Management of anastomotic leakage-induced tracheobronchial fistula following oesophagectomy: the role of endoscopic stent insertion

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Abstract

OBJECTIVES: Tracheobronchial fistulas are rare but life-threatening complications after oesophagectomy. Leakage of the oesophagointestinal anastomosis with inflammatory involvement of the tracheobronchial tree is the predominant reason for postoperative fistulization between the airways and the oesophagus or the gastric tube. Successful management is challenging and still controversially discussed. After promising results in the treatment of intrathoracic anastomotic leaks, we adopted endoscopic stent implantation as the primary treatment option in patients with anastomotic leak-induced tracheobronchial fistula. The aim of this study was to investigate the feasibility, the limits and the results of this procedure.

METHODS: Between January 2004 and December 2010, 222 consecutive patients underwent oesophageal resection mainly for oesophageal cancer. An anastomotic leak-induced tracheobronchial fistula was bronchoscopically verified in seven patients. Four patients received endoscopic implantation of either a self-expanding tracheal or oesophageal stent or both as primary treatment. Surgical re-exploration was mandatory in 2 patients because of necrosis of the pulled-up gastric tube or gangrene of the airways. One patient was conservatively managed.

RESULTS: Endoscopic stent placement was successfully accomplished in all 4 patients. Two patients received an oesophageal stent, one patient a tracheal stent and one patient both an oesophageal and a tracheal stent. Closure of the fistula was achieved in all cases and 3 patients finally recovered while one died by reason of respiratory failure. In both surgical re-explored patients resection of the gastric tube was performed, and in one patient, because of subtotal gangrene of the right bronchial tree, emergency pneumectomy was also mandatory. Both patients died due to severe sepsis and respiratory failure. The one conservatively treated patient died from severe pneumonia.

CONCLUSIONS: Treatment of anastomotic leak-induced tracheobronchial fistulas by means of oesophageal and tracheal stent implantation is feasible. If stent insertion is limited by gastric tube necrosis or bronchial gangrene, the prognosis is likely to be fatal.

Keywords: Tracheoesophageal fistula • Oesophagectomy • Anastomotic leakage • Endoscopic stent insertion

INTRODUCTION

Tracheobronchial fistula following oesophagectomy is a devastating condition associated with substantial morbidity and mortality [1]. It often results in respiratory failure, pulmonary sepsis and finally septic shock with fatal outcome [1]. Postoperative fistulization between the oesophagus, respectively, gastric tube and airways can occur as a consequence of intraoperative injury, ischaemic lesions due to devascularization of the trachea and main stem bronchi by extensive lymph node dissection, or leakage of the oesophagointestinal anastomosis with subsequent mediastinitis and inflammatory involvement of the tracheobronchial tree [1–3]. Anastomotic leaks are generally considered to be the predominant reason for acquired tracheobronchial fistulas following oesophagectomy. Leakage of intrathoracic anastomosis complicated by a tracheobronchial fistula is a crushing situation. Persisting contamination of respiratory system, mediastinum and pleural cavity results in rapidly progressing septic disease [1–3]. Despite the severity of this complication, there is no generally accepted therapeutic approach to postoperative tracheobronchial fistula [2, 4]. On the contrary, management is still controversially discussed and because of the rareness of this life-threatening complication, the literature comprises mainly case reports. Surgical re-exploration with primary closure of the fistula [5, 6], oesophageal diversion with resection of the gastric conduit, cervical esophagogastomy and feeding jejunostomy [4] have been suggested as well as conservative management with nil by mouth and nutrition via a feeding tube [7]. There are also a few case reports regarding endoscopic treatment [8]. However,
most of these studies are marred by very small numbers or refer to chronic fistulas long after initial oesophagectomy. Thus results remain inconclusive.

On the other hand, treatment of intrathoracic anastomotic leaks by means of endoscopic stent insertion has shown reliable good results in several studies. Our own experience with endoscopic stent placement was also favourable [9–11]. Therefore, we adopted endoscopic stent implantation as the primary treatment option in patients with anastomotic leak-induced tracheobronchial fistula, too. The aim of this study was to investigate the feasibility, the limits and the results of dealing with anastomotic leak-related tracheobronchial fistula by means of endoscopic stent implantation.

MATERIALS AND METHODS

The study comprises 222 consecutive patients who underwent oesophageal resection during a 7-year period between January 2004 and December 2010. All procedures were performed at the Department of General and Thoracic Surgery of the Klinikum Nuremberg Nord, which is a German tertiary care hospital. Our department is particularly dedicated to oesophageal surgery and serves as a referral centre for oesophageal disease to a population of approximately half a million people. A local Ethics Committee approved this retrospective study and waived the need for individual consent.

Patients

The median age in this series amounted to 62.4 years (Table 1). There were 185 male and 37 female patients. The predominant reason for surgery was oesophageal cancer (Table 1). There were 87 squamous cell carcinomas (39.2%), 88 adenocarcinomas of the oesophagogastric junction (AEG) Type I (39.6%), 30 AEG Type II (13.5%), which is a cancer of the gastric cardia with involvement of the distal oesophagus [12, 13], 4 AEG Type III, which is a cancer of the gastric cardia in the oesophagogastric junction (AEG) Type I (39.6%), 30 AEG Type I and 13 further lesions (Table 1). Prior to surgery functional operability was thoroughly assessed by cardiopulmonary diagnostics. If appropriate patients received preoperative hyperalimentation to improve poor nutritional status as well as chest physiotherapy and medical measures including inhalations regularly to improve impaired pulmonary function. A total of 55 patients had received neoadjuvant therapy, either neoadjuvant chemoradiotherapy (radiation dose 50.4 Gy) in the case of squamous cell carcinoma or neoadjuvant chemotherapy alone in the presence of adenocarcinoma of the AEG Type I–III.

In 160 cases, an open abdominothoracic en bloc oesophagectomy was performed (72.1%) with interposition of a pulled-up gastric tube and intrathoracic stapled end-to-side oesophagogastric anastomosis above the level of the tracheal carina [14]. Dissection nearby the airways was always performed with conventional surgical instruments and only sparse and careful employment of electrocautery. No ultrasonic shears, Ligasure® or similar devices were used in the region of the tracheobronchial tree. Twenty-five patients received extended total gastrectomy with transternal resection of the distal oesophagus and intrathoracic stapled end-to-side oesophagojejunostomy below the level of the tracheal carina (11.3%) [14]. Furthermore, 7 transmediastinal oesophagectomies (3.2%), 13 transthoracic oesophagectomies with delayed reconstruction (5.9%) [15], 5 limited resections of the distal oesophagus with jejunum interposition and stapled intrathoracic oesophagojejunostomy (merendino operation) [16] and 12 other procedures were carried out.

Diagnosis of anastomotic leakage and tracheobronchial fistula

If leakage of the intrathoracic anastomosis was clinically suspected, immediate endoscopy and computed tomography of the chest and abdomen were performed. Endoscopy was preferred to radiographic contrast-medium swallow for diagnosis of anastomotic leaks because of the possibility of direct visual examination of the anastomosis, quantification of the leak and determination of whether the pulled-up gastric tube is ischaemic or not. A straight decision, whether endoscopic stent implantation is reasonable or not, can be made out of the endoscopic aspect. Furthermore, computed tomography of the chest and abdomen is mandatory to rule out advanced pleural empyema or mediastinal abscess, which would require either percutaneous interventional or surgical drainage.

In case of assumed fistulization between the tracheobronchial tree and a dehisced intrathoracic anastomosis, bronchoscopy was carried out in addition to endoscopy of the oesophageal remnant and the pulled-up gastric tube. Bronchoscopy in combination with oesophagogastroscopy was used to determine the appropriate treatment strategy. Surgical re-exploration was unavoidable if the gastric conduit was ischaemic or necrosis of wide parts of the airways was encountered. Otherwise endoscopic stent insertion was preferred.

Table 1: Characteristics of patients and tumour entity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>%</th>
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<tr>
<td>Male</td>
<td>185</td>
<td>83.3</td>
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<tr>
<td>Female</td>
<td>37</td>
<td>16.7</td>
</tr>
<tr>
<td>Median age</td>
<td>62.4 years</td>
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<tr>
<td>Neoadjuvant chemoradio- or chemotherapy</td>
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<td>24.8</td>
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<td>Squamous cell carcinoma</td>
<td>87</td>
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<tr>
<td>AEG Type I</td>
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<td>AEG Type II</td>
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<td>AEG Type III</td>
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<tr>
<td>Neuroendocrine oesophageal carcinoma</td>
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<td>1.4</td>
</tr>
<tr>
<td>Others</td>
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<td>0.8</td>
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<tr>
<td>Benign oesophageal lesion</td>
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<td>3.7</td>
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Stent insertion

For closure of the anastomotic leak either a self-expanding, covered metal stent (Ultraflex; Boston Scientific, Natick, MA, USA) or a self-expanding, covered silicone stent (Polyflex; Boston Scientific) were endoscopically inserted. Stent placement was performed by a gastroenterologist well trained in interventional endoscopy. The exact position of the leakage was marked on the patient’s skin and afterwards the stent was inserted under
radioscopic guidance. After implantation the correct placement of the stent and the successful closure of the leak were always endoscopically and radioscopically controlled.

Fistulous openings of the distal trachea or the main stem bronchi were sealed by implantation of a self-expandable, covered Y-stent (Leufen aerstent; Leufen Medical, Aachen, Germany). Insertion of the tracheal bifurcation stent was always carried out by an experienced pulmonologist particularly trained in interventional bronchoscopy. Stent placement was performed via rigid bronchoscopy in general anaesthesia under radioscopic guidance. Afterwards, the correct location of the stent was confirmed by flexible bronchoscopy. Immediate cessation of air leakage proved successful closure of the fistula.

RESULTS

Intrathoracic leakage of the oesophageal—intestinal anastomosis was endoscopically verified in 27 patients. Additional fistulization between dehisced anastomosis and airways occurred in seven cases. Altogether 19 leaks were suitable for endoscopic stent insertion. Oesophageal stenting for leakage without tracheobronchial lesion was accomplished in 15 cases. Furthermore, four patients received endoscopic stent implantation for treatment of anastomotic leakage complicated by simultaneous fistulization into the airways. Re-thoracotomy was unavoidable in seven cases because of either ischaemic necrosis of the pulled-up gastric tube, advanced pleural empyema or gangrene of the airways. Two patients with tracheobronchial fistula were among those surgically re-explored sufferers. One patient with anastomotic leakage-induced fistula into the right main stem bronchus was managed conservatively including tracheostomy.

Results of patients with leak-induced tracheobronchial fistula

Altogether seven male patients with a median age of 65.1 years sustained an anastomotic leak-induced fistula into the tracheobronchial tree (Table 2). Two of them had received neoadjuvant chemoradiotherapy. Tumour entity was AEG Type I (4 cases), squamous cell carcinoma (two cases) and neuroendocrine carcinoma in one case. Abdominothoracic en bloc oesophagectomy with interposition of a pulled-up gastric tube and intrathoracic stapled anastomosis above the level of the tracheal carina had been carried out in all cases. Two-field lymphadenectomy was routinely performed (Table 2).

Fistulization originated always from a dehisced intrathoracic anastomosis. A lesion of the distal trachea was seen in three cases. Fistulous communication between the leak and right main stem bronchus was encountered in four cases (Fig. 1). Fistulas were always solitary without further openings into the tracheobronchial tree. Moreover, all lesions were early fistulae occurring within a few days after initial oesophagectomy. Endoscopy showed a viable gastric tube in five patients, while in two cases ischaemia of the conduit was revealed. In those two cases surgical re-exploration was mandatory.

Endoscopic stent insertion was performed in four patients suffering from tracheobronchial fistula. In two cases, only oesophageal stents were inserted. Successful stent placement closed the

Table 2: Characteristics of patients with anastomotic leakage-induced tracheobronchial fistula

<table>
<thead>
<tr>
<th>Case number</th>
<th>1</th>
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<td>78</td>
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<td>Neoadjuvant chemoradiotherapy</td>
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<td>Neuroendocrine carcinoma</td>
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<td>Squamous cell carcinoma</td>
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<td>AEG Type I</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Abdomino-thoracic en bloc oesophagectomy</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Insertion of a covered oesophageal stent</td>
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<td>Oesophageal and tracheal stent in combination</td>
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<tr>
<td>Insertion of a covered tracheal stent</td>
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<tr>
<td>Re-thoracotomy with resection of the gastric tube</td>
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<tr>
<td>Conservative management</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Definite closure of leak and fistula</td>
<td>+</td>
<td>+</td>
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anastomotic leak completely and the fistula into the airways simultaneously ceased. Fistula-related respiratory symptoms, like cough, aspiration and dyspnoea, stopped immediately. Both patients breathed spontaneously and were not in need of mechanical ventilation. Following definite healing of the anastomotic leak, the stents were removed without any difficulty 6 weeks after initial implantation. During stent explantation complete healing and closure of the fistula was endoscopically verified.

In another case, the fistula did not cease despite successful placement of an initial oesophageal stent. Therefore, an additional tracheal stent was inserted. Afterwards the communication into the respiratory system was completely sealed and the patient recovered. He was finally transferred to a rehabilitation facility specialized on pulmonary disorders. Stent removal was intended following full recuperation. However, computed tomography showed early mediastinal recurrence of his very malignant neuroendocrine/small cell G4 carcinoma when he was admitted for stent explantation 8 weeks after the initial stent insertion. Therefore, both stents remained in situ and he received chemoradiotherapy. He died 6 months later from rapid progressing neoplastic disease with local recurrence and distant metastasis.

One patient experienced mainly respiratory failure caused by a small fistula between the distal trachea and the anastomosis (Fig. 2). Hence a tracheal stent was initially inserted (Fig. 3). Owing to advanced pneumonia, pulmonary sepsis and respiratory failure, he needed ongoing mechanical ventilation. Sophisticated management of artificial ventilation did not prevent accumulation of carbon dioxide with subsequent respiratory acidosis. Thus he received pumpless extracorporeal lung assist (iLA Membrane Ventilator®; Novalung, Heilbronn, Germany). Notwithstanding improved gas exchange and multifaceted sepsis therapy including haemodynamic monitoring and management as well as adjunctive therapies, he ultimately sustained septic shock with fatal multi-organ failure.

Conservative management was preferred in one patient during the initial year of this study. He postoperatively experienced dehiscence of the intrathoracic anastomosis and subsequently developed an inflammatory fistula into the right main stem bronchus. Endoscopy showed a vital gastric tube with a rather small leakage. Hence a tracheotomy was carried out 6 days after the primary oesophagectomy and a nasogastric tube was inserted into the conduit for decompression and internal drainage. Despite adequate sepsis therapy and ventilatory support as less invasive as possible lethal necrotizing pneumonia could not be averted.

The two remaining patients suffering from leak-induced tracheobronchial fistula were not suitable for endoscopic stent insertion. A 72-year-old man, who had en bloc oesophagectomy because of AEG Type I, developed ischaemic necrosis of the tip of the pulled-up gastric tube followed by anastomotic leak and finally fistulization into the right main stem bronchus. Stent implantation was impossible by reason of ischaemia of the gastric conduit and hence re-thoracotomy with take-down of the anastomosis, resection of the ischaemic tube and cervical oesophageostomy as well as feeding jejunostomy was carried out 17 days after the initial oesophagectomy. Furthermore the fistulous opening within the membranous part of the right principle bronchus was closed by suture, which was reinforced by a pedicled muscle flap. Despite all treatment efforts he died from septic multi-organ failure 14 days after re-thoracotomy.
Moreover, a 62-year-old patient suffering from squamous cell carcinoma sustained ischaemia of the interposed gastric tube with succeeding anastomotic leakage 6 days after en bloc oesophagectomy. He had a history of alcohol abuse with poor nutritional condition and already preoperatively impaired functional performance status. Oesophagogastroscopy showed leakage related to ischaemia of the upper parts of the conduit. Bronchoscopy revealed not only a fistulous opening within the right main stem bronchus, but also advanced gangrene of the right airways with necrosis of the membranous parts of the intermediate and upper lobe bronchus (Figs 1 and 4, and Supplementary Video 1). Upon re-thoracotomy ischaemia of the gastric tube as well as subtotal gangrene of the airways was confirmed. Repair of the right tracheobronchial tree was not feasible due to the extent of necrosis and the advanced inflammatory destruction caused by severe mediastinitis. Therefore, resection of the ischaemic gastric tube together with right pneumectomy was carried out as the ultimate ratio. The bronchial stump was reinforced with a pedicled muscle flap obtained from the Musculus serratus anterius. Furthermore tracheotomy, cervical oesophagostomy and jejunostomy for enteral nutrition were performed. Short initial stabilization of his condition followed.

However, bronchopleural fistula leading to fatal respiratory failure occurred on the fourth day after re-operation.

DISCUSSION

Reports of acquired non-malignant oesophagotracheal and oesophagobronchial fistulas of inflammatory origin were first published in medical journals within the last decades of the nineteenth century [17]. Close contact between the oesophagus and the tracheobronchial tree favours contagious spread of infectious disease from one to the other. Inflammatory erosion of the adjacent structures was the common mechanism of fistulation [17]. The first successful surgical repair of such an oesophagotracheal fistula caused by actinomycosis was reported in 1896 [18]. Following some further reports of single cases, a large series from the Mayo Clinic was published in 1966 [19]. Henceforth, straight surgical repair with division and closure of the fistulous channel became the established treatment of choice [17, 20].

Fistulization between a dehisced intrathoracic anastomosis following oesophagectomy and the respiratory system can also be considered as acquired fistula of inflammatory origin. However, the situation differs in many ways from fistulization caused by infectious disease. These diseases are amendable by antibiotic therapy, and the general anatomic situs within the mediastinum has not been changed because of which limited operative procedures are still feasible. In case of intrathoracic anastomotic leakage, actually inflammatory erosion of the tracheobronchial tree takes place, too. However, previous oesophagectomy, lymphadenectomy and gastric pull-up or intestinal interposition have irreversibly altered the anatomic situs. The blood supply of the interposed conduit is fragile and ischaemic necrosis is therefore a main reason for leakage of the anastomosis. So the initial situation is much more complex. In the presence of a dehisced anastomosis, fistulization into the respiratory system is actually an epiphenomenon. It accompanies the underlying problem of anastomotic leakage. Thus different treatment strategies primarily dealing with the leak are mandatory.

Despite the severity of this complication, no generally accepted management exists. There is rather considerable diversity of opinion regarding the optimal therapeutic approach.

Re-thoracotomy with take-down of the dehisced anastomosis, resection of the pulled-up gastric tube, tracheal repair by interposing a muscle flap and creation of a cervical oesophagostomy has been proposed by some work groups [4, 5]. The alimentary tract is later reconstructed by colonic interposition. Obvious advantage is the immediate elimination of the septic focus by removal of the leaking anastomosis [4]. Furthermore, no gastric tube of dubious viability remains. This extensive procedure with delayed reconstruction is considered to be particularly suitable in the case of ischaemic necrosis of the gastric or intestinal conduit. However, results are marred by substantial morbidity and mortality. So, in the case of a viable gastric tube, other less invasive procedures are preferred by most surgeons.

Re-thoracotomy with careful preservation of a vital gastric tube, meticulous division of the fistula and interposition of a pedicled muscle or pericardial flap has been suggested [5, 6, 21]. However, this procedure still requires re-thoracotomy and results have been inconclusive. Often repeated procedures are mandatory until definite closure of the fistula is achieved. Conservative management with antibiotics, enteral nutrition via jejunostomy, non-invasive respiratory support and chest physiotherapy has also been proposed [7]. Notwithstanding some encouraging results, definite healing of the fistula is tedious and lengthy. Accelerating spontaneous closure by endoscopic means has been discussed, too. In some case reports, good results have been achieved by repeated endoscopic application of fibrin glue within the fistulous channel [1, 22]. However, in other series results of endoscopic fibrin glue were disappointing [4]. Thus far, no larger series regarding endoscopic stent insertion in case of early, anastomotic leakage-induced tracheobronchial lesions has been published. The few existing studies rather report on chronic oesophagotracheal fistulas occurring months or even years after initial oesophagectomy [23]. These results cannot readily be applied on an early, leak-induced fistula, which comes about within days after initial surgery.
While tracheobronchial fistula following oesophagectomy is very rare, anastomotic leakage is rather frequent. In recent years, closure of those intrathoracic leaks by means of endoscopic stent insertion has shown promising results [10]. Our own experience has also been favourable [9]. Thus, we decided to adopt stent insertion as the primary treatment option in patients with leak-induced oesophagotracheal fistula as well. However, an indispensable condition is the viability of the gastric tube [9, 10]. In case of ischemic necrosis of the conduit, re-thoracotomy with take-down of the anastomosis and diversion is still the only remaining option.

In our series, we encountered altogether 27 postoperative anastomotic leaks. This is in accordance with other studies, where anastomotic leakage rates between 4 and 12% have been reported for the last two decades [24]. Seven leaks were complicated by fistulization into the airways (3.1% of all patients). This is comparable with other series, which also showed incidence for this complication around 3% [1]. Furthermore, all fistulas of our series followed abdominothoracic en bloc oesophagectomy with intrathoracic anastomosis. This finding is in conformity with previous reports [1]. Orringer and Iannettoni encountered only one tracheoesophageal fistula in a huge series comprising 856 patients with transthiatal oesophagectomy and cervical anastomosis [25]. Therefore, leakage of an intrathoracic anastomosis can be considered as risk factor for development of postoperative tracheobronchial lesions, while cervical anastomosis seems to be rather save regarding this complication.

Stent insertion was feasible in all four patients and closure of leakage as well as of the fistula was accomplished (Fig. 3). Moreover, stent placement was successfully carried out in 15 further cases of intrathoracic anastomotic leak without fistulization into the respiratory system. Hence, we conclude that endoscopic stent implantation is feasible not only for anastomotic leaks, but also for closure of leakage-induced tracheobronchial lesions. One patient of the initial year of our study period was managed conservatively and finally died from pulmonary sepsis. Obviously persisting contamination of the airways through the fistulous communication between the leak and the right main stem bronchus inhibited recuperation and resulted in necrotizing pneumonia. Retrospectively we would now prefer stent insertion and would no longer opt for conservative treatment without stent. In our opinion, endoscopic stent insertion has the great advantage of providing immediate closure of the leakage. No further contamination of the mediastinum, pleural cavity or respiratory system takes place after successful stent placement has been accomplished. On the other hand, conservative treatment without stent or other endoscopic measures like clip application or instillation of fibrin glue does not immediately seal the leak or fistula. The leakage rather continues so that recuperation is hardly feasible. Hence, we give preference to endoscopic stent implantation.

While stent insertion was technically feasible, results were also encouraging. Three out of four patients who received endoscopic stenting for leak-induced tracheobronchial fistula recovered well. Furthermore, 11 of the 15 patients with stent insertion because of anastomotic dehiscence without tracheobronchial complication recuperated well. Complete healing of the defect with subsequent removal of the stent was achieved in two cases with fistula and in 11 cases of leakage without fistula into the airways. Naturally these results are fairly limited by the retrospective design of our single-centre study. However, prospective or randomized trials regarding such an uncommon postoperative event as leak-induced tracheobronchial lesion are not to be expected. Therefore, we conclude from our findings that endoscopic stent insertion in the case of anastomotic leakage-induced tracheobronchial lesions in the early postoperative period following oesophagectomy is not only feasible but shows encouraging results.

In our series, we encountered ischemic necrosis of the pulled-up gastric tube complicated by tracheobronchial fistula in two cases. If the conduit is not longer viable, neither leak nor fistula is amendable by endoscopic stent implantation. Despite surgical re-exploration including all necessary procedures, it was not possible to save those patients from death due to septic multi-organ failure.

In conclusion, treatment of anastomotic leak-induced tracheobronchial fistula following oesophagectomy by means of endoscopic stent insertion is feasible and shows encouraging results. However, prognosis is likely to be fatal if stent implantation is limited by ischemic necrosis of the pulled-up gastric tube or gangrene of the airways.

**SUPPLEMENTARY MATERIAL**

Supplementary material (Video 1) is available at **EJCTS** online.

**Conflict of interest:** none declared.

**REFERENCES**


