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Best evidence topic

# Should oesophageal stents be used before neo-adjuvant therapy to treat dysphagia in patients awaiting oesophagectomy? Best evidence topic (BET)

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ABSTRACT

Patients who develop significant dysphagia secondary to a potentially curable oesophageal cancer pose a significant clinical problem. Their nutritional needs can be met either by dietary supplementation, insertion of an oesophageal stent or through nasogastric or surgical feeding tube placement. We sought to determine whether, in patients about to start neo-adjuvant therapy prior to oesophagectomy, the use of oesophageal stent improves clinical outcomes. A best evidence topic in upper gastrointestinal surgery was written according to a structured protocol in order to answer this question. Two hundred and forty eight papers were found, of which eleven level III and one level IV study were considered to best address the clinical question. These indicate that whilst oesophageal stents do successfully relieve dysphagia throughout neoadjuvant therapy, they are not consistently associated with maintenance of, or improvement in, serum albumin or body weight. They are, however, commonly associated with stent migration and chest discomfort, both of which may frequently result in the need for stent removal or replacement. There is additional evidence within the manuscripts reviewed to demonstrate that the use of oesophageal stents in the neoadjuvant setting can lead to significant complications in a small proportion of patients which can compromise opportunity for curative surgery. The use of stents in this situation cannot be recommended.



## 1. Introduction

Oesophageal malignancy commonly presents with dysphagia and weight loss. Given that subsequent malnutrition is associated with poorer outcomes for both neoadjuvant therapy and surgery, maintaining adequate nutrition during neoadjuvant treatment is vital [1,2]. Strategies to address nutritional requirements include dietary supplementation, nasojejunal tube placement and feeding jejunostomy insertion. Each method has specific risks and advantages. Oesophageal stents, for example, have the benefit of permitting enteral nutrition without a visible feeding tube or the requirement to connect to a feeding pump. However, little is known about their efficacy or safety. We constructed a best evidence search according to a structured protocol, as described in a manuscript published within the *International Journal of Surgery* [3]. This BestBET, part of a series designed to answer clinically relevant questions and allow clinicians to rapidly review the literature on a defined topic, reviews the use of oesophageal stents in patients undergoing neoadjuvant therapy prior to planned oesophagectomy.

## 2. Clinical scenario

You are in the outpatient clinic with a 73 year old man with oesophageal cancer. Staging investigations, including computer tomography, endoscopic ultrasound and positron emission tomography have shown a surgically resectable T3N1 oesophageal adenocarcinoma. He has become severely dysphagic and is about to embark on neo-adjuvant chemotherapy. The patient is worried about losing weight and asks about the possibility of an oesophageal stent to alleviate his swallowing problems whilst awaiting potentially curative surgery. You elect to review the literature in

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**Table 1**
Best evidence papers.

| Article & level of evidence | Patient group assessed | Type of stent used | Outcomes assessed | | Summary of findings | Comments |
|---|---|---|---|---|---|---|
| Christie A. 2001. USA. [4] Level III: Follow up study | One hundred patients within a single tertiary referral centre with either oesophageal malignancy or lung cancer (7%) and dysphagia. | Expandable metal stent. (Ultraflex). | Relief of dysphagia | | Dysphagia relieved up to the time of oesophagectomy in 14/16 patients (88%). 2/16 (12,5%) required a feeding tube for nutritional supplementation. | Only a small subset of patients had stents to cover neoadjuvant CT. No comment is made on change in objective markers of nutrition, nor on impact on progression to surgery. |
| | | | Complications | | Two complications specific to those undergoing neoadjuvant therapy noted; one patient had stent placed in the proximal oesophagus and developed stent erosion into the T1 vertebral body, requiring subsequent neurosurgical drainage, whilst another developed a mediastinal abscess related to an occult stent perforation and erosion. This recurred following oesophagectomy and the patient died from sepsis. | |
| Bower M. 2009. USA. [5] Level III: Follow up study. | Twenty five patients within a single tertiary referral centre between January 1998 and July 2008 with oesophageal malignancy and stricture causing significant dysphagia. All had undergone neoadjuvant CRT after stent placement with a view to subsequent surgical resection. | Self expanding silicone-covered stent. (Polyflex). | Complications | Immediate | 1/25 (4%) experienced chest discomfort, alleviated with oral analgesics. | No note is made of the proportion for whom stent insertion was not a technical success. Stent placement is compared to 19 patients with feeding tubes placed and 14 nonstented patients maintained on oral diet, all of whom underwent neoadjuvant therapy. |
| | | | | Early | 2/25 (8%) required nasoduodenal tubes to support nutrition. | |
| | | | | Late | 6/25 (24%) experienced stent migration, 5/6 (83.3%) of whom required removal of the stent. | |
| | | | Change in dysphagia score | | Dysphagia significantly improved from 3.5/4 to 1.3/4 ($p < 0.001$) | |
| | | | Change in serum albumin | | Mean serum albumin significantly improved by 0.14 g/dL ($p < 0.001$) over the course of neoadjuvant CRT. | |
| | | | Change in body weight | | No significant change in body weight over the course of neoadjuvant CRT. | |
| | | | Progression to surgical resection. | | 14/25 (56%) patients with stents placed proceeded to surgical resection. | |
| Adler D. 2009. USA. [6] Level III: Follow up study | Thirteen patients within a single tertiary referral centre between April 2006 and November 2007 with oesophageal malignancy and stricture causing dysphagia. All were planned to have neoadjuvant therapy prior to undergoing planned oesophageal resection. | Self expanding silicone-covered stent. (Polyflex) | Technical success of stent insertion | | 11/13 (85%) stents inserted successfully, with 2/13 (15%) requiring immediate revision; 7/13 (54%) required dilation of stricture for insertion. | There is no discussion of objective markers of changes in nutrition. |
| | | | Complications | Immediate | 12/13 (92.3%) experienced chest discomfort, 1 (7.7%) of whom required stent removal and replacement due to severe pain. | |
| | | | | Early/Late | Stent migration occurred in 6/13 (46%), five of whom required stent removal. 2/13 (15%) patients required PEG feeding for supplemental nutrition. | |
| | | | Change in dysphagia score | | Mean dysphagia score significantly improved from 3.0/4 to 1.1 ($p = 0.005$) at 1 week, 0.8 ($p = 0.01$) at 2 weeks, 0.9 ($p = 0.02$) at three weeks and 1.0 ($p = 0/008$) at four weeks follow up. | |
| | | | Progression to surgery | | 3/13 (23%) of patients progressed to surgery. | |
| Siddiqui A. 2009. USA. [7] Level III: Follow up study | Thirty six patients within a single tertiary referral centre with oesophageal malignancy and significant dysphagia undergoing neoadjuvant therapy prior to planned oesophageal resection. | Self expanding silicone-covered stent. (Polyflex) | Technical success of stent insertion | | 11/12 (92%) stents inserted successfully, with 2/12 (17%) requiring predilation. One stent not inserted due to failure to traverse stricture, with the patient subsequently receiving a jejunostomy tube. | Complications not categorised by time at which they occurred. |
| | | | Change in dysphagia score | | | |

(*continued on next page*)

**Table 1** (*continued*)

| Article & level of evidence | Patient group assessed | Type of stent used | Outcomes assessed | | Summary of findings | Comments |
|---|---|---|---|---|---|---|
| | | | | | Significant improvement from baseline (3.1) at eight weeks (1.2; $p < 0.005$). | |
| | | | Change in body weight | | Significant increase from baseline (60.5 kg) at eight weeks (65.0 kg; $p < 0.001$). | |
| | | | Change in mean serum albumin | | Significant increase from baseline (2.8 g/dL) at eight weeks (3.5 g/dL; $p < 0.001$). | |
| | | | Complications | | 8/11 (73%) patients developed chest discomfort following the procedure, all managed with oral agents.<br>4/11 (36%) patients developed stent migration at a mean time of 3.5 weeks; all were asymptomatic. | |
| Lopes T. 2010. USA [8]<br>Level III: Follow up study | Eleven patients within a single tertiary referral centre with oesophageal malignancy causing dysphagia. All were planned to have neoadjuvant therapy prior to undergoing planned oesophageal resection. | Fully covered self-expandable metal stent. (ALIMAXX-E) | Technical success of stent insertion | | 10/11 (90.9%) stents successfully inserted, nine of whom required predilation. 1/11 (9.1%) stents placed too proximally with the patient subsequently receiving an NJ tube instead. | Most stents were considered to have satisfied their purpose and were removed at a mean of 100.4 days (50% removed due to satisfying their purpose, 10% because of migration and 10% due to complications developing). As such, the authors state that the improvement in dysphagia score may be attributable to the success of neoadjuvant therapy. |
| | | | Complications | Immediate | 3/10 (30%) experienced chest discomfort, relieved by oral agents. | |
| | | | | Delayed | 2/10 (20%) experienced stent migration, one of whom required stent removal for recurrent dysphagia. 1/10 (10%) developed tracheoesophageal fistulation, requiring stent removal. | |
| | | | Change in dysphagia score | | Dysphagia significantly improved by 3.12/4 at one month ($p < 0.05$), sustained at three and six months follow up. | |
| | | | Stent removal | | 8/10 (80%) stents removed, 5 (50%) of which were planned and 3 (30%) due to complications. Removal was universally described as easy. | |
| | | | Microscopic reaction to stent | | 6/8 (75%) stents associated with ulceration, 6/8 (75%) with granulation, 4/8 (50%) with polyps and 1/8 (12.5%) became embedded. | |
| | | | Progression to surgical resection | | 2/10 (20%) patients progressed to surgery. | |
| Langer F. 2010. Austria. [9]<br>Level III: Follow up study | Thirty eight patients within two tertiary referral centres, 29 of whom had oesophageal malignancy. The remainder had cardia (8) or subcardial (1) gastric cancer. | Self expanding silicone-covered stent (13)<br>(Polyflex: 13)<br>Self-expanding metal stents (25):<br>Niti-S (1)<br>Ultraflex (7)<br>Hanaro (5)<br>Choo (2)<br>DoStent (1): | Technical success of stent insertion | | 37/38 (97.4%) stents inserted successfully, with 1/38 (2.6%) leading to perforation and necessitating acute oesophagectomy. 12/38 (32%) required dilation. | Data provided for proportion of stents of each type which migrated during the study, with 2/13 (15.4%) self expanding plastic stents (Polyflex) migrating, compared with 10/25 (40%) of self expanding metal stents (6/10 (25%) Niti-S; 2/7 (28.6%) Ultraflex; 2/5 (40%) Hanaro; 0/2 Choo; 0/1 DoStent). |
| | | | Complications | Immediate | Immediate stent migration in 2/38 (5.3%) patients; one requiring stent repositioning and one requiring stent exchange. | |
| | | | | Early/Late | Early stent migration in 3/38 (7.9%), two requiring stent exchange and one requiring overstenting.<br>Late stent migration seen in 7/38 (18.4%) patients, causing a covered perforation requiring stent removal in one, and requiring restenting in another patient.<br>One stent caused erosion of the aortic wall at day 61. | |
| | | | Change in dysphagia score | | Dysphagia score significantly improved from 3.0/4.0 to 0.6/4.0 ($p < 0.05$). | |
| | | | Change in serum albumin | | | |

**Table 1** (*continued*)

| Article & level of evidence | Patient group assessed | Type of stent used | Outcomes assessed | | Summary of findings | Comments |
|---|---|---|---|---|---|---|
| | | | | | Serum albumin did not change in those who subsequently underwent surgery (39.9 vs 39.1 mg/dL) but significantly fell in those who did not undergo surgery, regardless of stenting (40.0 vs 29.7 mg/dL; $p < 0.05$). | |
| | | | Progression to surgical resection | | 12/38 (31.6%) failed to progress to surgery; 6 (15.8%) due to disease progression, 4 (10.5%) due to reduced performance status, 1 (2.6%) due to pneumonia and 1 (2.6%) due to cisplatin-induced encephalopathy and sepsis. | |
| Brown R. 2011. USA [10] Level III: Follow up study. | Thirty two patients within two-institutions between May 2008 and March 2010 with oesophageal malignancy. ( | Self expanding silicone-covered stent. (Polyflex) | Technical success of insertion | | Successful in 32/32 (100%) patients; 28/32 (87.5%) requiring dilatation of the stricture. | No intraoperative complications were noted to have resulted from the presence of a stent. |
| | | | Complications | Immediate | None | |
| | | | | Early | 1/32 (3.1%) patient experienced chest discomfort, managed on oral agents. | |
| | | | | Late | Stent migration in 8/32 (25%); two of whom required intervention for recurrent dysphagia. | |
| | | | Change in dysphagia score | | Significantly decreased from 2.1/4 to 0.6/4 ($p < 0.001$) within 48 h of stent placement, with improvements sustained until resection. | |
| | | | Change in weight | | Significantly decreased from 84.5 kg to 77.3 kg ($p < 0.01$) between pre-stent stage and resection; 1/32 (3.1%) patient required jejunostomy insertion due to significant weight loss. | |
| | | | Change in serum albumin | | Significantly decreased from 4.0 mg/dL to 3.6 mg/dL ($p = 0.03$) between pre-stent stage and resection. | |
| | | | Progression to surgical resection | | 12/32 (37.5%) did not proceed to oesophagectomy; 4 (12.5%) due to poor performance status, 8 (25%) because of disease progression. | |
| Pellen M. 2012. UK. [11] Level III: Follow up study | Sixteen patients within a single tertiary-referral centre between April 2006 and November 2008 with oesophageal malignancy and stricture causing significant dysphagia. | Self expanding removable nitinol braided polyethylene-covered alloy metal stent (SX-Ella HV) | Technical success of insertion | | Successful in 16/16 (100%). | No comment is made on the proportion of patients requiring dilatation prior to stent placement. |
| | | | Complications | Immediate | None reported. | |
| | | | | Early/Late | Distal migration in 43.8% (7/16); 2 (12.5%) of whom required intervention due to small bowel obstruction and dysphagia. Food bolus obstruction in 2/16 (12.5%). | |
| | | | Progression to surgical resection | | 6/16 (37.5%) did not progress: 1 (6.25%) due to poor nutrition, 1 (6.25%) at patient's request, 1 (6.25%) due to excellent RT response, 3 (18.8%) due to disease progression. | |
| | | | Change in dysphagia score | | Significantly decreased from 2.5/4 to 1.1/4 ($p = 0.001$). | |
| | | | Change in weight | | No significant change: 69.6 kg vs 67.4 kg ($p = 0.070$) | |
| | | | Change in albumin | | No significant change: 32.8 g/L vs 32.0 g/L ($p = 0.440$) | |
| Griffiths E. 2012. UK. [12] Level III: Cohort study | Twenty two patients within a single tertiary referral centre between July 2008 and February 2011 receiving oeophageal stents, nine of whom had oesophageal malignancy. | Woven polydioxanone biodegradable stent. (BD SX-ELLA) | Technical success of insertion | | Successful in 21/22 (96%) of patients. Placement failed in one patient due to failure of the stent to load on to the loading mechanism. | Technical success rate and change in dysphagia score are reported for all indications, rather than specifically for the indication reviewed within this manuscript. |
| | | | Complications | Immediate | None reported. | |
| | | | | Early | Of the 9 patients undergoing neoadjuvant therapy, 1/9 (11%) required insertion of a SEMS at 2 | |

(*continued on next page*)

**Table 1** (*continued*)

| Article & level of evidence | Patient group assessed | Type of stent used | Outcomes assessed | | Summary of findings | Comments |
|---|---|---|---|---|---|---|
| | | | | | months and 2 (22%) required supplementary feeding via jejunostomy and a fine bore NJ tube within 12 weeks of stenting. | |
| | | | Progression to surgical resection | | 6/9 (66%) did not proceed to surgery; 1 (11%) because of disease progression, two (22%) because of failure to gain sufficient weight and three (33%) because they became unfit for surgery. The additional 3/9 (33%) did progress to surgery but were not resected due to the recognition of disseminated disease. | |
| | | | Change in dysphagia score | | Significantly improved from 3.0/4 to 2.0/4 ($p = 0.0001$) at a median of 47 days. | |
| Krokidis M. 2013. UK. [13] Level III: Follow up study | Eleven patients within a single tertiary-referral centre between January and December 2011 with oesophageal malignancy. | Woven polydioxanone biodegradable stent (BD SX-ELLA) | Technical success of insertion | | Successful in 11/11 (100%); 5 (45%) of whom required dilation. | No note is made of whether patients received CT, RT or CRT. Mean follow up time was 102 days but it is difficult to determine the range time times at which dysphagia scores were estimated. |
| | | | Complications | Immediate | None reported. | |
| | | | | Early (<30 days) | Precluded oral nutrition in 3/11 (27%): 18% (2) experienced proximal migration and 9% (1) developed aspiration pneumonia secondary to fistulation at level of bronchial tree. | |
| | | | | Late (>30 days) | Stent dysfunction in 5/11 (45%) at a mean time of 97.8 days; 2 (18%) died at days 32 and 42 due to tracheoesophageal fistulation, 3 (27%) required restenting. | |
| | | | Mean stent patency rate | | 71.5 days (SD 68.3) | |
| | | | Progression to surgical resection | | 1/11 (9%) progressed to surgery despite requiring NJ feeding due to stent dysfunction. 3/11 (27%) had patent stents and were awaiting surgery at 52–130 days follow up. | |
| | | | Change in dysphagia score | | Significantly decreased from 3 to 1.9 ($p = 0.001$) in 8/11 (72%) at study end point. | |
| Martin R. 2014. USA. [14] Level III: Follow up study | Fifty two patients within two tertiary referral centres with oesophageal malignancy. | Self expanding silicone-covered stent. (Polyflex) | Complications | | 1/52 (1.9%) required feeding jejunostomy placement due to poor nutritional intake. 3/52 (5.8%) required stent replacement following migration. | No note of technical success of stent insertion or progression to surgery. The author's closing claim that 'consideration of stents instead of feeding tubes should be initiated as first line in dysphagia palliation' is perhaps not supported without data relating to progression to surgery. |
| | | | Change in dysphagia score | | Significantly improved from an average baseline of 66.6 to 1.1 ($p < 0.001$) at 1 week after stenting and 11.1 ($p < 0.001$) during neoadjuvant therapy. | |
| | | | Change in serum albumin | | No significant change; 4.0 g/dL at baseline compared with 3.9 g/dL ($p = 0.3$) at completion of neoadjuvant therapy. | |
| | | | Change in performance status | | No significant change; Karnofsky score of 90 at baseline, compared with 94.4 ($p = 0.170$) at completion of neoadjuvant therapy. | |
| | | | Change in body weight | | No significant change in body weight; 84.5 kg at baseline compared with 81.3 kg ($p = 0.57$) at completion of neoadjuvant therapy. | |
| | | | Quality of life measures relating to eating restriction (QLQ-C30 score) | | Significant improvement in median response to trouble enjoying meals at one week (4 vs 2; $p = 0.004$). Significant improvement in median response to early satiety from baseline of 4 at one week (2; $p = 0.012$) and during | |

**Table 1** (*continued*)

| Article & level of evidence | Patient group assessed | Type of stent used | Outcomes assessed | | Summary of findings | Comments |
|---|---|---|---|---|---|---|
| | | | | | neoadjuvant therapy (2; $p = 0.001$). Significant improvement in median response to taking a long time to complete meals from 4 at baseline to 3 ($p = 0.016$) at one week after stenting. Significant improvement in median response to difficulty eating from a baseline of 4 to 2 at 1 week ($p = 0.015$) and 1 ($p = 0.002$) during neoadjuvant therapy. | |
| Siddiqui A. 2012. USA. [15] Level IV: Retrospective case series. | Fifty five patients within two tertiary referral centres between October 2006 and August 2011 with oesophageal malignancy. | Fully covered self-expandable metal stents. (ALIMAXX-E: 22) (WallFlex: 29) (Evolution: 4) | Technical success of insertion | | 55/55 (100%) successfully inserted, none requiring oesophageal dilatation. | Three different stent types used but specific results for each stent used are not shown, nor is justification for the stent type utilised. Average weight results were not available for four patients. |
| | | | Complications | Immediate | 8/55(15%) experienced chest pain, necessitating stent removal in 2/55 (3.6%). | |
| | | | | Early | 1/55 (1.8%) required stent removal for uncontrollable reflux. 1/55 (1.8%) experienced self-limiting odynophagia. 1/55 (1.8%) required endoscopic management of food bolus obstruction. | |
| | | | | Late | Stent migration occurred in 17/55 (31%) after a mean of 44 days, with 1/55 (1.8%) requiring stent replacement for recurrent dysphagia. 1/55 (1.8%) required oesophageal repair and oesophagostomy for perforation sustained whilst undergoing neoadjuvant therapy. | |
| | | | Progression to surgical resection | | 8/55 (15%) underwent attempted curative resection. | |
| | | | Change in dysphagia score | | Mean dysphagia score significantly improved from a baseline of 2.4 at 1 week after stenting (1.0; $p < 0.001$). | |
| | | | Change in weight | | There was no significant change in weight at one month after stenting when compared with baseline; 149 vs 153 pounds ($p = -0.59$). | |

order to determine whether an oesophageal stent would be likely to relieve his dysphagia and improve his clinical outcomes.

## 3. Three-part question

In patients undergoing neo-adjuvant therapy prior to oesophagectomy, does the use of oesophageal stent for the relief of dysphagia afford improved parameters relating to nutritional status, including change in weight and serum albumin, without negatively impacting on morbidity, progression to surgery and overall survival?

## 4. Search strategy

A Medline search limited to the time period of 1st January 1946 to 1st March 2014 was operated using the Ovid interface probed for the following terms: (oesophagectomy [All Fields] OR oesophageal neoplasia [All Fields]) AND (neoadjuvant therapy [All Fields] OR neoadjuvant chemotherapy OR neoadjuvant chemoradiotherapy OR pre-operative chemotherapy OR pre-operative chemoradiotherapy OR pre-operative radiotherapy) AND (stent OR nutrition) AND (outcomes). Results were limited to papers published in the English language and those relating to Humans. Any manuscript addressing the use of oesophageal stents during neoadjuvant therapy prior to oesophagectomy was assessed in detail.

## 5. Search outcome

Two hundred and forty eight papers were found using the described search strategy, after which abstracts were independently reviewed by both authors and those which were not deemed relevant were excluded from further analysis. Of the 248 abstracts initially identified, twelve manuscripts were identified that provided the best evidence to answer the clinical question. A total of 237 manuscripts were excluded from further analysis; 35 of which did not relate to the use of stents, 53 which were not directly applicable to oesophageal pathology and/or oesophageal malignancy, 115 of which related to the post-operative use of stents and the remainder of which constituted review articles or isolated case reports.

## 6. Discussion

Eleven level III follow up studies and one level IV retrospective case series were identified to be relevant to the research question, as illustrated within Tables 1 and 2 [4–15].

**Table 2**
Summary of key findings, by stent type and year of publication.

| | No. of patients | Neo-adj therapy[a] | Stent type studied | Insertion | | Significant improvement in dysphagia? | Change in mean serum albumin | Change in weight | Complications (%) | | | % Requiring supplementary tube feeding | % Requiring unplanned stent removal/replacement | % Progression to surgical resection[b] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | % Success | % Requiring dilation | | | | Chest discomfort | Stent migration | Erosion or fistulation | | | |
| Christie A; 2001 | 100 | CT/CRT | SEMS | NR | NR | Y | NR | NR | 0 | 0 | 12 | 12 | 12 | NR |
| Bower M; 2009 | 25 | CRT | SEPS | 100 | 56 | Y | ↑ | ↔ | 0 | 20 | 0 | 8 | 20 | 56 |
| Adler D; 2009 | 13 | CRT | SEPS | 85 | 54 | Y | NR | NR | 92.3 | 46 | 0 | 15 | 15 | 23 |
| Siddiqui A; 2009 | 36 | CRT | SEPS | 92 | 17 | Y | ↑ | ↑ | 73 | 36 | 0 | 0 | 0 | NR |
| Lopes T; 2010 | 11 | CRT | SEMS | 91 | 82 | Y | NR | NR | 30 | 20 | 10 | 0 | 30 | 20 |
| Langer F; 2010 | 38 | CT/CRT | SEP/MS | 97 | 32 | Y | ↓ | NR | NR | 32 | 9 | 3 | 29 | 52.6 |
| Brown R; 2011 | 32 | CT/CRT | SEPS | 100 | 87.5 | Y | ↓ | ↓ | 3.1 | 25 | 0 | 3.1 | 0 | 62.5 |
| Pellen M; 2012 | 16 | CT | SEMS | 100 | NR | Y | ↔ | ↔ | 0 | 44 | 0 | 0 | 0 | 62.5 |
| Griffiths E; 2012 | 22 | CT | SEBS | 96 | NR | Y | NR | NR | 0 | NR | NR | 22 | 66 | 0 |
| Krokidis M; 2013 | 11 | CT/CRT | SEBS | 100 | 45 | Y | NR | NR | 0 | 18 | 18 | 9 | 27 | 0–27 |
| Martin R; 2014 | 52 | CT/CRT | SEPS | NR | NR | Y | NR | NR | NR | 6 | NR | 1.9 | 5.8 | NR |
| Siddiqui A; 2012 | 55 | CRT | SEMS | 100 | 0 | Y | NR | ↔ | 15 | 31 | 1.8 | 0 | 3.6 | 15 |

Key: NR – Not recorded/measured, Y–Yes, N–No, ↔–No change (stable), ↑–Significant increase seen, ↓–Significant decrease seen, SEBS–Self expanding biodegradable stent, SEMS–Self expanding metal stent.

[a] CT–Chemotherapy; CRT–Chemoradiotherapy.

[b] Without requiring additional nutritional supplementation via nasojejunal or feeding jejunostomy tube. Results are shown as a percentage of those who had stents successfully inserted.

Nine series provide information relating to the technical success of stent insertion, rates of which vary between 85 and 100% [6–13,15]. Failures are attributed within the studied series to an inability to traverse strictures, proximal stent placement, failure of the stent loading mechanism and one perforation which necessitated acute oesophagectomy [7–9,12]. Eight manuscripts reported the use of pre-dilatation prior to stent placement, rates of which varied between 17 and 85.5% [5–10,13,14]. Adler et al. additionally note that two of the thirteen patients included within their series required immediate revision of stent placement [6].

Placement of an oesophageal stent significantly improved overall dysphagia scores in all twelve studies reviewed [4–15]. This improvement is noted to occur within 48 h of stent placement and is reported to continue for the duration of follow up in three studies respectively extending to four, eight and 24 weeks, and to time of resection in a further two studies [4–15]. Supplementary feeding tube placement was nevertheless required due to recurrent dysphagia by two of 100 patients reported by Christie et al., by two of 25 patients reported by Bower et al. and by one of 11 patients identified by Krokidis et al. [4,5,13].

As is summarised within Table 2, there was no consistent improvement seen in markers of nutritional status, with mixed reports of both weight and serum albumin levels increasing, decreasing or remaining unchanged following stent insertion [5,7,9–11,15].

Rates of progression to surgical resection vary significantly between manuscripts from a nadir of 0%, reported with the use of biodegradable stents by Griffiths et al., to a peak of 56% [5,6,8–13,15]. Noting that 33% of patients with biodegradable stents inserted within their 2012 study progressed to theatre but were deemed unsuitable for intervention at the time of attempted resection, Griffiths et al. additionally highlight that 66% were deemed unfit for surgery pre-operatively, two thirds of whom had failed to gain sufficient weight [12]. Pellen et al. provide further analysis of poor rates of progression to surgical resection, noting that just one of the six patients within their sixteen strong cohort who failed to progress to surgery did so as a result of poor nutritional status, with three experiencing significant disease progression [11]. These findings are supported by Brown et al. who identify that whilst two thirds of their patients who failed to progress to resection did so because of disease progression, one third had experienced a significant decline in their performance status [10]. Whilst Langer et al. report cisplatin-induced encephalopathy and pneumonia as prohibiting resection in twelve of their patients who failed to progress to surgery, they too additionally identify disease progression and reduced performance status as principal factors underlying failed surgical resection [9].

There are numerous reports of complications arising within the studied series. Christie et al. identify two patients who developed significant complications, including one death from sepsis secondary to the development of a mediastinal abscess following stent erosion [4]. A further patient required neurosurgical drainage after stent erosion into the T1 vertebral body caused an abscess [4]. Bower et al. make note of six (24%) patients who experienced stent migration, all of whom had responded to neoadjuvant therapy [5]. One patient additionally experienced chest discomfort significant enough to warrant readmission [5]. This immediate complication of stent placement is reiterated by Siddiqui's 2007 series, which reported that 73% of patients were affected by chest pain, and Adler's 2009 prospective level III study of thirteen patients undergoing SEPS placement [6,7]. Within this population, 92.3% (12) patients experienced chest discomfort which was severe enough in 7.7% (1) to warrant stent removal and replacement [6]. Stent migration is again recognised as a complication, affecting six (46%) patients, five of whom required removal of their stent [6].

Thirty percent of patients within Lopes' analysis experienced chest discomfort and an additional 30% (3) required stent removal for complications [8]. Two of these patients had experienced stent migration whereas one developed tracheoesophageal fistulation [8]. Serious stent related complications were additionally reported by Langer et al., including perforation ($n = 1$), mediastinitis ($n = 1$), tracheoesophageal fistulation ($n = 2$), bleeding ($n = 1$) and jejunal perforation ($n = 1$) [9]. Of clinical relevance, 18.5% of the patients in this study required endoscopic intervention (either stent replacement or repositioning) due to stent migration [9].

Despite successful initial stent placement in 11/11 patients studied by Krokidis et al., early complications occurred in 3/11 (27.2%), none of whom were subsequently able to be fed orally [13]. One patient experienced proximal stent migration within two days of its deployment, leading to vocal cord dysfunction and tracheobronchial aspiration secondary to a tracheoesophageal fistula [13]. A second patient experienced proximal stent migration, again within the first 48 h of placement, presenting as aspiration and haematemesis [13]. The third developed pneumonia secondary to a fistula to the bronchial tree which developed after three weeks [13]. Importantly, two of the eight patients with sustained stent placement died due to the development of tracheosophageal fistulae at days 42 and 62 [13].

Finally, Siddiqui et al. identified pain as a significant consequence of stent placements within their 2012 series of 55 patients, with two of the 13 patients requiring stent removal due to the severity of their discomfort [15]. Further, stent migration occurred in 17 (31%) patients, with a further patient undergoing a delayed perforation [15]. In spite of this, Brown et al. report just 3.1% (1) of the patients within their analysis experiencing chest discomfort, though eight (25%) experienced stent migration, albeit with only two requiring endoscopic intervention [10].

## 7. Clinical bottom line

Stent placement is effective for relieving dysphagia in patients undergoing neo-adjuvant chemotherapy but does not consistently translate to maintenance or improvement in either weight or serum albumin levels. Stents placed for this indication additionally consistently require reintervention due either to migration or chest pain and are associated with both significant variation in the rate of patients progressing to curative surgery and uncommon life threatening complications including oesophageal perforation, medinastinitis, aortic erosion and tracheo-oesophageal fistulation. The use of stents in this scenario cannot be supported.

## Ethical approval

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## Author contribution

EAG devised the clinical question posed by this article, and both EAG and CMJ performed a literature review to answer the question posed. Abstracts were sifted by both authors and a database formed by CMJ. Each article included within this manuscript was read by both authors and its findings summarised by both authors, as tabulated. CMJ wrote the first draft of the manuscript and both CMJ and AEG contributed to subsequent reviews.

## Conflicts of interest

The authors declare that they have no conflicts of interest relating to this article.

## References


[1] J.M. Daly, F.N. Weintraub, J. Shou, E.F. Rosato, M. Lucia, Enteral nutrition during multimodality therapy in upper gastrointestinal cancer patients, Ann. Surg. 221 (1995) 327–328.

[2] A. Windsor, M. Braga, R. Martindale, R. Buenos, R. Tepaske, L. Kraehenbuehl, A. Weimann, Fit for surgery: an expert panel review on optimising patients prior to surgery, with a particular focus on nutrition, Surgeon 2 (2004) 315–319.

[3] O.A. Khan, J. Dunning, A.C. Parvaiz, R. Agha, D. Rosin, K. Mackway-Jones, Towards evidence-based medicine in surgical practice: best BETs, Int. J. Surg. 9 (2011) 585–588.

[4] A. Christie, P.O. Buenaventura, H.C. Fernando, N.T. Nguyen, T.L. Weigel, P.F. Ferson, J.D. Luketich, Results of expandable metal stents for malignant esophageal obstruction in 100 patients: short-term and long-term follow up, Ann. Thorac. Surg. 71 (2001) 1797–1802.

[5] M. Bower, W. Jones, B. Vessels, C. Scoggins, R. Martin, Nutritional support with endoluminal stenting during neoadjuvant therapy for esophageal malignancy, Ann. Surg. Oncol. 16 (11) (2009) 3161–3168.

[6] D.G. Adler, J. Fang, R. Wong, J. Wills, K. Hilden, Placement of polyflex stents in patients with locally advanced esophageal cancer is safe and improves dysphagia during neoadjuvant therapy, Gastrointest. Endosc. 70 (4) (2009) 614–619.

[7] A.A. Siddiqui, C. Glynn, D. Loren, Y. Kowalski, Self-expanding plastic esophageal stents versus jejunostomy tubes for the maintenance of nutrition during neoadjuvant chemoradiation therapy in patients with esophageal cancer: a retrospective study, Dis. Esophagus 22 (2009) 216–222.

[8] T.L. Lopes, M.A. Eloubeidi, A pilot study of fully covered self-expandable metal stents prior to neoadjuvant therapy for locally advanced esophageal cancer, Dis. Esophagus 23 (2010) 309–315.

[9] F.B. Langer, S.F. Schoppmann, G. Prager, F. Tomaselli, U. Pluschnig, M. Hejna, R. Schmid, J. Zacherl, Temporary placement of self-expanding oesophageal stents as bridging for neo-adjuvant therapy, Ann. Surg. Oncol. 17 (2010) 470–475.

[10] R.E. Brown, A.E. Abbas, S. Ellis, S. Williams, C.R. Scoggins, K.M. McMasters, R.C.G. Martin, A prospective phase II evaluation of esophageal stenting for neoadjuvant therapy for esophageal cancer: optimal performance and surgical safety, J. Am. Coll. Surg. 212 (4) (2011) 582–588.

[11] M.G.C. Pellen, S. Sabri, A. Razack, S.Q. Gilani, P.K. Jain, Safety and efficacy of self-expanding removable metal esophageal stents during neoadjuvant chemotherapy for resectable esophageal cancer, Dis. Esophagus 25 (2012) 48–53.

[12] E.A. Griffiths, C.J. Gregory, K.G. Pursnani, J.B. Ward, R.C. Stockwell, The use of biodegradable (SX-ELLA) oesophageal stents to treat dysphagia due to benign and malignant esophageal disease, Surg. Endosc. 26 (2012) 2367–2375.

[13] M. Krokidis, C. Burke, S. Spiliopoulos, P. Gkoutzios, O. Hynes, I. Ahmed, R. Dourado, T. Sabharwal, R. Mason, A. Adam, The use of biodegradable stents in malignant oesophageal strictures for the treatment of dysphagia before neoadjuvant treatment or radical radiotherapy: a feasibility study, Cardiovac Interv. Radiol. 36 (2013) 1047–1054.

[14] R.C.G. Martin, R.M. Cannon, R.E. Brown, S.F. Ellis, S. Williams, C.R. Scoggins, A.E. Abbas, Evaluation of quality of life following placement of self-expanding plastic stents as a bridge to surgery in patients receiving neoadjuvant therapy for esophageal cancer, Oncologist 19 (2014) 259–265.

[15] A.A. Siddiqui, A. Sarkar, S. Beltz, J. Lewis, D. Loren, T. Kowalski, J. Fang, K. Hilden, D.G. Adler, Placement of fully covered self-expandable metal stents in patients with locally advanced esophageal cancer before neoadjuvant therapy, Gastrointest. Endosc. 76 (1) (2012) 44–51.