requires a sufficient drainage of the mediastinum.[1–6] However, to date, there is no 'gold standard' in the therapeutic interventions that aim to achieve these goals. Most surgeons recommend an aggressive surgical approach to achieve low mortality rates.[1–6] Other clinicians prefer a consequent conservative treatment for esophageal perforation within some extent similar mortality rates.[10,14] The study of Vogel *et al.* demonstrated a good clinical outcome for patients with esophageal perforation undergoing an aggressive conservative treatment of sepsis and control of esophageal leaks (Table 7). Comparable data were demonstrated by Martinez *et al.* showing a successful aggressive conservative treatment in a series of iatrogenic perforations with 100% survival.[14] In our study, the overall hospital mortality rate was low with 6.8% (3 of 44 patients). For iatrogenic perforations, more often conservative or interventional therapy was performed than in patients with a Boerhaave syndrome who mostly underwent surgery. That is, because iatrogenic perforations are mainly early detected and well-contained perforations with minimal mediastinal soilage, so that a nonoperative approach appears to be a successful therapeutic modality. On the other hand, the Boerhaave syndrome is generally associated with extensive mediastinal contamination and devitalized borders of the esophageal lesion, so that a surgical therapy is needed. In our opinion, there should be no inflexible standard therapy for esophageal perforation, but rather an individualized approach for each patient. If a patient with esophageal perforation already shows signs of sepsis or possible organ failure, a surgical treatment should be considered as a necessary option to successfully remove the septic focus. However, if the patient is still in a stable health condition, it has to be evaluated by which therapeutic management – conservative, interventional, or surgical – a septic illness can be avoided. In this process, the etiology, location, and size of perforation, as well as the overall health status, physiologic reserve of the patient, and the extent of associated injuries, should be useful critical determinants.

In the last years, an alternative approach has been proposed in the therapy of esophageal perforation by using a SEMS.[23] In fact, in this series, a quite high number of patients with perforations were treated with an esophageal stent. Mainly, these patients had an iatrogenic perforation based on a benign disease. Based on our experience, endoscopic treatment of esophageal perforation can be considered as a safe alternative to conservative or operative treatment options, despite possible complications like stent migration or the difficulty of stent removal.[23] However, it is essential to combine stent implantation with additional supportive treatment to achieve the best outcome.

Our study results suggest that the interval between perforation and the initiation of treatment is perhaps the most crucial factor in the outcome of patients with esophageal perforation. Even though the number of patients in this study is too low to assess any significant results, this finding is consistent with several recent studies. In the large review of 726 patients with esophageal perforation by Brinster *et al.*, the overall mortality rate in patients with treatment delayed by 24 hours or more was 27% compared to 14% in patients with a treatment initiated within 24 hours.[2] Similar results were reported by Eroglu *et al.* and Kiernan *et al.* showing that the mortality among patients treated within 24 hours of sustaining the injury was substantially less than among those for whom diagnosis and treatment were delayed.[3,4]

In conclusion, the diagnostic interval should be kept as short as possible by a fast and an aggressive diagnostic. Depending predominantly on the etiology and site of the perforation, an immediate, individual-

ized approach for each patient should be chosen, in order to prevent septic complications of this potentially fatal disease.

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