BJR

https://doi.org/10.1259/bjr.20170935

Received: 05 December 2017 | Revised: 22 May 2018 | Accepted: 04 June 2018

Cite this article as:
Kaltsidis H, Mansoor W, Park J-H, Song H-Y, Edwards DW, Laasch H-U. Oesophageal stenting: Status quo and future challenges. *Br J Radiol* 2018; **91**: 20170935.

REVIEW ARTICLE

Oesophageal stenting: Status quo and future challenges

[1]HARRY KALTSIDIS, PhD, FRCP, [2]WASAT MANSOOR, MBChB, MRCP, PhD, [3]JUNG-HOON PARK, PhD, [3]HO-YOUNG SONG, MD, [4,5]DEREK WILLIAM EDWARDS, and [4,5]HANS-ULRICH LAASCH, Dr med, MRCP, FRCR

[1]Department of Gastroenterology, Manchester University Hospitals NHS Foundation Trust, Manchester, UK
[2]Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK
[3]Department of Radiology and Research Institute of Radiology, Asan Medical Center & University of Ulsan College of Medicine, Seoul, Korea
[4]Department of Radiology, The Christie NHS Foundation Trust, Manchester, UK
[5]Department of Natural Sciences, University of Chester, Chester, UK

Address correspondence to: Prof. Hans-Ulrich Laasch
E-mail: *HUL@christie.nhs.uk*

ABSTRACT

Oesophageal stents are widely used for palliating dysphagia from malignant obstruction. They are also used with increasing frequency in the treatment of oesophageal perforation, as well as benign strictures from a variety of causes. Improved oncological treatments have led to prolonged survival of patients treated with palliative intent; as a consequence, stents need to function and last longer in order to avoid repeat procedures. There is also increasing need for meticulous procedure planning, careful selection of the device most appropriate for the individual patient and planned follow-up. Furthermore, as more patients are cured, there will be more issues with resultant long-term side-effects, such as recalcitrant strictures due to radiotherapy or anastomotic scarring, which will have to be addressed. Stent design needs to keep up with the progress of cancer treatment, in order to offer patients the best possible long-term result. This review article attempts to illustrate the changing realities in oesophageal stenting, differences in current stent designs and behaviour, as well as the pressing need to refine and modify devices in order to meet the new challenges.

INTRODUCTION

In the UK Registry of Oesophageal Stenting (ROST) median survival of patients was 90 days in 2004.[1] At that time stent insertion was the final palliative measure and further oncological treatment was a rare exception. In this database, a clear rise in late complications was observed, with 60% of patients surviving longer than 6 months requiring a further procedure for recurrent symptoms. Today many more patients receive additional treatments after stent insertion and the improved prognosis has a bearing on long-term performance of the *in situ* prostheses. This article aims to illustrate how the approach to oesophageal stenting needs to become more considered in the light of advancing cancer treatment.

IMPACT OF MODERN CHEMOTHERAPY

Recent evidence has shown that early intervention for symptomatic relief in patients with oesophago-gastric (OG) cancer improves survival and quality of life (QOL).[2] Currently, self-expanding metal stents are considered the standard of care for managing cancer-related dysphagia. However, new and improved chemotherapy regimens, the mainstay of treatment for advanced OG cancer, may in fact be capable of improving the symptoms of dysphagia by superior control of the disease locally. Stenting can then be reserved as an option at a later stage of the disease if symptoms recur. In neoadjuvant studies, improvement in dysphagia score following administration of chemotherapy has been reported as high as 70–96%, with concurrent improvement in QOL scores for those patients.[3] In the palliative setting, second-line docetaxel-based regimes showed similar improvement in dysphagia and general quality of life.[4]

Stent insertion to alleviate dysphagia is most commonly used in the context of advanced (Stage IV) disease, which unfortunately coincides with the initial presentation in most patients. The median survival in this group of patients has improved steadily since the early 1970s. Lately however, with the introduction of newer biological therapies, survival in this group is exceeding 12 months.[5] Patients presenting at earlier stages and who are amenable to potentially curative treatments are unfortunately quite likely to relapse and require palliative systemic and local treatments at a later stage.[6]

Until recently, identical standard chemotherapy regimens were considered for all patients with the same stage of disease irrespective of individual tumour characteristics. Most commonly, eligible patients with advanced OG cancer would receive combination chemotherapy regimens based on a platinum-5 fluoropyrimidine (5-FU) doublet.[5] This treatment is associated with significant toxicities, which would often affect the patient's fitness and performance status significantly and even render them unfit for either further treatments or interventions, such as palliative stenting that may have been required. This was exemplified in a recent large multi centre UK study, where only 14% of patients were fit enough to receive second-line therapy following standard therapy.[6] As a result, stenting was considered at an earlier stage in the patient's pathway and before chemotherapy with its toxicities limits interventional options. Improved insight into the importance of optimising QOL has brought the "one fits all" policy under scrutiny. With the emergence of less toxic biological agents and the concept of "Personalised Medicine", there is increasing interest in tailoring oncological treatment to the profile of individual cancers. Distinct molecular subtypes of OG cancer have been identified and these subtypes have allowed for patient stratification and trials of targeted therapies based on mutations and over expression of proteins identified within the subtypes.[7] This approach has undoubtedly resulted in better survival outcomes as well as better preservation of patients' performance status during these generally less toxic treatments. As a consequence, patients stay fitter for longer allowing more opportunity for further therapy and intervention. An early landmark example of this success was the ToGA trial, testing the Her-2 inhibitor Trastuzumab. This was the first targeted biological agent to be tested in OG cancers overexpressing the Her-2 receptor. This phase III multicentre trial demonstrated a median survival of 16 months for high Her-2 expressing patients receiving cisplatin/ 5-FU (CF) and trastuzumab compared to 11.8 months for patients only receiving CF.[8] This was the first time a regimen had managed to extend median survival for advanced stage OG patients beyond 12 months. Progress in improving survival has also been achieved in recent years with a number of successful second-line studies using both traditional chemotherapy agents such as the taxanes[4] and emerging biological agents such as the VEGF2 inhibitor, Ramucirumab.[9,10] Furthermore, there has been much interest in the immunotherapies targeting the check point inhibitors. Early results using Program Death Receptor Ligand-1 (PD-L1) antagonists demonstrate a promising response signal[11] and efficacy in second- and third-line patients.[12] The majority of first- and second-line studies are yet to be reported on.

Dysphagia continues to be an important burden which impacts significantly on QOL and reduces a patient's chance to utilise the treatments available. 40% of patients with OG cancers present with problematic dysphagia.[13] Whereas previously, early stenting was adopted as a universal strategy, this is no longer the case. On the other hand, as survival improves and treatments become less toxic, more and more repeat interventions will be required in the same patient to maintain the functionality of a stent. Previously, permanent stents were placed prior to commencing chemotherapy in the vast majority of patients, whereas now more options such as temporary and late stenting and biodegradable stents are available. Delaying stent intervention may become more common practice as more effective chemotherapy agents become available. However, it is also important to note that as patients go through the OG cancer pathway, the effects of dysphagia can become more prominent and the efficacy of the chemotherapeutic agents in trying to abrogate this problem become less effective. Delays in correcting dysphagia often cause rapid deterioration in body mass index and QOL. This then leads to poor tolerance for chemotherapy and increased incidence of dose delays and chemotherapy stoppages.[14]

A potential complication in patients with *in situ* stents receiving chemotherapy is increased probability of stent migration, since successful local response will reduce the tumour mass and the ability of the stricture to effectively anchor the prosthesis.[15] Stent migration in this setting may be entirely asymptomatic if a sizable oesophageal lumen has been restored and the stent resides in the stomach or passes without difficulty through the bowel without causing obstruction. However there is a small risk of impaction and the resultant risk of perforation and peritonitis, so a reasonable attempt at stent retrieval ought to be considered whenever the overall prognosis and patient-related factors advocate such an approach. Biodegradable stents have been relatively recently introduced to clinical practice and theoretically would be ideal in this clinical scenario (*i.e.* temporary stenting while awaiting the effect of chemotherapy). However more data are needed before they have an established place in the algorithm of management of these patients. As our understanding and experience with more efficacious forms of oncological treatments evolves, we will hopefully be in a position to select the most appropriate type of oesophageal stent for each individual patient and minimise the number of repeat interventions needed to control dysphagia.

STENT CONSTRUCTION AND BEHAVIOUR

A vast range of stents are now available for all parts of the GI tract: In 2017 there were approximately 35 versions of oesophageal stents available from 10 manufacturers in the UK. Although some of their characteristics have been charted, there is neither consistency in the terminology used to describe their specific features, nor consensus on what constitutes optimal behaviour.[16] This makes choosing the most suitable stent difficult.

Definitions

- Radial force: The force with which the stent expands from its compressed state
- Axial rigidity: The resistance of the stent to flexion
- Flexibility: The ability to bend
- Conformability: The ability to stay bent without trying to return to a straight configuration
- Stent shortening: The amount a stent contracts as it is expands on deployment to its nominal diameter
- Laser-cut stent: A construction where a solid tube is perforated to add flexibility
- Braided stent: The traditional woven stent, where wires only cross each other (also termed "crossing wire" or "S-type")
- Knitted stent: A woven stent, where wires hook around each other, allowing longitudinal compression (also termed "hooked wire" or "D-type")

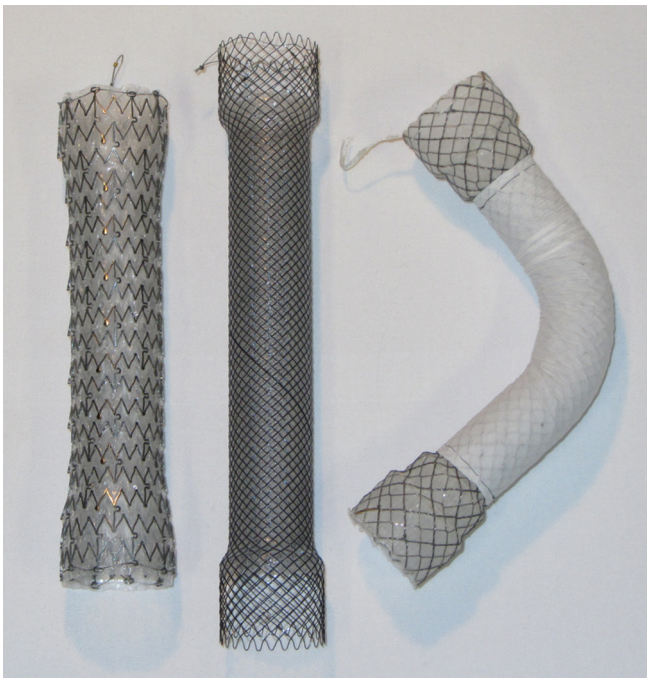
The ideal stent is delivered through a small access system, is easy to place accurately, expands reliably, causes no discomfort and does not displace or obstruct.

At present the majority of oesophageal stents are contained in an 18 Fr/6 mm delivery system. This is smaller than the 11–12 mm diameter of a therapeutic gastroscope. In contrast to enteral stents, these systems are too large for deployment even through a 3.7 mm working channel, hence deployment under endoscopic view can only be undertaken with the endoscope alongside the delivery system for visual inspection, making this a more invasive procedure than radiologic placement. Modified enteral stents are available for through-the-scope (TTS) delivery, but these lack some of the features of dedicated oesophageal stents. When stents are compressed into their delivery system, they elongate to a variable degree, which — depending on their size and construction - can be as much as twice the nominal size in large colonic stents. Conversely, on release the stent will shorten, as it expands. This ratio is usually quantified as the degree of shortening of the elongated stent. Example: A 12 cm stent, which measures 18 cm in the delivery system is 150% of nominal length, but shortens by 33% during full expansion. However if the stricture is very resilient, immediate stent expansion and shortening may not occur and the expected stent length may be exceeded by a large amount. Stent diameter should relate to the mid-portion, the "trunk" of the stent, usually between 18 and 20 mm. The ends or "heads" of the stent will be significantly larger than this, typically an additional 5–8 mm. This is to help anchor the stent and provide a seal against the oesophageal wall to avoid bypassing of food. The length of the stent is dictated by the length of the target lesion and the adjacent anatomy. For example a stricture of the very distal oesophagus may be better served by using a longer stent extending into the stomach than impacting the distal end in the curve of the gastro-pesophageal junction. In contrast a high tumour in the cervical oesophagus may only allow for minimal overstenting to avoid causing globus sensation. There is little evidence to guide on selecting the length of a stent. The stricture needs to be adequately covered, but excessive length reduces oesophageal peristalsis more. The stent should at least exceed the extent of the strictured segment by the length of the stent heads, which tend to be 15–25 mm long each.

Most stents are of a "dog bone shape", symmetrical to the mid-point of the stent and with perpendicular joints with the heads (Figure 1). Some stents have flared ends and some have additional features to reduce displacement ("migration").

Stent materials, notably polyester and polydioxanone are completely radiolucent, but the radiopacity of shape-memory alloys is low. Stents tend to have three groups of markers of a denser material, such as gold, to allow better identification on fluoroscopy. Sets of three to four markers are applied to both ends of the stent and in the middle. Unless an asymmetrical placement is required the latter can be centred on the middle of the stricture for stent release.

Figure 1. Different oesophageal stents (from left): Laser-cut EndoMaxx stent (Merit), Braided Evolution stent (Cook), Knitted Egis stent (S&G Biotech).

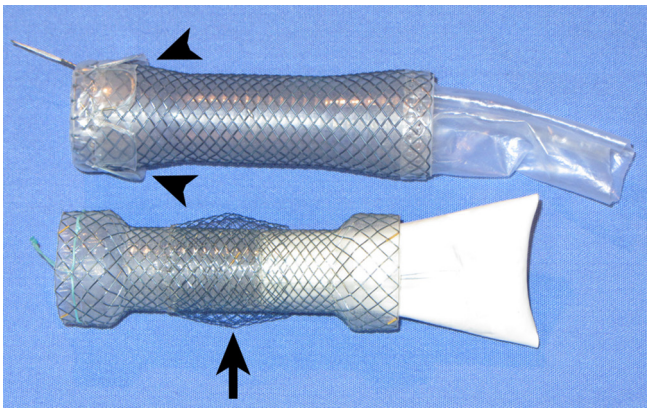


To help endoscopic visualisation delivery systems tend to have a yellow marker on the delivery system indicating the top of the stent.

While the conventional squamous cell carcinoma of the oesophagus is reducing in incidence due to regression in risk factors, the incidence of adenocarcinoma of the lower oesophagus and cardia is increasing and now accounts for around 70% of cases in the Western world. Stents placed with the lower end in the stomach have a 3–4 times greater risk of accidental displacement than stents in the oesophagus proper, and a number of approaches have been tried to address this.

Two stents have external anchors, either as a collar, which hooks over the edges of the stricture or an additional segment of bare stent to embed in the mucosa (Figure 2), whereas others work on advanced designs of the metal stent skeleton, in order to absorb peristaltic forces (Figure 3). The latter approach may be a better option for patients with oesophageal perforation which may require temporary or permanent occlusion, but who do not have an associated stricture. Examples are tracheo-oesophageal fistulae from external invasion by a bronchial carcinoma, benign perforation as a complication of oesophageal dilatation or leaks after bariatric surgery.[17] In the absence of a significant stricture a larger stent should be considered to achieve sufficient fixation against the oesophageal wall.[18] A straight rather than a dog-bone shaped profile is preferable to achieve complete apposition of the stent to the oesophageal wall throughout its length and there is a stent specifically licensed for this (Figure 4). A version of this is also available for emergency stenting of bleeding varices.[16]

Figure 2. Anti-migration stents: (top) Ella-HV plus (Ella-CS) with anchoring collar (arrowheads), (bottom) Niti-S double stent (TaeWoong Medical) with bare fixation segment (arrow).



If the perforation is from external malignancy, subsequent removal is usually not indicated and the ideal stent may be a partially covered colonic stent (Figure 5), although this application would be regarded as "off-label". Partially covered stents allow the uncovered ends to embed in the normal mucosa. This will stimulate hypertrophic overgranulation of the mucosa, which will fix the stent and preclude migration, but also make removal much more difficult.

Stent maintenance is becoming a core issue with improved patient survival and the ability to remove stents is likely to become more and more important.

Stent covers

A number of materials have been used to cover the bare stent skeleton so tumour growth cannot occlude it. Polyurethane has found to be not bio-resistant enough, with early degradation rates of 5–8% in an acidic environment.[15,19] External silicone membranes are vulnerable to mechanical damage during loading into the delivery system or deployment, but applied in a liquid form, silicone encases the wires individually and fills the gaps between them. It is inert and relatively stable, but fixes the wires against each other, reducing conformability. Expanded polytetrafluoroethylene (ePTFE) is less elastic, but when applied as an external membrane provides a more durable barrier against tumour ingrowth,[15,19] without affecting the movements of the stent interstices. A number of stents combine silicone as well ePTFE coverings of different parts of the stent.

Figure 3. Conformability of a knitted stent (Egis, S&G Biotech).

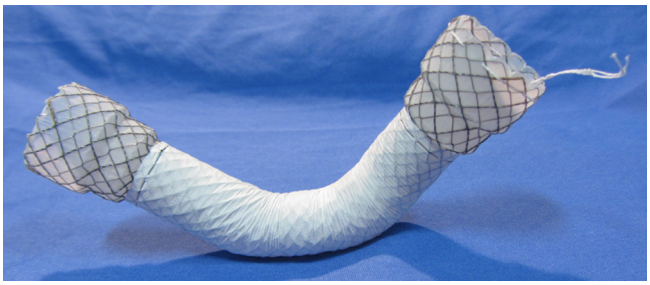
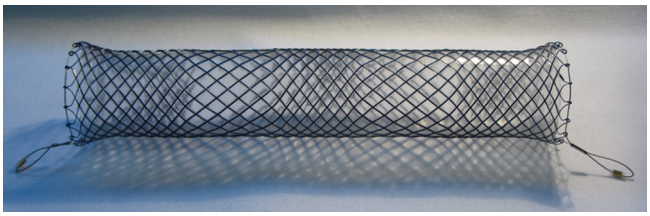


Figure 4. Ella Seal stent (Ella-CS) for benign perforations, also licensed for compressing variceal haemorrhage (Danis version). Note the varying braiding angle..



Biodegradable stents

At present there is only one biodegradable (BD) GI stent, specifically licensed only for benign oesophageal strictures (Figure 6). Off-label experience in other parts of the GI-tract has confirmed the reliable, timely disintegration of the polydioxanone filament in the bile duct, small and large bowel and in malignant conditions.[20–23]

Although currently BD stent placement in malignant strictures is off-licence, there is potentially a growing role for this in patients, who have a good life expectancy, while they are awaiting relief of dysphagia from further chemotherapy. The ideal algorithm however, still needs to be established.

Removable stents

Given the risks of long-term stent placement, easy retrievability of a stent should be regarded as an essential feature in reducing the rate of potential late complications. Stent removal has a high success rate if the prosthesis has not spontaneously migrated and most stent-related complications can be avoided by the timely removal when indicated.[15,24]

Figure 5. (Straight) Partially covered, double knitted colonic stents; (left) Egis (S&G Biotech); (right) ComVi (Taewoong Medical).

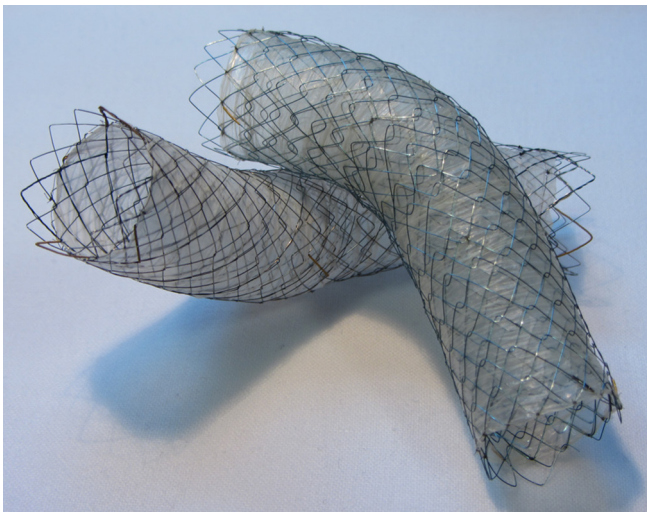
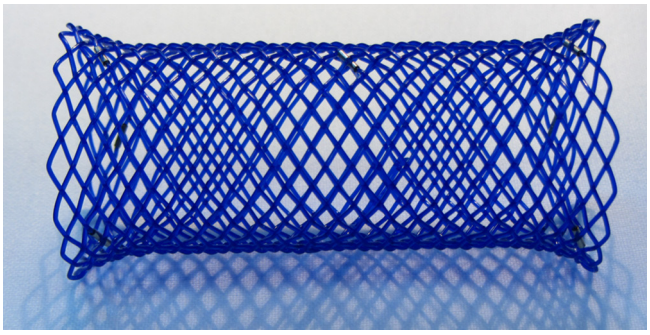


Figure 6. Biodegradable Ella-SX BD oesophageal stent (Ella-CS).



A relatively new concept is temporary stenting in potentially curable patients, who undergo neoadjuvant treatment. Initial studies have shown encouraging results in specialist centres, avoiding the need for enteral feeding in patients with limiting dysphagia.

For patients who have a poor prognosis, *e.g.* less than 3 months, the option of removing the stent is not of major importance. Increasingly, however, patients are outliving their primary stent, causing recurrence of symptoms. This is either because of tumour overgrowth, perishing of the stent cover allowing tumour ingrowth, stent fracture or stent migration.

Tumour overgrowing the stent an end is often associated with failed local control of the tumour and overall unfavourable prognosis; further stent insertion is usually appropriate and easy in this setting.

Stent failure is an emerging problem, either reflecting disruption of the covering membrane or fracture of the wire skeleton (Figure 7). Nitinol fracture is likely to be a consequence of metal corrosion from continued exposure to gastric acid, but clinical and laboratory data are awaited.

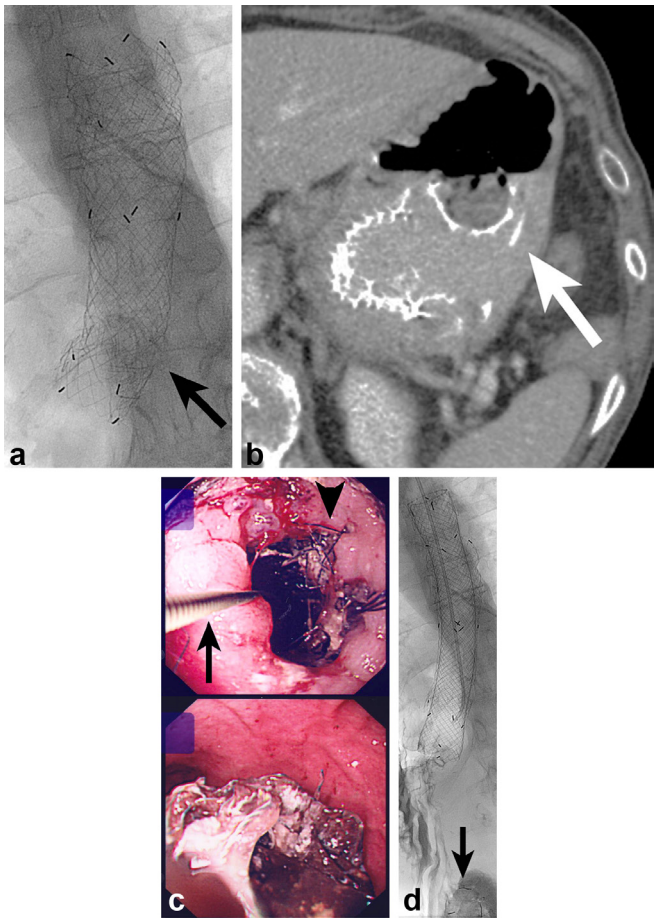
The ability to remove a failed stent is a bonus in a patient with recurrent dysphagia, as the clinical result of secondary stent insertion is dependent on stent expansion and conformability to the original anatomy.

Anti-reflux valves

Stents placed across the lower oesophageal sphincter precipitate free regurgitation of gastric content (Figure 8). Many studies have debated the importance of gastro-oesophageal reflux and the importance of reducing oesophageal pH,[25–29] but the essential issue is avoiding aspiration of gastric contents in a supine position. The fundus and cardia represent the lowest points of the stomach, when lying down. Consequently any gastric content will empty into the thoracic oesophagus when the patient has gone to bed, posing a high risk of aspiration and resulting pneumonia. This is not addressed by prescribing proton pump inhibitors.

Anti-reflux valves are not designed to just prevent the symptoms of acid reflux; they are supposed to reduce the rate of oesophageal

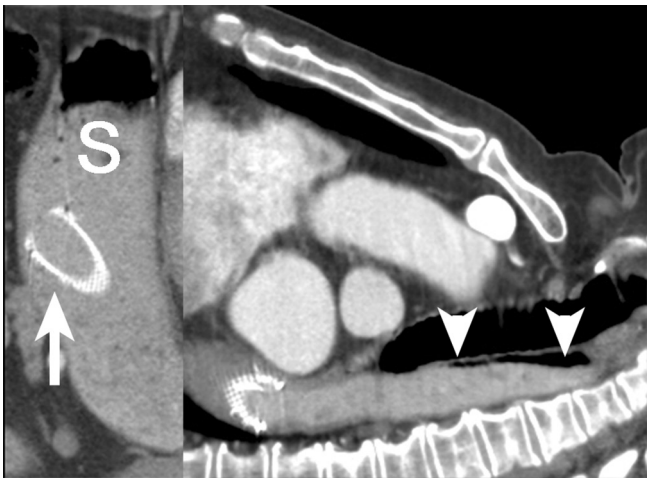
Figure 7. (A) Radiograph showing irregular widening of a stent with angulation of the distal head (arrow) indicating degradation of the nitinol. (B) Axial CT showing disintegration of the intragastric stent portion and dislocation of the distal head (arrow). (C) Endoscopy images show wire fractures (arrowhead), which precluded stent removal and a guide wire (arrow) inserted for secondary stenting (top). Inspection of the stomach after further stent insertion demonstrates the stent fragment in the stomach (bottom). (D) Fluoroscopic image showing the coaxial Ella-HV rescue stent, as well as the distal fragment (arrow).



regurgitation of gastric content and the risk of aspiration pneumonia and have been shown to be cost-effective.[30] Most designs are of a "wind-sock" construction, which collapses with the increase in gastric pressure (Figure 9). Secondary insertion of valved stents and "retro-fit" valves has been shown to reduce patients' symptoms with debilitating heartburn and laryngo-pharyngeal reflux from open stents.[31,32]

Stent construction seems to have largely evolved around marketing opportunities rather than scientific evidence and it is precisely the application of scientific outcomes combined with better understanding of the emerging needs of patients that needs to drive future device development.

Figure 8. Montage of 2 sagittal CT reconstructions acquired in a supine position showing the stomach content (S) emptying through the distal end of an open stent (arrow) freely into the upper oesophagus (arrowheads).



CURRENT CHALLENGES

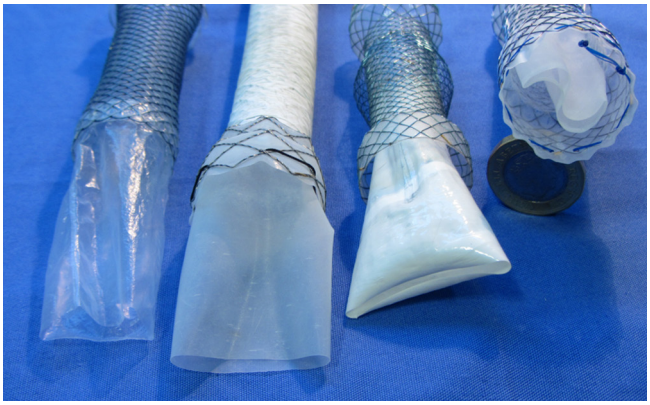
Migration

Oesophageal stent migration is a common occurrence and can be classified into four patterns, depending on the final position of the stent.[24] An understanding of these mechanisms is important for successful management. Risk factors for migration are stent placement across the cardia, longer patient survival and further oncological therapy.

In the setting of palliative stenting for malignant oesophageal obstruction the frequency of stent migration ranges in different series from 0 to 40 per cent.[33–35] Migration is 3–4 times more likely to occur if the stent crosses the gastro-oesophageal junction (GOJ). Adenocarcinoma of the lower oesophagus and cardia is now by far the commonest variant and in the UK the average migration of stents placed across the cardia was 16.7% in 2004.[1]

Approximately every other oesophageal cancer diagnosed is at an advanced stage, with the only therapeutic interventions feasible being palliative chemotherapy and stenting aiming to relieve dysphagia.[36] Stents are also increasingly used for management of benign conditions such as perforations, fistulae and non-malignant strictures (peptic, radiation-induced, caustic, anastomotic, etc.). In a recent retrospective study, migration was noted in 36% of patients in the benign group and was identified as the most important factor in limiting the therapeutic efficacy of this intervention.[37] Partially covered and uncovered SEMS (UC-SEMS) migrate less, due to inflammatory reaction and formation of granulation tissue within the uncovered part of the mesh, which effectively anchors the stent. As a consequence such stents should be considered as permanent and—as a principle—must be avoided for temporary stenting in benign disease. Should removal of an uncovered stent become necessary at a later date this requires challenging manoeuvres,[38,39] which carry the risk of perforation and may well fail.

Figure 9. Different types of valved oesophageal stents (from left): Ella HV plus (Ella-CS), Egis (S&G Biotech), Niti-S (Taewoong Medical), Hanaro (MI Tech).



Besides choosing a stent with specific anti-migration properties, there are several strategies to reduce the risk of migration. The following are some important points to be considered by prior to placing a stent and in order to minimise the risk of migration:

- The underlying pathology must be clearly defined. If it is cancer, the prognosis and expected survival needs to be discussed with the oncology team. *It is far better to defer a planned procedure if this information is unavailable then to proceed on the basis of inaccurate information.* If a patient is treated with palliative intent and the survival expectancy is short then a partially covered SEMS may be a sensible choice, due to the markedly reduced risk of migration; the issues regarding removability may be irrelevant in this setting.
- The vast majority of stents migrate distally, due to the intrinsic peristalsis of the oesophageal musculature; "balancing" a stent in a way that the proximal end is at least a long or slightly longer than the distal may reduce the risk of migration. The exception is a stent with a fixation system at the proximal end, which engages the top of the stricture.
- In very short malignant strictures, strictures of the GOJ or when stents are used for indications without stricture (*e.g.* perforation, fistula), the risk of spontaneous migration is very high; in such situations the use of a partially covered stent should be considered at the index intervention. The obvious concern is, of course, removability of a stent used for a benign indication. Techniques for removing partially covered stents are discussed below.
- For most patients with a distally migrated stent the priority is to relieve recurrent dysphagia which is usually achieved by placement of a new prosthesis across the stricture. The migrated stent is usually located in the relatively capacious gastric antrum and rarely causes significant symptoms. It may be difficult to remove it at the time of rescue stenting, as it may not be possible to pass an endoscope through the stricture. If the migrated stent needs to be retrieved, this can be done more safely at a later stage after the stricture has been re-dilated by the secondary stent.
- There are several endoscopic techniques for reducing migration of a standard fully covered stent. Anchoring the stent by mechanically fixing the upper rim of the stent to the oesophageal mucosa has been successful using endoclips,[40,41]

"over the-scope" clips (OTSC)[42] and an endoscopic suturing device.[43,44] The latter appears particularly useful in benign indications,[45] as the sutures are easier to remove than clips.

- Partially covered stents are not designed to be removed, hence the reluctance to use them in anything other than palliation of malignant dysphagia.[46] The endoscopic approach for removing such an embedded prosthesis involves some form of thermal ablation of the granulation tissue which has grown through and fixes the uncovered stent segment. This is usually achieved with the use of argon plasma coagulation (APC), which is a safer non-contact method of ablation with controlled depth of coagulation compared to monopolar diathermy. This approach is certainly time-consuming, technically demanding and associated with complications.[47] An alternative approach involves the deployment of a second—fully covered—stent within the lumen of the embedded stent (stent-in-stent technique).[48–50] The pressure exerted onto the granulation tissue causes ischaemia and necrosis. After 1–2 weeks first the inner and then the outer stentis removed. It is important to choose a secondary stent that matches the size and profile of the initial stent or has a marginally larger diameter. If the initial, partially covered stent does not have a purse string, the use of an endoscopic overtube should be considered to avoid injury to the upper oesophagus and cricopharyngeus.

In summary, stent migration is the most frequent complication of oesophageal stenting and a significant cause of morbidity and recurrent hospitalisation. Detailed knowledge of the patients' condition and prognosis, selection of the most appropriate prosthesis and a combined, interdisciplinary, collaborative approach is essential to ensure the best possible outcomes for patients. Ongoing research into development of stents with novel anti-migratory properties is needed to address these issues.

OTHER COMPLICATIONS OF OESOPHAGEAL STENT PLACEMENT

Oesophageal stenting is an invasive interventional procedure; however, it appears that the risk profile is relatively favourable compared to other interventions of similar nature. In one retrospective series, there were no procedure-related deaths over a 2-year period follow up and risk of re-intervention was 17%.[51] The UK registry however demonstrated a steady increase of re-intervention over time, reaching 60% at 6 months.[1] With the increasing survival of patients with advanced oesophageal cancer, more and more patients will present for re-intervention.

Recurrent dysphagia

Swallowing deteriorates again in approximately one third of patients because of food impaction, tumour ingrowth/overgrowth, inflammatory granulation tissue formation (usually at proximal end of *in situ* prosthesis), stent migration, stent fracture and unfavourable angulation/position of the fragments or a combination of the above.[52,53] Patients need good dietary advice. Spontaneous food bolus obstruction is mostly caused by soft, doughy bread, stringy vegetables or tough meat. However it may herald other problems such as beginning tumour occlusion stent collapse or fracture. Tumour in- and overgrowth can easily be overcome by co-axial placement of a further prosthesis covering the ingrowing tissue. Migrated stents with resulting recurrence of the malignant stricture as well as fractured stents can generally be treated in a similar manner by coaxial deployment of another stent. Wherever feasible the index stent should be removed or endoscopically repositioned, but in embedded stents this may be a 2–3 stage-long process. Careful consideration of the pros and cons for each individual patient is necessary to tailor the endoscopic intervention to each patient's needs and expectations. Factors such as prognosis/life expectancy, desired outcome and patient's preference are of paramount importance in making the right decisions.[53–55]

Fistula formation

Fully covered stents are used to treat oesophageal fistulae of either malignant or benign origin.[56]

However very infrequently, stents can themselves fistulate—usually into the respiratory tract. Tracheo-oesophageal fistula (TOF) formation as a consequence of stent placement is an uncommon but life-threatening complication and has been reported in 3–5% of cases. TOF is associated with stricture location and chemo-radiotherapy. The latter association is likely due to mucosal injury and ischaemia. Pressure necrosis is caused by high radial expansion forces of some stents and is more likely to happen at the ends of a rigid stent with a large head. Angulation of the surrounding anatomy may increase pressure, if the stent is too stiff to conform to it.[57] Surgical options are usually very limited and in the first instance deployment of a further fully-covered stent across the defect is an adequate treatment option, given the limited life expectancy for the vast majority of these patients.

Retrosternal pain

This is a common occurrence in up to 15% of patients post placement of a SEMS across a malignant stricture.[38] This is probably an underestimate and in reality over 50% of patients experience a degree of discomfort after the procedure, related to stent expansion and possibly local inflammatory response. Predisposing factors are large diameter stents, rigid stent construction and previous treatment, particularly radiotherapy.[58] Stent removal is rarely required to control the pain and use of opioid-based analgesia for up to 7–10 days is sufficient in most cases. In addition to that, short-term administration of a smooth muscle relaxant, such as hyoscine butyl bromide reduces oesophageal spasm and may help with pain control.

Airway compression

Oesophageal stents may exert pressure on the adjacent trachea or main bronchi. Unless these are encased by tumour, these are strong enough structures to be displaced rather than compressed. However if the tumour surrounds these or previous radiotherapy has caused a degree of tracheomalacia, pressure from the expanding stent may cause significant airway narrowing. If a planning CT indicates pre-existing airway narrowing and certainly if the patient has stridor, insertion of an airway stent should be considered prior to oesophageal stenting.

CONCLUSION

The context of oesophageal stent insertion is changing. Increasing importance needs to be placed on patients' life expectancy and further chemo- and hormone-receptor treatment, when selecting patients for stenting.

Insertion of a permanent metal stent is no longer the ideal palliation in all patients with malignant dysphagia and critical assessment of how to best meet the patient's nutritional needs is essential. Temporary measures such as short-term insertion of a naso-gastric tube, placement of a removable metal or a biodegradable stent and gastrostomy are likely to have an increasing role in managing patients with advanced GO cancer.

Careful assessment of treatment options at multi disciplinary meetings prior to referral and close patient review after stent insertion are becoming more important than ever. Patients need to be carefully counselled regarding the options and given direct access to the interventional team in the event of recurring dysphagia.

The limitations of this review reflect the development of stent technology by trial and error. Devices have not been developed on the basis of an understanding of the forces within the diseased oesophagus and its complex biochemical milieu, but by available materials and commercial marketing advantages. Most evidence is of low grade, based on case series or small comparative studies. When stents were very much a "last resort" device in patients with a very short life expectancy, this was not that important. But the increasing survival of patients with additional palliative treatment requires much better understanding of the factors affecting stent performance and a more critical appraisal of each patient.

ACKNOWLEDGMENT

HUL has acted as technical advisor to Ella-CS and S&G Biotech in the past.

REFERENCES

1. Laasch H-U, Lee S, Moss J, Roobottom C, Kinsman R, Walton P. *British Society of Interventional Radiology. ROST - Registry of Oesophageal Stenting, First Report 2004*. Henley-on-Thames: Dendrite Clinical Systems; 2004.
2. Temel JS, Greer JA, El-Jawahri A, Pirl WF, Park ER, Jackson VA, et al. Effects of early integrated palliative care in patients with lung and GI cancer: a randomized clinical trial. *J Clin Oncol* 2017; **35**: 834–41. doi: https://doi.org/10.1200/JCO.2016.70.5046
3. Cools-Lartigue J, Jones D, Spicer J, Zourikian T, Rousseau M, Eckert E, et al. Management of dysphagia in esophageal adenocarcinoma patients undergoing neoadjuvant chemotherapy: can invasive tube feeding be avoided? *Ann Surg Oncol* 2015; **22**: 1858–65. doi: https://doi.org/10.1245/s10434-014-4270-9
4. Ford HE, Marshall A, Bridgewater JA, Janowitz T, Coxon FY, Wadsley J, et al.COUGAR-02 Investigators Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. *Lancet Oncol* 2014; **15**: 78–86. doi: https://doi.org/10.1016/S1470-2045(13)70549-7
5. Waddell T, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D.European Society for Medical Oncology (ESMO)European Society of Surgical Oncology (ESSO)European Society of Radiotherapy and Oncology (ESTRO) Gastric cancer: ESMO-ESSO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2013; **24**(Suppl 6): vi57–vi63. doi: https://doi.org/10.1093/annonc/mdt344
6. Cunningham D, Starling N, Rao S, Iveson T, Nicolson M, Coxon F, et al.Upper Gastrointestinal Clinical Studies Group of the National Cancer Research Institute of the United Kingdom Capecitabine and oxaliplatin for advanced esophagogastric cancer. *N Engl J Med* 2008; **358**: 36–46. doi: https://doi.org/10.1056/NEJMoa073149
7. Bass AJ, Thorsson V, Shmulevich I, Reynolds SM, Miller M, Bernard B, et al. Comprehensive molecular characterization of gastric adenocarcinoma. *Nature* 2014; **513**: 202–9. doi: https://doi.org/10.1038/nature13480
8. Bang YJ, Van Cutsem E, Feyereislova A, Chung HC, Shen L, Sawaki A, et al.ToGA Trial Investigators Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. *Lancet* 2010; **376**: 687–97. doi: https://doi.org/10.1016/S0140-6736(10)61121-X
9. Fuchs CS, Tomasek J, Yong CJ, Dumitru F, Passalacqua R, Goswami C, et al.REGARD Trial Investigators Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet* 2014; **383**: 31–9. doi: https://doi.org/10.1016/S0140-6736(13)61719-5
10. Wilke H, Muro K, Van Cutsem E, Oh SC, Bodoky G, Shimada Y, et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol* 2014; **15**: 1224–35. doi: https://doi.org/10.1016/S1470-2045(14)70420-6
11. Muro K, Bang Y, Shankaran V, Geva R, Catenacci DVT, Gupta S, et al. LBA15A phase 1B study of pembrolizumab (PEMBRO; MK-3475) in patients (PTS) with advanced gastric cancer. *Annals of Oncology* 2014; **25**(suppl_4): 1–41. doi: https://doi.org/10.1093/annonc/mdu438.15
12. Boku N, Kang Y-K, Satoh T, Chao Y, Kato K, Chung HC, et al. 617OA Phase 3 Study of nivolumab (Nivo) in previously treated advanced gastric or gastroesophageal junction (G/GEJ) cancer: Updated results and subset analysis by PD-L1 expression (ATTRACTION-02. *Annals of Oncology* 2017; **28**(Suppl 5): v209–v68. doi: https://doi.org/10.1093/annonc/mdx369.001
13. Office for National Statistics. Cancer Statistics: Registrations Series MB1. Available from: http://www.statistics.gov.uk/statbase/Product.asp?vlnk=8843.
14. Tan BH, Brammer K, Randhawa N, Welch NT, Parsons SL, James EJ, et al. Sarcopenia is associated with toxicity in patients

undergoing neo-adjuvant chemotherapy for oesophago-gastric cancer. *Eur J Surg Oncol* 2015; **41**: 333–8. doi: https://doi.org/10.1016/j.ejso.2014.11.040
15. Park JH, Song HY, Kim JH, Jung HY, Kim JH, Kim SB, Lee H, et al. Polytetrafluoroethylene-covered retrievable expandable nitinol stents for malignant esophageal obstructions: factors influencing the outcome of 270 patients. *AJR Am J Roentgenol* 2012; **199**: 1380–6. doi: https://doi.org/10.2214/AJR.10.6306
16. Gamsjäger M, Heghedus A, Resch H, Bodlaj G. Use of the Ella Danis stent in esophageal bleeding due to severe reflux esophagitis. *Endoscopy* 2016; **48**(Suppl 1): E127. doi: https://doi.org/10.1055/s-0042-104652
17. Eisendrath P, Cremer M, Himpens J, Cadière GB, Le Moine O, Devière J. Endotherapy including temporary stenting of fistulas of the upper gastrointestinal tract after laparoscopic bariatric surgery. *Endoscopy* 2007; **39**: 625–30. doi: https://doi.org/10.1055/s-2007-966533
18. Siersema PD, Homs MY, Haringsma J, Tilanus HW, Kuipers EJ. Use of large-diameter metallic stents to seal traumatic nonmalignant perforations of the esophagus. *Gastrointest Endosc* 2003; **58**: 356–61. doi: https://doi.org/10.1067/S0016-5107(03)00008-7
19. Na HK, Song HY, Kim JH, Park JH, Kang MK, Lee J, et al. How to design the optimal self-expandable oesophageal metallic stents: 22 years of experience in 645 patients with malignant strictures. *Eur Radiol* 2013; **23**: 786–96. doi: https://doi.org/10.1007/s00330-012-2661-5
20. Petrtýl J, Brůha R, Horák L, Zádorová Z, Dosedel J, Laasch HU. Management of benign intrahepatic bile duct strictures: initial experience with polydioxanone biodegradable stents. *Endoscopy* 2010; **42**(Suppl 2): E89–E90. doi: https://doi.org/10.1055/s-0029-1243880
21. Stivaros SM, Williams LR, Senger C, Wilbraham L, Laasch HU. Woven polydioxanone biodegradable stents: a new treatment option for benign and malignant oesophageal strictures. *Eur Radiol* 2010; **20**: 1069–72. doi: https://doi.org/10.1007/s00330-009-1662-5
22. Rejchrt S, Kopacova M, Brozik J, Bures J. Biodegradable stents for the treatment of benign stenoses of the small and large intestines. *Endoscopy* 2011; **43**: 911–7. doi: https://doi.org/10.1055/s-0030-1256405
23. Janík V, Horák L, Hnaníček J, Málek J, Laasch HU. Biodegradable polydioxanone stents: a new option for therapy-resistant anastomotic strictures of the colon. *Eur Radiol* 2011; **21**: 1956–61. doi: https://doi.org/10.1007/s00330-011-2131-5
24. Park JH, Song HY, Shin JH, Cho YC, Kim JH, Kim SH, et al. Migration of retrievable expandable metallic stents inserted for malignant esophageal strictures: incidence, management, and prognostic factors in 332 patients. *AJR Am J Roentgenol* 2015; **204**: 1109–14. doi: https://doi.org/10.2214/AJR.14.13172
25. Dua KS, Kozarek R, Kim J, Evans J, Medda BK, Lang I, et al. Self-expanding metal esophageal stent with anti-reflux mechanism. *Gastrointest Endosc* 2001; **53**: 603–13. doi: https://doi.org/10.1067/mge.2001.114054
26. Laasch HU, Marriott A, Wilbraham L, Tunnah S, England RE, Martin DF. Effectiveness of open versus antireflux stents for palliation of distal esophageal carcinoma and prevention of symptomatic gastroesophageal reflux. *Radiology* 2002; **225**: 359–65. doi: https://doi.org/10.1148/radiol.2252011763
27. Homs MY, Wahab PJ, Kuipers EJ, Steyerberg EW, Grool TA, Haringsma J, et al. Esophageal stents with antireflux valve for tumors of the distal esophagus and gastric cardia: a randomized trial. *Gastrointest Endosc* 2004; **60**: 695–702. doi: https://doi.org/10.1016/S0016-5107(04)02047-4
28. Wenger U, Johnsson E, Arnelo U, Lundell L, Lagergren J. An antireflux stent versus conventional stents for palliation of distal esophageal or cardia cancer: a randomized clinical study. *Surg Endosc* 2006; **20**: 1675–80. doi: https://doi.org/10.1007/s00464-006-0088-2
29. Power C, Byrne PJ, Lim K, Ravi N, Moore J, Fitzgerald T, et al. Superiority of anti-reflux stent compared with conventional stents in the palliative management of patients with cancer of the lower esophagus and esophago-gastric junction: results of a randomized clinical trial. *Dis Esophagus* 2007; **20**: 466–70. doi: https://doi.org/10.1111/j.1442-2050.2007.00696.x
30. Nunes CC, Waechter FL, Sampaio JA, Pinto RD, Alvares-Da-Silva MR, Pereira-Lima L. Comparative post-operative study of prostheses, with and without an anti-reflux valve system, in the palliative treatment of esophageal carcinoma. *Hepatogastroenterology* 1999; **46**: 2859–64.
31. Hirdes MM, Vleggaar FP, Laasch HU, Siersema PD. Technical feasibility and safety of a new, implantable reflux control system to prevent gastroesophageal reflux in patients with stents placed through the lower esophageal sphincter (with video). *Gastrointest Endosc* 2012; **75**: 174–8. doi: https://doi.org/10.1016/j.gie.2011.08.037
32. Davies RP, Kew J, Byrne PD. Treatment of post-stent gastroesophageal reflux by anti-reflux Z-stent. *Cardiovasc Intervent Radiol* 2000; **23**: 487–9. doi: https://doi.org/10.1007/s002700010113
33. Battersby NJ, Bonney GK, Subar D, Talbot L, Decadt B, Lynch N. Outcomes following oesophageal stent insertion for palliation of malignant strictures: A large single centre series. *J Surg Oncol* 2012; **105**: 60–5. doi: https://doi.org/10.1002/jso.22059
34. Doosti-Irani A, Mansournia MA, Rahimi-Foroushani A, Haddad P, Holakouie-Naieni K. Complications of stent placement in patients with esophageal cancer: A systematic review and network meta-analysis. *PLoS One* 2017; **12**: e0184784. doi: https://doi.org/10.1371/journal.pone.0184784
35. Wagh MS, Forsmark CE, Chauhan S, Draganov PV. Efficacy and safety of a fully covered esophageal stent: a prospective study. *Gastrointest Endosc* 2012; **75**: 678–82. doi: https://doi.org/10.1016/j.gie.2011.10.006
36. Stahl M, Mariette C, Haustermans K, Cervantes A, Arnold D.ESMO Guidelines Working Group Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2013; **24**(Suppl 6): vi51–vi56. doi: https://doi.org/10.1093/annonc/mdt342
37. Bakken JC, Wong Kee Song LM, de Groen PC, Baron TH. Use of a fully covered self-expandable metal stent for the treatment of benign esophageal diseases. *Gastrointest Endosc* 2010; **72**: 712–20. doi: https://doi.org/10.1016/j.gie.2010.06.028
38. Wang MQ, Sze DY, Wang ZP, Wang ZQ, Gao YA, Dake MD. Delayed complications after esophageal stent placement for treatment of malignant esophageal obstructions and esophagorespiratory fistulas. *J Vasc Interv Radiol* 2001; **12**: 465–74. doi: https://doi.org/10.1016/S1051-0443(07)61886-7
39. Song HY, Lee DH, Seo TS, Kim SB, Jung HY, Kim JH, et al. Retrievable covered nitinol stents: experiences in 108 patients with malignant esophageal strictures. *J Vasc Interv Radiol* 2002; **13**: 285–92. doi: https://doi.org/10.1016/S1051-0443(07)61722-9
40. Kato H, Fukuchi M, Miyazaki T, Manda R, Faried A, Takita J, et al. Endoscopic clips prevent self-expandable metallic stent migration. *Hepatogastroenterology* 2007; **54**: 1388–90.
41. Vanbiervliet G, Filippi J, Karimdjee BS, Venissac N, Iannelli A, Rahili A, et al. The role of clips in preventing migration of fully covered metallic esophageal stents: a pilot comparative study. *Surg Endosc* 2012; **26**:

53–9. doi: https://doi.org/10.1007/s00464-011-1827-6
42. Mudumbi S, Velazquez-Aviña J, Neumann H, Kyanam Kabir Baig KR, Mönkemüller K. Anchoring of self-expanding metal stents using the over-the-scope clip, and a technique for subsequent removal. *Endoscopy* 2014; **46**: 1106–9. doi: https://doi.org/10.1055/s-0034-1377916
43. Yang J, Siddiqui AA, Kowalski TE, Loren DE, Khalid A, Soomro A, et al. Esophageal stent fixation with endoscopic suturing device improves clinical outcomes and reduces complications in patients with locally advanced esophageal cancer prior to neoadjuvant therapy: a large multicenter experience. *Surg Endosc* 2017; **31**: 1414–9. doi: https://doi.org/10.1007/s00464-016-5131-3
44. Wright A, Chang A, Bedi AO, Wamsteker EJ, Elta G, Kwon RS, et al. Endoscopic suture fixation is associated with reduced migration of esophageal fully covered self-expandable metal stents (FCSEMS). *Surg Endosc* 2017; **31**: 3489–94. doi: https://doi.org/10.1007/s00464-016-5374-z
45. Ngamruengphong S, Sharaiha RZ, Sethi A, Siddiqui AA, DiMaio CJ, Gonzalez S, et al. Endoscopic suturing for the prevention of stent migration in benign upper gastrointestinal conditions: a comparative multicenter study. *Endoscopy* 2016; **48**: 802–8. doi: https://doi.org/10.1055/s-0042-108567
46. van Halsema EE, Wong Kee Song LM, Baron TH, Siersema PD, Vleggaar FP, Ginsberg GG, et al. Safety of endoscopic removal of self-expandable stents after treatment of benign esophageal diseases. *Gastrointest Endosc* 2013; **77**: 18–28. doi: https://doi.org/10.1016/j.gie.2012.09.001
47. Fiocca F, Cereatti F, Antypas P, Donatelli G. Argon plasma coagulation: a less-expensive alternative to the "stent-in-stent" technique for removal of embedded partially covered esophageal stents. *Gastrointest Endosc* 2016; **83**: 453. doi: https://doi.org/10.1016/j.gie.2015.08.067
48. Aiolfi A, Bona D, Ceriani C, Porro M, Bonavina L. Stent-in-stent, a safe and effective technique to remove fully embedded esophageal metal stents: case series and literature review. *Endosc Int Open* 2015; **3**: E296–E299. doi: https://doi.org/10.1055/s-0034-1391419
49. Hirdes MM, Siersema PD, Houben MH, Weusten BL, Vleggaar FP. Stent-in-stent technique for removal of embedded esophageal self-expanding metal stents. *Am J Gastroenterol* 2011; **106**: 286–93. doi: https://doi.org/10.1038/ajg.2010.394
50. Vasilikostas G, Sanmugalingam N, Khan O, Reddy M, Groves C, Wan A. 'Stent in a stent'-an alternative technique for removing partially covered stents following sleeve gastrectomy complications. *Obes Surg* 2014; **24**: 430–2. doi: https://doi.org/10.1007/s11695-013-1163-0
51. Schoppmann SF, Langer FB, Prager G, Zacherl J. Outcome and complications of long-term self-expanding esophageal stenting. *Dis Esophagus* 2013; **26**: 154–8. doi: https://doi.org/10.1111/j.1442-2050.2012.01337.x
52. Didden P, Spaander MC, Bruno MJ, Kuipers EJ. Esophageal stents in malignant and benign disorders. *Curr Gastroenterol Rep* 2013; **15**: 319. doi: https://doi.org/10.1007/s11894-013-0319-3
53. Didden P, Kuipers EJ, Bruno MJ, Spaander MC. Endoscopic removal of a broken self-expandable metal stent using the stent-in-stent technique. *Endoscopy* 2012; **44**(Suppl 2 UCTN): E232. doi: https://doi.org/10.1055/s-0032-1306795
54. Homs MY, Steyerberg EW, Kuipers EJ, van der Gaast A, Haringsma J, van Blankenstein M, et al. Causes and treatment of recurrent dysphagia after self-expanding metal stent placement for palliation of esophageal carcinoma. *Endoscopy* 2004; **36**: 880–6. doi: https://doi.org/10.1055/s-2004-825855
55. Homann N, Noftz MR, Klingenberg-Noftz RD, Ludwig D. Delayed complications after placement of self-expanding stents in malignant esophageal obstruction: treatment strategies and survival rate. *Dig Dis Sci* 2008; **53**: 334–40. doi: https://doi.org/10.1007/s10620-007-9862-9
56. Mullan D, Najran P, Shepherd D, Li A, Laasch H-U. Minimally invasive treatment strategies for tracheoesophageal fistulae. *Digestive Disease Interventions* 2018; **02**: 011–17.
57. Laasch HU, Nicholson DA, Kay CL, Attwood S, Bancewicz J. The clinical effectiveness of the Gianturco oesophageal stent in malignant oesophageal obstruction. *Clin Radiol* 1998; **53**: 666–72. doi: https://doi.org/10.1016/S0009-9260(98)80293-6
58. Verschuur EM, Steyerberg EW, Kuipers EJ, Siersema PD. Effect of stent size on complications and recurrent dysphagia in patients with esophageal or gastric cardia cancer. *Gastrointest Endosc* 2007; **65**: 592–601. doi: https://doi.org/10.1016/j.gie.2006.12.018