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REVIEW

Anastomotic leak after oesophagectomy and stent implantation: a systematic review

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Abstract Anastomotic leaks following oesophageal cancer resection have a high mortality. Stents have an established position in the palliation of dysphagia due to malignancy and in treating malignant perforation or fistula. They are increasingly used for benign conditions such as spontaneous oesophageal perforation with encouraging results. In this systematic review we examine the available evidence and attempt to define the role of stents in the management of oesophageal anastomotic leaks after resection for cancer. It is evident from the review that plastic- and metal-covered stents are an effective strategy for the treatment of anastomotic leaks. Vigilance is required as complications such as stent migration and incomplete sealing are not uncommon. Further clinical studies with greater methodological rigor in terms of sample size and study design may confirm that stents have an important contribution to make in the management of oesophageal anastomotic leak.

Keywords Oesophagectomy · Stent implantation · Management of anastomotic leaks

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Introduction

Anastomotic leaks following oesophageal cancer resection have an incidence of up to 17% and a mortality of up to 60% [1, 2]. There is no standardised approach for treating patients with symptomatic leaks. Management can include surgical intervention [3–6] percutaneous drainage [4, 6], antibacterial and antifungal treatment and nutritional support [7]. Stents have an established position in the palliation of dysphagia due to malignancy and in treating malignant perforation or fistula [3, 4]. They are increasingly used for benign conditions such as spontaneous oesophageal perforation with encouraging results [3]. Endoluminal stents are increasingly being deployed to treat oesophageal leaks following cancer resection [6]. Although this is an attractive therapeutic option, it is not without its hazards. Our aim was to evaluate the safety and efficacy of this strategy and define its role in the management of patients who have undergone oesophageal resection for cancer.

Materials and methods

A literature search of the current Ovid MEDLINE database (up to the end of 2009) and allied versions (Cumulative Index to Nursing and Allied Health Literature; Evidence Based Medicine of Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effects; International Pharmaceutical Abstracts) was performed independently by the authors. The subject heading "oesophagectomy," "oesophageal cancer," "gastric pull-up", "leak" and "cervical anastomosis" were included in title and/or abstract. The searches were limited to English language

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articles and human trials. The evidence was assessed using accepted guidance [8].

Results

Type of literature retrieved

The literature search found 24 different studies related to stent treatment of oesophageal anastomotic leak following cancer resection (Table 1). A total of 201 patients that had received a stent were analysed [6, 9–31]. A history of neoadjuvant treatment prior to resection was identified in only four cases. Studies were heterogeneous in terms of type, number of patients, site and size of the defect, previous intervention prior to stent and other parameters of evaluation. Due to the heterogeneous nature of reports identified, the best evidence synthesis method was therefore used rather than a formal meta-analysis. Four studies were case reports. Fifteen articles were retrospective reviews of large unselected series of cases where stents were used for a variety of indications. Data concerning thoracic oesophageal anastomotic leaks was extracted from these studies wherever possible (Tables 2, 3). Remaining reports consisted of retrospective and prospective series of cases in which a stent was used in the management of thoracic oesophageal anastomotic leak. The single series of cervical anastomotic leaks is discussed separately and not included in Tables 2 and 3 [28].

Initial management of the leak

Several different descriptions of the site of anastomotic defect were described (Table 1). These included 'intrathoracic oesophageal', 'cervical anastomosis', 'proximal oesophagus', 'mid-oesophagus', oesophago-gastric junction', 'thoracic anastomotic leak,' 'upper oesophagus,' and 'distal oesophagus'. In the majority of series, the leak could be broadly classified as either cervical (leading to an oesophago-cutaneous fistula) or intrathoracic resulting in an endo-pleural, mediastinal, bronchial or tracheal fistula. The size of the defect varied from 10 to 70% of the anastomotic circumference. Therapeutic intervention had often occurred prior to deployment of a stent. This usually involved percutaneous drainage [26, 29]. Reopening of the neck wound to evacuate pus and debris together with regular endoscopic lavage and debridement was used in a series of cervical anastomotic leaks [28]. Surgical re-exploration with debridement plus or minus an attempt at repair was performed prior to stent insertion several studies [9, 15–18] In four studies, there were no details available of interventions leading up to a stent [10, 14, 19, 20].

The time interval prior to stent implantation was variable (Table 1). Measurement of the number of days as a mean, median and range was used by majority of studies. A few studies reported standard deviation and confidence intervals. The minimum time interval from the original operation prior to stenting ranged from 4 to 10 days. The maximum time ranged from 83 to 611 days. In 11 studies, no information could be obtained regarding the interval prior to stent insertion.

Outcome of plastic stent deployment

Two main types of covered stent were used: plastic and metal. The Polyflex woven plastic stent (Rüsch AG, Wiesbaden, Germany) consists of an outer wall of polyester netting embedded in silicone that forms the inner lining. Sizes used ranged from 23 to 25 mm flare with 18–21 mm body and lengths of 90–150 mm. Sizes were generally selected according to leak size and location. Stents were placed when patients were either intubated under general anaesthesia or under sedation with analgesia. Radiological assistance was often used. There was a high rate of sealing of post-resection leak with a plastic stent (Table 2). This ranged from 50 to 100%. Overall, sealing of a leak occurred in 68 out of 86 (79%) cases when a plastic stent was used (Table 2). Stent migration occurred in most series with an incidence of 9–75% (22% overall). Stent replacement or insertion of an additional stent was necessary in 11–100% of cases (19% overall). Major complications were seldom reported but mainly involved a requirement for further salvage surgery or persistent non-sealing of the leak. Time taken before resumption of oral nutrition was variable and depended on confirmation of healing (by resolution of clinical symptoms and radiological and endoscopic evidence of a seal). Stents were removed in the majority of series as early as 1 week after insertion (for migration) and as late as 4 months. In-hospital mortality ranged from 22 to 50%. The overall incidence of in-hospital mortality was 10 out of 86 cases (12%).

Outcome of metal stent deployment

Several different types of covered metal stents were used for treatment. These included Ultraflex (Boston Scientific, Watertown, MA), Telestep Wallstent (Schneider, Minneapolis, MN), Gianturco Rosch Z Stent (Cook, Bjaeverskov, Denmark), Wilson-Cook prosthesis, Choo Stent (MI Tech, Seoul, Korea), Mushroom covered metallic stent (Micro-Tech Company, Nanjing, East China). The length of stents used for thoracic leaks ranged from 100 to 120 mm with end diameters of 22–28 mm and waist diameters of 18–23 mm. One series exclusively treated cervical oesophagogastric anastomotic leaks. An Ultraflex tracheal stent of

Table 1 Initial management of oesophageal anastomotic leak patients that subsequently received a stent (articles in chronological order)

Author	Type of study	*N*	Neoadjuvant treatment	Location of leak/fistula	Intervention prior to stent (number)	Interval in days prior to stent
Segalin et al. [9]	Case report	1 (4)*	None	Pleura	Surgical repair and drainage	N/A
Roy-Choudhury et al. [6]	Not clear if prospective or retrospective over 52 months	14	None	Pleural	"Conservative" treatment	N/A
Doniec et al. [10]	Retrospective series 1996–2002	18 (21)*	None	Pleura; abdomen	N/A	N/A
Evrard et al. [11]	Prospective observational study (1999–2003)	4 (21)*	None	N/A	Fibrin glue ($n = 1$)	N/A
Gelbmann et al. [12]	Prospective series 2002–2003	5 (9)*	None	Pleura ($n = 2$)	None	13–65
Hünerbein et al. [13]	Not clear if prospective or retrospective (1998–2003)	9	None	Pleura	Pleural drainage	N/A
Langer et al. [14]	Prospective observational study (2000–2003)	18 (24)*	None	Pleura	N/A	4–65
Schubert et al. [15]	Observational study (2000–2003)	11 (12)*	None	Pleura	Endoscopic lavage and debridement; external drainage	10–45
Han et al. [16]	Observational study (2002–2005)	7 (8)*	None	Pleural ($n = 7$); abdomen ($n = 1$)	Peri-anastomotic and pleural drainage	5–30
Peters et al. [17]	Case reports	3	Chemoradiation ($n = 1$)	Pleura ($n = 2$), mediastinum ($n = 1$)	Surgical debridement ($n = 2$)	7–83
Freeman et al. [18]	Prospective observational study over 30 months	5 (21)*	None	Pleura ($n = 2$); tracheobronchial ($n = 3$)	Surgical repair	N/A
Holm et al. [19]	Retrospective case review (2002–2006)	4 (30)*	None	N/A	N/A	N/A
Karbowski et al. [20]	Retrospective study	1 (30)*	None	N/A	N/A	N/A
Nowakowski et al. [21]	Observational study	6	None	Pleura	Pleural drainage ($n = 3$)	N/A
Ott et al. [22]	Prospective observational study over 3 years	6 (12)*	None	Pleura	N/A	N/A
Scharf et al. [23]	Case report	1	Chemoradiation ($n = 1$)	Mediastinum	Surgical lavage and drainage	N/A
Profili et al. [24]	Case reports	2 (3)*	None	Pleura	Pleural drainage ($n = 3$)	5–12
Kauer et al. [25]	Retrospective study (1998–2005)	10	None	Pleura	N/A	N/A
Tuebergen et al. [26]	Non-randomised observational (1999–2006)	22 (32)*	None	Pleura, mediastinum, abdomen	Percutaneous drainage and surgical intervention	4–611

Table 1 continued

Author	Type of study	N	Neoadjuvant treatment	Location of leak/fistula	Intervention prior to stent (number)	Interval in days prior to stent
Zisis et al. [27]	Retrospective observational (2004–2006)	9	Chemoradiation ($n = 1$); chemotherapy ($n = 2$)	Pleura ($n = 7$); trachebronchial ($n = 2$)	Surgical exploration ($n = 2$)	8–28
Lindenmann et al. [28]	Not clear if prospective or retrospective (2003–2006)	6	None	Neck	Wound debridement ($n = 5$)	10–14
Leers et al. [29]	Retrospective series 2002–2007	15 (31)*	None	Pleura, mediastinum	Pleural drainage	N/A
Turkyilmaz et al. [30]	Retrospective review 1989–2008	2 (25)*	None	N/A	N/A	N/A
Dai et al. [31]	Prospective series 2001–2007	22	None	N/A	None	0–14

N/A, data not available or impossible to extract from the study

* Studies where the relevant data of a specific subset of cases of interest were extracted from a larger, more heterogeneous group

60 mm length with 22 mm end and 20 mm waist was used [28]. All six leaks were sealed successfully. Stent migration occurred in two cases, both of which required replacement. Three patients developed an oesophageal stenosis that required dilatation. There was no mortality.

For thoracic oesophageal leaks, the success of metal stent placement was reported to be high. Seal rates from 57 to 100% of cases were reported (Table 3). Out of 109 cases, metal stents achieved sealing of the defect in 62 cases (57%). This was less than for plastic stents. However, stent migration and replacement rates were less than for plastic stents at 6 and 4% overall, respectively. Serious complications were more frequent with metal stents (15%) compared with 7% for plastic stents. These consisted of persistent leaks or fistulation, oesophageal stenosis, haemorrhage and conduit necrosis (Table 3). Once again, the time taken before resumption of oral nutrition was variable and depended on confirmation of healing. Stents were removed in the majority of studies where this information could be obtained (Table 3). In-hospital mortality was 4% for metallic stents.

Discussion

Twenty-four studies were identified and included in this review. Two different types of stent were used for the treatment of oesophageal leak: plastic or covered metal stent. Published studies generally reported a high proportion of patients with defects completely healed. Overall, using pooled results extracted from all studies, seal rates for plastic stents were higher than metal stents for thoracic anastomotic leaks (Tables 2, 3). Data from cervical anastomotic leaks were limited to a single series of six cases where all of the defects healed using a metal tracheal stent together with cervical wound debridement [28]. Morbidity associated with stenting was not infrequent. Stent migration is inevitable either by chance or iatrogenic when the device is removed after successful healing or for a stent exchange. Vigilance is required once a stent is implanted by radiological upper GI series and endoscopy. Migration should be suspected if there is any deterioration in the patient's condition. Migration may be managed by endoscopic retrieval and repositioning or replacement [11, 22, 25]. Alternatively a suture can be attached to the top of the stent and secured to the patient's ear to discourage distal migration [16]. This study used a mushroom-shaped stent with a 50 mm wide distal flare designed to sit across an oesophagogastrostomy. This stent produced good results with successful healing in all seven cases. Unfortunately, this is the only series where this device has been used. Transmural oesophageal sutures can be used to secure the stent during insertion to prevent migration [32]. Incomplete

Table 2 Outcome of plastic (polyflex) stent insertion for thoracic oesophageal anastomotic leak (articles in chronological order)

References	*n**	Defect sealed	Stent exchange or addition performed	Migration of stent	Other major complications	Time until stent removal	In-hospital mortality
Evrard et al. [11]	4	4 (100%)	0	3 (75%)	None	1 week–4 months	None
Gelbman et al. [12]	5	3 (60%)	1 (20%)	0	Non sealing ($n = 2$)	Yes ($n = 3$)	2 (40%)
Hünerbein et al. [13]	9	8 (89%)	7 (78%)	2 (22%)	None	Routinely after 2 weeks and replaced as necessary	None
Langer et al. [14]	18	16 (89%)	2 (11%)	4 (22%)	Revisional surgery ($n = 2$)	Day 22–70 post insertion of stent ($n = 5$)	4 (22%)
Schubert et al. [15]	11	11 (100%)	0	1 (9%)	None	Median time of stent retrieval 4 weeks (range 2–8 weeks)	None
Freeman et al. [18]	5	N/A	N/A	N/A	N/A	N/A	None
Holm et al. [19]	4	N/A	N/A	N/A	None	N/A	None
Karbowski et al. [20]	1	1 (100%)	0	0	None	N/A	None
Ott et al. [22]	6	3 (50%)	N/A	4 (67%)	None	N/A	3 (50%)
Scharf et al. [23]	1	0	1 (100%)	0	Resection of anastomosis	Yes	None
Dai et al. [31]	22	21 (95%)	5 (23%)	5 (23%)	Revisional surgery ($n = 1$); reoperation for replacement of stent ($n = 1$)	7–62 days	1 (5%)
Overall	86	67 (78%)	16 (19%)	19 (22%)	7 (8%)	N/A	10 (12%)

N/A, data not available or impossible to extract from the study

* Studies where the relevant data of a specific subset of cases of interest were extracted from a larger more heterogeneous group

sealing around the proximal end of a stent was more commonly seen with metallic stents than with plastic. This has been the authors' experience so far with two metal stents used to treat oesophageal leaks. If this occurs, remedial measures have been attempted with variable success including application of endoclips to the top of the stent [25], insertion an additional stent inside the previous one [10] or salvage surgery [14, 31]. Serious complications occurred more frequently with metal stents compared with plastic stents in our analysis. In spite of this, in-hospital mortality was more frequently reported with plastic stents. Stents were seldom used alone to treat anastomotic leaks. Almost every study reported intervention prior to stenting that typically included commencement of intravenous broad-spectrum antibiotics, drainage of collections (pleural, mediastinal and abdominal) and nutritional support (Table 1). In addition surgical exploration and debridement was often performed. In-hospital mortality was high in two studies in which no intervention was reported prior to stenting [12, 22]. There is no clear evidence from the literature favouring the timing of stent insertion. The earliest that a stent has been used is 4 days following the original operation [14, 26]. This suggests that a philosophy of early stent insertion has been considered by some authors. The author would favour surgical re-exploration in large leaks (>70% of circumference) or if a leak occurred in the first 2 or 3 days after surgery. Stents have also been deployed much later after other interventions failed. Series tend to report a mixture of approaches depending on the clinical course of the patient. Another confounding issue for stent insertion is that there needs to be expertise available and a suitable range of types and sizes of implants to deal with variations and optimise the chance of success. Although it is an attractive therapeutic option, stent insertion for an acute anastomotic leak is not always available. Whenever a stent is used, it should be part of a surgical management package that includes early diagnosis, management of systemic sepsis, adequate drainage, nutritional and multi-organ support and timely intervention for stent complications. It is difficult to draw conclusions from these data regarding the benefit of stent implantation for oesophageal anastomotic leak. Case series to date are generally too small, heterogeneous and retrospective in nature. It would be ethically difficult to conduct a randomised-controlled trial of stent insertion in such patients, but it would be helpful to see some larger prospective studies of stent insertion in specific patient populations. Deployment of a plastic stent rather than a metal stent seems to be more likely to be successful. Both types of stent cause complications and therefore require careful monitoring prior to removal if and when appropriate. To date there has been no data demonstrating an economical advantage for insertion

Table 3 Outcome for metal stent insertion for thoracic oesophageal anastomotic leak

References	*n**	Defect sealed	Stent exchange or addition performed	Migration of stent	Other major complications	Time until stent removal	In-hospital mortality
Segalin et al. [9]	1	1 (100%)	0	0	None	20 days	None
Roy-Choudhury et al. [6]	14	8 (57%)	N/A	0	Food bolus obstruction ($n = 3$); bleed from stent erosion ($n = 1$); persistent leak ($n = 1$)	N/A	None
Doniec et al. [10]	18	N/A	N/A	N/A	Oesophageal stenosis, broken stent cover	N/A	N/A
Han et al. [16]	7	7	0	0	None	18–48 days	None
Peters et al. [17]	3	3 (100%)	0	0	Oesophageal stenosis ($n = 1$)	7–10 weeks	None
Kauer et al. [14]	10	9 (90%)	4 (40%)	4 (40%)	Persistent leak ($n = 1$)	After 4–6 weeks ($n = 5$); excreted in faeces ($n = 3$)	2 (20%)
Nowakowski et al. [21]	6	6	0	0	None	None removed	None
Profili et al. [16]	2	2 (100%)	1 (50%)	1 (50%)	None	Not removed	None
Tuebergen et al. [9]	22	17 (77%)	2 (9%)	N/A	Persistent leak ($n = 5$)	4–426 days	N/A
Zisis et al. [10]	9	7 (78%)	0	1 (11%)	Conduit necrosis ($n = 1$); tracheo-oesophageal fistula ($n = 2$)	N/A	2 (22%)
Leers et al. [29]	15	N/A	N/A	N/A	None	N/A	None
Turkyilmaz et al. [30]	2	2 (100%)	0	0	Late gastrointestinal haemorrhage ($n = 1$)	Not removed	None
Overall	109	62 (57%)	7 (4%)	6 (6%)	16 (15%)		4 (4%)

N/A, data not available or impossible to extract from the study

* Studies where the relevant data of a specific subset of cases of interest were extracted from a larger more heterogeneous group

of a stent for anastomotic leak. Surgery should probably remain the 'gold-standard' for dealing with a large dehiscence or early leak occurring in the first several days after initial resection.

Conflict of interest None.

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