Recurrent oesophageal cancer complicated by tracheo-oesophageal fistula: improved palliation by means of parallel tracheal and oesophageal stenting

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Abstract

OBJECTIVES: Recurrent oesophageal carcinoma complicated by the development of a tracheo-oesophageal fistula is a crushing condition. In this situation, endoscopic double stenting may provide a quick and safe option for palliation.

METHODS: The outcomes of patients who received endoscopic parallel stent implantation for tracheo-oesophageal fistula due to recurrent oesophageal cancer at a German tertiary referral hospital between 2006 and 2013 were reviewed in a retrospective case study.

RESULTS: A total of 9 patients were identified (mean age 59.9 years). Tumour entity was squamous cell carcinoma, adenocarcinoma and neuroendocrine cancer of the oesophagus in 5, 3 and 1 case, respectively. The mean interval between primary treatment and recurrence was 19.2 months. Successful double-stent placement was always feasible. Complete closure of the communication between oesophagus and respiratory system was accomplished in all cases by stent implantation. There were no stent-associated complications. The mean survival following stent insertion was 64 days (6–121 days). After successful double stenting, 5 patients were fit enough to receive palliative chemo- or radiotherapy. Seven patients were finally discharged home after adequate oral intake had been achieved. Fatal aspiration pneumonia with respiratory failure occurred in 2 cases.

CONCLUSIONS: Endoscopic parallel stent implantation provides an easy and ubiquitous available technique for closure and palliation of tracheo-oesophageal fistula caused by recurrent oesophageal cancer. Immediate sealing of the fistula and relief of symptoms related to aspiration is achieved while hazardous operations are avoided. Therefore, we recommend endoscopic parallel stent insertion as the treatment of choice in case of tracheo-oesophageal fistula caused by recurrent oesophageal cancer.

Keywords: Oesophageal carcinoma • Tracheobronchial fistula • Endoscopic stent • Palliative care

INTRODUCTION

The recurrence of oesophageal carcinoma following treatment in initially curative intention is a devastating situation which is associated with severe morbidity and poor health-related quality of life [1]. Recurrent carcinoma is usually diagnosed in an advanced stage and, therefore, only palliative treatment options are available for most cases. An average survival of ~3 months is to be expected [1]. Cancer-related fistulization between the oesophagus and the tracheobronchial tree adds further difficulty. Unless closure of the fistula is achieved, death from pulmonary sepsis is imminent [2, 3]. Surgical options are limited by local tumour growth, previous operations and radiotherapy as well as by an impaired functional status.

Here, endoscopic stent insertion may provide a reasonable alternative. In general, endoscopic stenting can be carried out either as implantation of a single stent or as parallel stenting of both the trachea and the oesophagus [4]. Several series showed that the results following the placement of only one stent are marred by a substantial rate of initial treatment failure [5, 6]. Furthermore, early reopening of the fistula is rather frequently encountered [4, 5]. Against this background, parallel stenting of the oesophagus and the airway may help to improve the outcome regarding closure of the fistula as well as keeping it closed [7]. On the other hand, double-stent insertion may also lead to more stent-related complications as vascular erosion [8]. Therefore, the aim of this case series is to investigate the results of parallel stenting for tracheo-oesophageal fistula caused by recurrent oesophageal carcinoma.
MATERIALS AND METHODS

All cases of malignant tracheo-oesophageal fistula caused by recurrent oesophageal carcinoma who received treatment at our institution were included in a retrospective analysis. The study period was between 2006 and 2013. The Klinikum Nuremberg is one of Germany’s largest tertiary referral hospitals and a major centre for thoracic surgery in Southern Germany. The study was approved by a local ethics committee and the need for written consent was waived because of the retrospective design.

Initial therapy

The patients of this study had previously received either definitive chemoradiotherapy or oesophagectomy for potentially curable oesophageal carcinoma. Multimodality treatment comprising either neoadjuvant or adjuvant chemoradiation in combination with oesophagectomy was also carried out.

Definitive chemoradiotherapy meant two cycles of platinum-based chemotherapy (Cisplatin and 5-FU) given concurrently with 66 Gy of external beam radiotherapy followed by two cycles of adjuvant chemotherapy. Neoadjuvant chemoradiotherapy consisted of two cycles of platinum-based chemotherapy (Cisplatin/S-FU) administered concurrently with 50.4 Gy of external beam radiotherapy. Oesophagectomy was performed as transthoracic en bloc oesophagectomy with two-field-lymphadenectomy and interposition of a pulled up gastric tube with intrathoracic stapled anastomosis above the level of the tracheal carina.

Diagnosis of tracheo-oesophageal fistula

Relapse of oesophageal carcinoma was always confirmed by histological examination of biopsies obtained from the recurrent tumour. If fistulization between the oesophagus and the airways was clinically suspected, endoscopy was immediately performed. Oesophagoscopy and bronchoscopy were both carried out to assess whether the fistula was amendable by endoscopic stent insertion or not. Compared with contrast medium swallow, endoscopy enables straight visualization of the fistula and provides information regarding the size and exact origin of the fistulous orifice in the airways. Furthermore, the grade of cancer-associated stenosis can be estimated in both systems. In addition to endoscopy, all patients underwent multislice computed tomography (CT) of the chest and abdomen.

Endoscopic stent implantation

For closure of the fistula, either a self-expanding, covered metal stent (Ultraflex; Boston Scientific, Natick, MA, USA) or a self-expanding, nitinol wire stent with complete silicone covering (Leufen aixstent Oesophagus; Leufen Medical, Aachen, Germany) was endoscopically inserted into the oesophagus. In general, stents with a length from 10 to 12 cm and a diameter of either 20 or 24 mm were used. Stent placement was performed by an experienced team comprising a gastroenterologist well trained in interventional endoscopy and a senior thoracic surgeon with great experience in oesophageal surgery. The exact position of the fistula 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 fistula 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). Lesions within the more proximal parts of the trachea which had no relationship to the carina were closed by placement of either a self-expanding silicone stent (Dumon Stent; Novatech SA, France) or a self-expanding, covered nitinol wire stent (Leufen aerstent; Leufen Medical, Aachen, Germany). Insertion of the tracheal stent was always carried out by a well-coordinated team comprising an experienced pulmonologist particularly trained in interventional bronchoscopy and a senior thoracic surgeon. Stent placement was performed via rigid bronchoscopy in general anaesthesia under radioscopic guidance. Afterwards correct location of the stent was confirmed by flexible bronchoscopy. Immediate cessation of air leakage proved successful closure of the fistula.

RESULTS

A total of 9 patients with a mean age of 59.9 years were included into this study. There were 7 men and 2 women. Squamous cell carcinoma, adenocarcinoma and neuroendocrine carcinoma of the oesophagus were encountered in 5, 3 and 1 case, respectively. Seven patients had previously undergone oesophagectomy, whereas 2 had received definitive chemoradiotherapy for squamous cell carcinoma of the upper third of the oesophagus. In the surgical managed patients, the localization of the oesophageal cancer was usually below the level of the tracheal bifurcation with an average upper tumour margin at a 33 cm distance to the dental arch.

All treatments were carried out in curative intention for potentially curable oesophageal cancer without distant metastases or functional inoperability. During the study period, ~300 oesophagectomies were performed at our institution. The 7 surgical cases of this study had an uneventful postoperative course following transthoracic en bloc oesophagectomy and the pathohistological examination of the specimen always showed clear margins free of cancer. Multimodality treatment was applied in altogether 4 cases; 3 patients received neoadjuvant chemoradiotherapy, while 1 patient underwent adjuvant chemoradiation. An uneventful course was also observed in the 2 cases of definitive chemoradiotherapy and a complete response with no residual tumour was found after conclusion of the treatment.

The mean time between end of the primary treatment and recurrence of oesophageal cancer was 19.2 months (2–57 months). Loco-regional tumour recurrence was recognized in all cases and led to cancer-induced fistulization between the airways and the oesophagus. Furthermore, 4 patients sustained distant metastases in addition to their loco-regional problem. All 9 patients showed signs of aspiration pneumonia and most of them also complained about moderate dysphagia and persistent weight loss.

Parallel stenting was intende at all cases. The decision, which stent to be placed at first, was made in dependence on the endoscopic findings and the respiratory condition of each patient. In cases with considerable stenosis of the trachea or critical respiratory function due to a large defect of the tracheal wall, implantation of the tracheal stent was carried out in the first place (Figs 1–4). A pre-existing tracheal stenosis can deteriorate substantially when an
oesophageal stent is firstly inserted. Radial force following full expansion of the oesophageal stent may cause severe compression of the already stenosed trachea resulting in acute respiratory failure.

Figure 1: Recurrent oesophageal carcinoma. Recurrent squamous cell carcinoma of the oesophagus in a 54-year old man 26 months after transthoracic oesophagectomy with two-field-lymphadenectomy. CT shows loco-regional cancer recurrence within the mediastinum with close contact to the membranous part of the trachea (A). Bronchoscopy reveals broad tumour invasion into the trachea with considerable tracheal stenosis (B) and oesophagoscopy shows recurrent cancer at the level of the intrathoracic anastomosis involving the gastric conduit (C).

Figure 2: Parallel stenting. The result after successful double stenting is shown for the patient of Fig. 1. At first, a tracheal bifurcation stent was inserted followed by an oesophageal stent. Afterwards, radioscopy proofs correct stent placement (A). Contrast medium swallow shows closure of the fistula (B). No contrast medium occurs within the airways while it freely passes through the oesophagus and the gastric conduit (B).
On the other hand, patients with high-grade stenosis of the oesophagus and no significant narrowing of the airways underwent oesophageal stenting at first.

Correct stent placement was achieved in all cases and we encountered no difficulties during the procedure (Figs 1–4). Double stenting was carried out quickly with only a few days separating the two interventions. Implantation of the oesophageal stents was accomplished in conscious sedation, whereas general
anaesthesia was required for insertion of the tracheal stents via rigid bronchoscopy. There were no anaesthesia-related complications. Following stent placement, immediate extubation with spontaneous breathing was feasible in all but 1 patient. This patient suffered from severe aspiration pneumonia and was already preoperatively ventilator dependent. Double stenting did not cause relevant pain following the procedure and besides from usual pain relievers the patients did not require a special pain management.

After successful parallel stent implantation, oral intake could be resumed in all patients besides the one who continued to require mechanical ventilation. He died 6 days later from fulminate pulmonary sepsis resulting in septic shock with multiorgan failure. The remaining 8 patients recuperated quite well and 5 of them were fit enough to start with radio- or chemotherapy in palliative intention. The other 3 sufferers received best supportive care. Altogether 7 patients managed to recover well enough to leave hospital. They were discharged home and continued to receive either best supportive care provided by their family physicians and our outpatient department or palliative treatment provided by the outpatient department in cooperation with oncologists and radiotherapists. One patient died 41 days after parallel stent implantation while still being in hospital and receiving treatment for pneumonia.

The mean survival following endoscopic stent insertion was 64.3 days. Leaving out the 1 patient who died shortly after stent placement, the remaining 8 had an average survival of 71.6 days. Three of them survived >90 days and the longest observed survival was 121 days. During that time, we encountered neither major stent-related problems nor reopening of the fistula. One elective change of an oesophageal stent was performed 7 weeks after initial stent placement. The stent was replaced by a 2 cm longer stent because of local tumour growth and damage to the silicone covering. Complete dislocation of an inserted oesophageal stent was not observed. Slight migration of the oesophageal stents without clinical relevance or symptoms occurred but was always amendable by endoscopic reintervention with repositioning of the existing stent. Sufficient stent placement was always endoscopically controlled before the patients were discharged home. No dislocation or migration of the tracheal stents was recognized.

In the 5 cases who underwent palliative radio- or chemotherapy, we found a mean survival of 73.25 days. Five of the 7 patients who had recovered well enough to be discharged home were finally readmitted to our hospital and died from progressing cancer including pathological fracture of the femur neck, cerebral oedema due to brain metastases and deteriorating pulmonary function. Assumably due to cardiac arrest, 1 died suddenly and unexpected while being in our outpatient department for the follow-up on the 82nd day following stent placement. Hitherto he had had an unexceptional postinterventional course. The patient showing the longest survival of altogether 121 days chose not to return to the hospital and eventually died at home in presence of her relatives.

DISCUSSION

Despite all progress in the treatment of potentially curable oesophageal carcinoma, recurrence of the disease is still observed in many cases following initially curative management. Here, the results from the USA, Japan and Europe are not materially different [1, 9, 10]. Tumour recurrence was observed in 233 of 590 patients (40%) who had received oesophagectomy at a major centre for oesophageal surgery in the USA [9]. A similar recurrence rate of 43% has been reported from Japan and a current series from the Netherlands comprising 1088 patients who had undergone oesophagectomy at the University of Amsterdam between 1993 and 2010 also recorded recurrent cancer in 45% of all cases [1, 10].

Recurrence of oesophageal carcinoma is usually associated with a dismal prognosis and the survival is poor. Several large series have shown an average survival of only a few months. In the above-mentioned study from the USA, mean survival of 9 months for patients receiving palliative therapy was found whereas the survival was only 3 months in untreated cases [9]. The Dutch series also recognized a mean survival of only 3 months following diagnosis of recurrence of oesophageal cancer [1].

Despite the fact that oesophageal cancer is one of the most frequent malignancies worldwide [11], fistulization into the tracheobronchial tree is a rather rarely encountered condition [12]. An extensive retrospective review of all cases of oesophageal cancer at the Memorial Sloan-Kettering Cancer Center in New York between 1926 and 1988 observed the occurrence of a tracheobronchial fistula in only 161 of 3543 cases (4.5%) [13]. An even lower rate of 0.9% was recorded in an autopsy series from the Duke University Medical Center comprising 2440 cases of post-mortem examinations in patients who had suffered from oesophageal cancer [14]. However, higher incidence rates have also been reported [15]. A series from South Africa including 1135 patients who were treated for oesophageal carcinoma at the Natal University found the existence of a tracheobronchial fistula in altogether 184 patients [16]. On the other hand, the analysis comprised only those patients receiving intubation of the oesophagus in palliative intention because of incurable oesophageal carcinoma, whereas the total number of cases during the study period of 5 years amounted to ~2500 [16].

Adequate management of tracheobronchial fistulas caused by oesophageal carcinoma has been controversially discussed in the pre-endoscopy era. At that time administration of a specific therapy for closure or exclusion of the fistula was mainly hampered by the predominantly poor performance status of the sufferers. As a consequence, therapy often not exceeded best supportive care. Accordingly, the results were rather discouraging. Several palliative surgical procedures had also been suggested. At this resection of the fistula and oesophageal exclusion (closure of the oesophagus above and below the fistula with oesophagostomy and gastrostomy) showed outcome not superior to best supportive care with a recorded 30-day mortality varying between 55 and 60% [13].

More promising results were achieved by surgical bypass procedures involving either the colon or the stomach for oesophageal substitution [13, 17, 18]. However, only a minority of the patients affected by cancerous fistulization are usually fit enough to undergo major surgery and despite the overall satisfying functional outcome, colonic or gastric interposition as bypass is still associated with a noteworthy rate of severe complications [18]. As a consequence, substantial morbidity and mortality have considerable limited the justification of bypass procedures as palliation for unresectable oesophageal cancer [19]. To avoid the adverse effects of major surgery in a patient population with already impaired performance status, oesophageal intubation was advocated as less invasive method for closure of tracheobronchial fistula caused by oesophageal cancer [16, 20, 21]. In the pre-endoscopy era, this was achieved either by pushing the prosthesis down via the
peroral route or by pulling the tube through the tumour from below via a gastric incision [16]. Nonetheless, this procedure was also associated with serious side effects as haemorrhage and perforation caused by passing the rigid plastic tube through the tumoural affected parts of the oesophagus.

With the advent of modern interventional endoscopy oesophageal intubation has completely been replaced by endoscopic insertion of self-expandable stents [4]. Here, the obvious advantage is that endoscopic stents can be placed without great effort through a routine procedure which is nearly ubiquitously available. Furthermore, immediate closure of the fistula is achieved and aspiration of gastrointestinal contents into the airway ceases. In addition to sealing, the fistulous connection stenosis and narrowing of the oesophagus are simultaneously amended by stent implantation leading to immediate relief of symptoms as dysphagia and odynophagia [4, 5]. Moreover, the prosthesis is only expanded within the target area which is much safer than passing a rigid tube through the whole oesophagus.

In general, placement of an oesophageal stent has been regarded as the treatment of choice for tracheobronchial fistula caused by oesophageal carcinoma [4]. Stenting of the oesophagus is more commonly available than airway stenting and has the convincing advantage of avoiding general anaesthesia as it is usually performed in conscious sedation. Moreover, dysphagia due to oesophageal stenosis is simultaneously relieved by the procedure. However, several larger series reporting on oesophageal stenting for malignant tracheo-oesophageal fistula have shown substantial rates of both primary and secondary treatment failure [5, 6].

Initial failure to close the fistula by placement of one single stent was recorded in 12 of 61 patients suffering from malignant oesophago-respiratory fistula in a Korean series [5]. Moreover, reopening of the fistula took place in 17 further cases so that only approximately half of the patients were sufficiently treated by single-stent placement [5]. A Hungarian series comprising a multitude of endoscopic procedures as endoscopic oesophageal push through intubation with Häring-Rüsch endoprothesis or implantation of self-expandable oesophageal stents found initial treatment failure in 44 of 188 patients which were suitable for an endoscopic intervention [6]. However, due to the long study period with inclusion of many cases from the 1980s and early 1990s, only 16 of the 188 patients had actually received a modern self-expanding stent.

On the other hand, endoscopic insertion of tracheal and tracheobronchial stents for malignant airway disease has shown reliable good results with little complications and good palliation of symptoms related to stenosis as well as to fistulization [22, 23]. Therefore, parallel stenting of the oesophagus and the airways combining the advantages of both procedures has been suggested for improved endoscopic management of malignant tracheo-oesophageal fistula [7, 24, 25]. However, there have also been reports on an increased risk of fatal haemorrhage following double-stent implantation [8].

We adopted parallel stenting as primary treatment option for several reasons. First of all, it is clearly established that patients with successful closure of the fistula have a significant longer survival than patients with persistent fistula [5]. In the already mentioned Korean series, survival in case of successful stent placement was 15.1 weeks compared with only 6.2 weeks in case of failed stent insertion (P < 0.05) [5]. In our series, we accomplished complete closure of the fistula in all 9 cases by double stenting. This is in accordance with previous results [7]. Therefore, we may assume that patients suffering from tracheobronchial fistula caused by oesophageal cancer have a survival benefit due to the higher success rate of parallel stenting. Moreover, reliable closure of the fistulous tract is crucial for providing further treatment. Only patients with completely sealed fistula are able to undergo palliative anticancerous treatment in the form of either chemotherapy or radiation.

The treatment for recurrence of oesophageal carcinoma has been shown to be associated with significant longer survival [9]. In their series comprising 233 patients with recurrent oesophageal carcinoma following oesophagectomy in curative intention DeMeester et al. were able to demonstrate that patients who were treated for the recurrence survived averagely 9 months compared with only 3 months in cases without anticancerous therapy (P < 0.001) [9]. All our patients were suffering from recurrent oesophageal carcinoma. Following successful closure of the fistula by double stenting, 5 of 9 were able to receive either chemo- or radiotherapy. So we may conclude that parallel stenting with its improved success rate does in all likelihood prolong the survival not only by more reliable closure of the fistula but also by enabling the patients to receive palliative treatment.

Furthermore, double stenting with improved closure of the fistula is assumingly the better method of palliation. Stenosis of the oesophagus as well as of the airways is dealt with and dysphagia is relieved with consecutive reduction of aspiration and pneumonic symptoms. As patients suffering from recurrent oesophageal carcinoma have only a very limited life expectancy quick and reliable palliation should be the aim of every treatment approach [1]. Here, parallel stenting may be more advantageous than single stenting.

In our series, we encountered none of the previously described complications of parallel stenting. We found no difficulties in weaning off mechanical ventilation after tracheal stent implantation in general anaesthesia. In all but 1 patient who had already preoperatively sustained pulmonary sepsis with respiratory failure immediate extubation was feasible. So the need for general anaesthesia for rigid bronchoscopy was not associated with any complications or deterioration of the respiratory condition of the sufferers. Furthermore, we found no problems related to the existence of two stents within the mediastinum as mechanical friction or pressure necrosis of the tissue situated between the two stents.

Fatal haemorrhage due to vascular erosion which has occasionally been reported following parallel stenting was not seen in our study population. Severe bleeding and even aortic erosion have also been observed in cases of single-stent placement and are not limited to cases with double stenting. Fatal haemorrhage is also caused by straight tumour infiltration into the large mediastinal blood vessels and is in all probability expression of an advanced and incurable intrathoracic cancer spread. Thus far, there is no proof that parallel stenting might increase the well-known risk of stent-related vascular erosion. The most recent Dutch series on recurrent oesophageal carcinoma showed an average survival of only 3 months [1]. Under these circumstances, the advantages of quick and reliable palliation countervail the possible risk of later vascular erosion. Furthermore, it is noteworthy that in our series 7 of 9 patients were eventually fit enough to be discharged home following successful double stenting.

In conclusion, parallel endoscopic stenting provides a safe and quick option for reliable closure of tracheobronchial fistula caused by recurrent oesophageal carcinoma. Against the background of a very limited life expectancy in case of recurrence of oesophageal cancer, the possible higher risk of stent-related complications due to insertion of two stents is justified by both the improved palliation of fistula-associated symptoms and the possibility to receive palliative anticancerous treatment with longer average survival. Parallel stenting is easily accomplished with a high rate of
technical success and no noteworthy procedure-related complications. Therefore, we recommend endoscopic stenting of both the airways and the oesophagus in case of recurrent oesophageal carcinoma.

Conflict of interest: none declared.

REFERENCES