A practical guide to the management of dysphagia in patients with metastatic esophageal cancer

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> Abstract: In patients with esophageal cancer, dysphagia can be a distressing symptom, subsequently resulting in weight loss and malnutrition. While luminal obstruction is a common complication, the optimal management approach remains undefined. Given the high morbidity and mortality of esophagectomy and esophageal bypass, surgical palliation has long fallen out of favor. Instead, various other palliative approaches are available, all of which are relatively effective, but differ in regards to time to benefit, durability and toxicity. The available literature is relatively limited, and decisions regarding how to manage dysphagia, and when to appropriately employ these various therapies, are left to individual judgment. Using a tertiary center experience and a review of the current literature, we would typically recommend either systemic chemotherapy or palliative external beam radiotherapy (EBRT) as initial measures. The benefits of chemotherapy include the high likelihood of symptomatic improvement, avoidance of delays in systemic therapy, and minimal locoregional toxicity. Radiotherapy would similarly be an effective initial approach and may be best suited for patients with low volume (oligo-metastatic) disease. For patients who develop progressive dysphagia later in their disease course, radiotherapy or SEMS placement are the main therapy options. We recommend against "double palliation," in which patients receive two palliative therapies simultaneously. Overall, decisions regarding management of malignant dysphagia should be individualized to consider the severity of the obstruction, the need for systemic therapy, prior therapy received, and finally the patient's life expectancy and personal wishes.

Keywords: Chemotherapy; malignant dysphagia; metastatic esophageal cancer; palliation; radiotherapy

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Introduction

Dysphagia, as a consequence of luminal obstruction and invasion into the muscularis propria, is a distressing symptom commonly encountered in patients with esophageal cancer. Most patients subsequently suffer from weight loss and malnutrition. Complete, or near complete obstruction, is a frequent reason for hospitalization in this

patient population.

While luminal obstruction is a common complication of esophageal cancer, the optimal management approach remains undefined. Given the high morbidity and mortality of esophagectomy and esophageal bypass, surgical palliation has long fallen out of favor. Instead, various other palliative approaches are available, all of which are relatively effective, but differ in regards to time to benefit, durability and Page 2 of 9 Annals of Esophagus, 2018

Table 1 Summary & comparison of various treatments for malignant dysphagia

Treatment	Time to benefit	Durability of response	Toxicity/adverse effects	Recommendations/indications
SEMS	Immediate	Relatively durable	Pain (up to 60%)	Refractory dysphagia despite chemotherapy and or EBRT
			Stent migration (4–36%)	Patients with esophageal perforations or tracheoesophageal fistulae
			Stent occlusion	
			GERD	
			Globus sensation	
			Bleeding	
EBRT	Several weeks [2–6]	Relatively durable	Fatigue, nausea, esophagitis, bleeding, strictures, and fistula,	Can be first line depending on patient need
				Can be used for those who progress after initial chemotherapy
Brachytherapy	Several weeks [2–6]	Less durable than EBRT	Perforation, esophagitis with ulceration, strictures, and fistulae	Refractory dysphagia despite chemotherapy and EBRT
Chemotherapy	Several weeks [1–3]	Relatively durable	Minimal loco-regional toxicity	Recommended as first-line treatment
				Can be used as second-line in select patients
Endoscopic tissue ablation	Variable	Less durable (often require repeat procedures)	Varies, though generally well tolerated. Adverse effects may range from minor cutaneous reactions to bleeding or perforation	Rarely utilized
				Reserved for patients who have either failed, refused, or are unfit for chemotherapy and/or EBF

SEMS, self-expanding metallic stents; EBRT, external beam radiotherapy; GERD, gastroesophageal reflux disease.

toxicity (*Table 1*). The available literature is relatively limited, and decisions regarding how to manage dysphagia, and when to appropriately employ these various therapies, are left to individual judgment.

To minimize unnecessary procedures and complications, it is best to utilize a multidisciplinary approach. In this review, the various treatment options for malignant dysphagia will be discussed, including self-expanding metallic stents (SEMS), radiotherapy, chemotherapy, and endoscopic interventions. In addition, common therapeutic pitfalls will be explored and the author's recommendations on management will be described.

SEMS

Mechanical relief of dysphagia though the use of luminal stents is well described. Self-expanding plastic stents (SEPS) have been available for years, but their use has largely been replaced by that of SEMS, due in part to greater efficacy and lesser toxicity (1). SEMS placement is relatively easy, and can be performed in the outpatient setting. Most importantly, dysphagia relief is often immediate.

Stent placement, however, is not without complication. Esophageal stenting has been associated with pain, bleeding, migration, globus sensation, and increased gastroesophageal reflux disease (GERD). While the literature is variable, pain may be experienced in up to 60% of patients who undergo stent placement. Of note, XRT in addition to stent placement increases the risk of prolonged pain (2). Though temporary pain is easily managed with short courses of narcotic analgesia, persistent pain can be difficult to manage, thus significantly impacting the patient's quality of life (QOL).

Stent migration has been reported to occur in up to 40% of patients (3). Though migration events may be clinically asymptomatic and discovered only at the time of routine radiography, symptomatic migration is common and may be serious. Patients often report recurrent dysphagia or

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chest pain. In cases of proximal dislodgement, patients may also experience globus sensation. Management of migrated stents has been a controversial topic, with some authors recommending a conservative approach and others, endoscopic removal. While migration to the stomach should not be considered an emergency, it is important to note that migration into the small bowel may lead to obstruction and perforation. Therefore, the consensus remains that migrated stents should be repositioned or removed whenever possible. Stents that have migrated past the reach of an endoscope should be monitored with serial radiographs. Two studies noted the decrease in migration rate to 8-15% with the use of large-diameter stents (25-28 mm), however these stents were also associated with higher rates of complications (i.e., hemorrhage, perforation, and fistulae). External fixation may also reduce the risk of stent migration (3).

Stent occlusion is another complication, and may occur from food impaction or tumor ingrowth/overgrowth. In regards to food impaction, patients are often recommended to begin with liquids and gradually build up to a soft diet following stent placement, as the stent can take up to 1–2 days to fully expand. Certain foods should be avoided, including bread, gristly meat, pithy fruit, and raw vegetables. Patients are encouraged to take frequent sips of warm or carbonated beverages between and during meals to help keep the stent clear (1).

To minimize tumor ingrowth, stents are now completely or partially covered with synthetic materials such as polyurethane or silicone. In distinguishing the two types of covered SEMS, partially covered stents typically have uncovered ends which allow some tissue ingrowth to minimize migration. Completely covered stents are therefore more likely to migrate, but can be more easily removed in the event the stent is poorly tolerated (2).

Care must also be given when placing stents across large tumors located in proximity to the trachea or at the gastroesophageal junction (GEJ). With the former, stent expansion may result in airway compression. In the latter, the stent may abut the gastric wall and occasionally become obstructed. Furthermore, stents placed across the GEJ have been noted to have a higher risk of migration and GERD. Stents with anti-reflux valves have been investigated and are available, however, it remains unclear if these devices are truly beneficial. Prior studies have been limited by small power and lack of an objective scale to measure reflux symptoms (4). At present, reflux is best managed with acid suppression and mechanical/lifestyle modifications (upright

positioning with meals and 30-degree head elevation with sleep).

One area of extreme value for SEMS is in managing esophageal perforations or tracheoesophageal fistulae. While the prognosis of these patients typically remains poor, rapid deterioration and death can be avoided. In some circumstance, patients will recover sufficiently to allow subsequent cancer directed therapy.

External beam radiotherapy (EBRT)

EBRT is frequently employed in the management of malignant dysphagia for patients with metastatic disease. EBRT is broadly available and improves symptoms in most patients. Furthermore, the response to RT is relatively durable with few delayed toxicities. Murray et al. reported the outcomes of palliative EBRT in 148 patients with unresectable esophageal cancer. In this retrospective analysis, the majority of patients received a cumulative dose of 20 Gy given over 5 fractions. Overall, 75% of patients obtained symptomatic improvement. Subsequent esophageal stenting or repeat radiotherapy was required in 26% and 3% of patients, respectively. Treatment was also relatively durable (median time to stent/retreatment was 4.9 months) and generally well tolerated (5).

It is important to recognize that the response to EBRT may be delayed, with full symptomatic benefit not becoming apparent for several weeks. In some patients, dysphagia may temporarily worsen and transient odynophagia may develop secondary to radiotherapy esophagitis. For patients who have severe dysphagia, an alternative route to provide nutrition and hydration may be required for a brief period.

Concurrent chemo-radiotherapy

Some clinicians advocate the use of definitive treatment doses (≥50.4 Gy) of radiotherapy with concurrent administration of chemotherapy (CRT) (6,7). The rationale for this approach is improved locoregional control with more durable palliation of dysphagia than would be expected with lesser doses of EBRT alone. It remains unclear, however, if this treatment approach is appropriate. For example, Penniment *et al.* reported the results of a randomized phase III trial comparing palliative RT to concurrent CRT in patients with advanced esophageal cancer. In this study, 220 patients received either palliative RT [35 Gy in 15 fractions (n=115) or 30 Gy in 10 fractions (n=105)] or CRT with cisplatin and 5-FU (n=111). There

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was no significant difference in dysphagia relief between the two groups (68% RT, 74% CRT, P=0.343). Furthermore, CRT was more toxic, and median overall survival and QOL were not improved with more aggressive therapy (8).

While definitive chemoradiotherapy (dCRT) is a standard of care for locally advanced/non-metastatic disease, in which long term survival is the principle treatment goal, the use of this treatment regimen in the metastatic setting should be discouraged, in the opinion of the authors. Given the other therapeutic options to palliate dysphagia and the relatively poor prognosis of patients with metastatic disease, palliative EBRT alone is usually sufficient to achieve symptomatic improvement without impairing QOL.

Esophageal brachytherapy (BT)

Esophageal BT is another relatively effective option, which has been well described in the literature. Esophageal BT enables the endoscopic delivery of high doses of RT to the esophageal wall while avoiding surrounding structures. The dose and schedule of therapy may vary based on practice patterns, with patients typically receiving anywhere between 7–28 Gy in fractions of 5–7 Gy (American Brachytherapy Society guidelines). Similar to EBRT, the benefit to this treatment may be delayed (9,10).

It remains unclear, however, how best to incorporate this treatment modality. BT has both been compared to and combined with several other available therapies. For example, Homs et al. reported the results of a small trial in which 202 patients with esophageal cancer and malignant dysphagia were randomized to stent placement or a single dose of 12 Gy BT. In this study, stent placement resulted in more rapid palliation of dysphagia. Long term dysphagia control, however, was more often achieved in patients who received BT. BT was also associated with slightly less complications and better QOL (11). Similar results were also reported by Bergquist et al., in which BT (3 fractions of 21 Gy) was compared to placement of a SEMS, and by Hanna et al. (12,13). Again, stent placement resulted in more immediate benefit, but outcomes overall were similar, and QOL remained superior in the BT group. Other authors suggest that a combination of EBRT and stent placement may be more advantageous then either modality alone in select patients, potentially exploiting the immediate relief of dysphagia with SEMS and diminishing late tumor ingrowth and overgrowth with BT (14).

It should be noted that EBRT is more effective than BT alone. Welsch et al. reported the results of a

retrospective analysis comparing BT, EBRT, and EBRT + BT. In this study, the 6-month dysphagia-free survival was approximately 90% in both the EBRT and EBRT + BT arms, compared to only 37% in patients who were treated with BT alone. Furthermore, only 7–8% of patients treated with EBRT +/- BT experienced worsening dysphagia, compared to 35% in the BT alone arm (15).

The ability to offer BT is limited to relatively few centers. Furthermore, the complications of esophageal BT can be significant, including esophagitis with ulceration, stricture, perforation and fistulae. The incidence of these toxicities is variable, and depends on the clinical context (tumor location, subsequent therapy, etc.). In the opinion of the authors, BT should be reserved for the few patients who have dysphagia despite chemotherapy and EBRT. The decision to employ BT over placement of an esophageal SEMS would then depend on local expertise, life expectancy, severity of dysphagia, need for immediate improvement, anatomic factors, and patient preference. BT is more likely to be beneficial in patients for whom delayed benefit is reasonable, and may therefore be preferred over SEMS in patients who have mild to moderate symptoms and a life expectancy expected to exceed 3 months.

Chemotherapy

A common misconception is that dysphagia must be addressed with a local therapy or procedure prior to initiation of chemotherapy in patients with metastatic disease. The assumption being chemotherapy-associated nausea and anorexia will exacerbate the patient's underlying nutritional deficit, and therefore be detrimental. While not readily appreciated, chemotherapy often provides symptomatic improvement with relief of dysphagia in the first few weeks of treatment.

We have previously reported, for example, the results of a single institution phase II trial of induction chemotherapy followed by surgical resection and post-operative adjuvant chemoradiotherapy in patients with locally advanced esophageal adenocarcinoma. In this trial, patients with clinical evidence for primary tumor extension beyond the muscularis (cT3 disease) or regional nodal metastases (N positive disease) were treated with 3 cycles of epirubicin, oxaliplatin, and fluorouracil (EOF) chemotherapy prior to surgical resection. Overall, ~80% of patients experienced resolution of dysphagia by the time of surgery. While not specifically reported, clinical improvement was often noted during the first cycle of therapy (16). In our own experience,

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the same phenomenon is noted in patients with metastatic disease. Chemotherapy often provides rapid relief of malignant dysphagia. This benefit mirrors systemic disease control, and therefore appears to last for several months.

Similar results were reported by Cools-Lartigue *et al.* They analyzed clinical outcomes and nutritional parameters of patients receiving neo-adjuvant chemotherapy for locally advanced esophageal cancer identified through a prospective database. Overall, 130 patients received preoperative chemotherapy between 2007–2012. A total of 78 patients reported severe dysphagia at presentation, of which 77 (96%) obtained improvement with chemotherapy. This improvement was often noted prior to the second cycle of chemotherapy. Only one patient required an esophageal stent and no patients required an enteral feeding tube. QOL was improved and there was no detrimental effect on nutritional parameters (17).

One obvious, but unique, feature of chemotherapy which distinguishes this modality from the others mentioned in this paper is the lack of esophageal toxicity. While the side effects of chemotherapy are well described, there is no significant risk of short or long term local toxicity. Furthermore, there is no delay in managing metastatic disease when chemotherapy is initially employed. In our experience, chemotherapy is effective even in patients who have complete luminal obstruction.

It must be noted, however, that the few studies which compare chemotherapy with other maneuvers to relieve dysphagia in patients with metastatic disease generally favor either SEMS or EBRT. For example, in one such study, Touchefeu *et al.* reported the results of a retrospective analysis comparing the effects of chemotherapy to that of SEMS for the management of severe dysphagia in inoperable esophageal or GEJ cancer. Forty-two patients received chemotherapy and twenty-nine underwent SEMS placement. After 4 weeks, dysphagia scores improved more frequently with SEMS than chemotherapy (93% *vs.* 67%, P=0.01) (18). Of the patients receiving chemotherapy, 18 patients (42.9%) required a SEMS to be secondarily placed. Likewise, 33.3% of patients who previously had a SEMS placed required a second stent (18).

In another study, Cwikiel *et al.* compared the results of radiotherapy, chemotherapy, and esophageal stent treatment. The palliative effects of chemotherapy and radiotherapy were evaluated retrospectively, whereas the effects of stent treatment were evaluated prospectively. Seventy eight of 140 patients (56%) who were treated with radiotherapy, 31 of 63 patients (49%) treated with

chemotherapy, and 53 of 66 (81%) treated with SEMS were free of dysphagia at the time of treatment completion (19).

Despite the possibility that chemotherapy may not be as effective at relieving dysphagia when compared to SEMS or EBRT, the authors still consider initial chemotherapy to be a reasonable treatment option for most patients with metastatic disease. This recommendation is based largely on the lack of local toxicity, the relatively rapid relief of dysphagia, and the avoidance of delays in treating metastatic disease.

Endoscopic esophageal dilation

Esophageal dilation is a technique used to achieve immediate relief of dysphagia in patients with both malignant and benign strictures. Similar to other endoscopic techniques, however, several repeat procedures are often required. The benefits are variable, but often less successful for malignant disease. Esophageal perforation is the most commonly reported complication of the procedure with reported rates estimated at 0.1–1%. Factors that place patients at higher risk for complications include the presence of a large hiatal hernia, a tortuous esophagus or a complex stricture. Though guidewire assistance and fluoroscopic control are recommended to reduce the associated risks, dilation is rarely performed due to limited efficacy and the concern for potential perforation (20,21).

Endoscopic tissue ablation

Relief of dysphagia can be obtained through various other endoluminal ablative therapies, including argon plasma coagulation (APC), neodymium doped:yttrium aluminum garnet (Nd:YAG) laser therapy, and photodynamic therapy (PDT). These approaches potentially allow recanalization of the esophagus through tissue destruction and subsequent tumor debulking. The reported literature is relatively limited, making it difficult to accurately describe the effectiveness of these techniques, distinguish which techniques are superior, and determine how best to employ these therapies. While these therapies provide relief of dysphagia in many patients, these techniques are rarely performed anymore secondary to their transient effects and the frequent necessity for repeated endoscopic procedures.

APC is a noncontact thermal ablative technique in which an electrical current is passed through argon gas that has been dispersed over the lesion. This results in tissue damage, with relatively limited tissue penetration Page 6 of 9 Annals of Esophagus, 2018

(2–4 mm) (22). Rupinski *et al.* reported the results of a small randomized trial in which 93 patients with malignant dysphagia and no prior therapy were treated with APC, APC + BT, or APC + PDT. In this study, 27 patients received APC alone. These patients were treated with APC every 2–4 days until improvement in dysphagia was demonstrated. Overall, patients underwent an average of 5.1 endoscopic treatments in the APC only arm, with a median dysphagia-free period of only 35 days. Of note, relief of dysphagia was more durable in the combination arms (APC + BT or APC + PDT). There was very little reported toxicity overall in the patients treated with APC. We cannot say whether the results of APC + BT or APC + PDT are better than could be achieved with BT or PDT alone (23).

Laser therapies have several applications in medicine, with Nd:YAG laser therapy being the most commonly employed. Gevers et al. reported the results of a retrospective review of patients with malignant dysphagia treated with plastic stents, SEMS, and laser therapy over 10 years at a single institution. Laser therapy was administered to 70 patients, most of whom had received some prior therapy, including chemotherapy/radiotherapy (10%) or dilation (54%). In this report, laser therapy was administered every 2-4 days until recanalization was achieved, and potentially repeated every 3-4 months, if required. Initial improvement in dysphagia was reported in 83% of patients after a mean of 2.5 sessions (range 1–7), and patients went on to have an average of 4.3 maintenance sessions. The palliative benefit lasted approximately 14 weeks, with 3 major complications (2 perforations, 1 major bleeding event). Similar symptomatic benefit was obtained in the patients treated with esophageal stents, although the complication rates were significantly higher than what was observed in patients treated with laser therapy. The authors concluded that laser therapy was as effective as stent placement, but with less complications. It should be noted, however, that the patients treated with stents had received more prior therapy, including prior laser treatment (24).

PDT is achieved with the endoscopic application of light therapy after the administration of a photosensitizing agent. The photosensitizer tends to accumulate in tumor tissues and generates reactive oxygen species once activated, resulting in tissue injury and necrosis (22). Lightdale *et al.* reported the results of a multicenter randomized trial in which 236 patients with malignant dysphagia were treated with either PDT or laser therapy with Nd:YAG. In this report, both therapies appeared similarly effective,

although PDT provided a higher objective tumor response at 1 month (32% vs. 20%, P<0.05), and more complete responses (9 vs. 2 patients). While minor toxicities including cutaneous reactions were more common in the PDT-treated patients, serious toxicity was more often seen with Nd:YAG. Esophageal perforation, for example, was observed more frequently with Nd:YAG (1% vs. 7%, P<0.05). The authors concluded that PDT was the preferred ablative therapy (25).

It must be emphasized that the efficacy and toxicity of any therapy will depend on several factors, notably prior therapy received. This makes extrapolation across disease settings difficult at best. The literature that informs us is also largely comprised of older retrospective studies and small randomized trials. Given the limitations of the data, evolution of technology with various devices and protocols of administration, as well as operator dependence, it is difficult to adequately define the value of these therapies and understand how best and when to employ them.

In our opinion, endoscopic ablative therapies have a relatively limited and historical role in the management of malignant dysphagia. These techniques, when employed, should be reserved for patients who have either failed, refused, or are unfit for chemotherapy and/or EBRT. The choice of an ablative therapy as opposed to BT or placement of a SEMS would be based on available expertise and individual clinical factors.

Supplemental nutrition

Significant dysphagia with subsequent weight loss and nutritional compromise is commonly encountered in esophageal cancer. Long-term artificial supplemental nutrition, however, is rarely required or appropriate. While nutritional support has been shown to increase fat mass, it has limited impact on patient survival, nutritional parameters, QOL, or sense of well-being (26). In addition, artificial nutrition may decrease QOL by exacerbating symptoms such as nausea and diarrhea. Also, artificial nutrition may increase the burden of medical devices and introduce complications including dislodgement and tube occlusion, as well as discomfort and infection at the site of entry. Given the various methods to palliate luminal obstruction, therefore, we generally discourage long-term placement of feeding tubes in patients with metastatic disease. Several groups including the American Society of Parenteral Nutrition, provide the same recommendation (27,28). Educating patients and family members on the natural course of terminal disease and frequent lack of Annals of Esophagus, 2018 Page 7 of 9

discomfort experienced from minimal food intake secondary to cancer related anorexia is required.

Occasionally, however, temporary enteral support is reasonable. For patients who have severe dysphagia and are unable to maintain hydration or meet minimal caloric requirements, but who are otherwise fit and are anticipated to obtain dysphagia relief from planned therapy, temporary nutritional support is useful. In our own practice, patients occasionally present with or develop complete obstruction prior to initiation of radiotherapy or chemotherapy. For these patients, we offer temporary nutritional support with an endoscopically placed nasoenteric tube. Once patients exhibit a clinical response to therapy, the tube is removed. Typically, this response can be obtained in just a few weeks.

Nasoenteric feeding tubes are often undesirable for patients for cosmetic reasons, may easily become dislodged, and given their thin caliber, may become occluded. It is for these reasons that many physicians consider total parenteral nutrition (TPN) or a SEMS to be preferable alternatives. In our opinion, however, nasoenteric support is superior to TPN as it is more physiologic, less expensive, and easier to employ over a short time frame. We prefer nasoenteric support over SEMS placement for patients who have not received prior therapy, as nutritional support is often transient in this setting, the feeding tubes are easily removed, and we feel the side effect profile for a nasoenteric feeding tube is superior to that of a SEMS. In our practice we reserve the use of SEMS until later in the disease course, when the remaining therapy options are not expected to provide relief of dysphagia.

When placing a nasoenteric feeding tube, one issue that arises is whether post-pyloric or pre-pyloric placement is preferential. The literature does not provide definitive evidence in favor of either location, but several factors should be considered. Pre-pyloric placement is easier to accomplish, is more physiologic, and allows administration of bolus feeding which is more convenient for patients. However, cancers of the GEJ, or those tumors which extend deeply into the stomach, may be associated with impaired gastric motility. For these patients, delivery of adequate nutrition may be impaired with pre-pyloric placement. Also, aspiration risk may be higher for patients with impaired esophageal motility from advanced cancer, and as a result of prior therapy, including EBRT. Therefore, at our institution, post-pyloric placement is preferred. These tubes are placed endoscopically, however, requiring operator expertise.

Ultimately, local experience and practice patterns

will determine care. We would suggest that temporary nutritional support is appropriate only in patients with a relatively favorable prognosis, whereas the same maneuvers at the end of life should be discouraged. Overall, we prefer post-pyloric nasoenteric feeding tubes when indicated, and discourage the use of gastrostomy or jejunostomy tubes as well as TPN.

Recommendations

For most patients with metastatic disease and malignant dysphagia, we would typically recommend either systemic chemotherapy or palliative EBRT as initial measures. The benefits of chemotherapy include the high likelihood of symptomatic improvement, avoidance of delays in systemic therapy, and minimal loco-regional toxicity. Radiotherapy would similarly be an effective initial approach and may be best suited for patients with low volume (oligo-metastatic) disease.

For patients who develop progressive dysphagia later in their disease course, radiotherapy or SEMS placement are the main therapy options. At our institution, for patients who receive initial chemotherapy but later develop dysphagia, EBRT is employed. We typically reserve the use of esophageal SEMS for those patients who experience recurrent moderate to severe dysphagia despite chemotherapy and EBRT, or for unfit patients with limited life expectancy. We rarely employ endoscopic ablative therapies for management of dysphagia. Second line chemotherapy is less likely to provide robust symptomatic benefit, and therefore, cannot be relied upon to relieve dysphagia.

Of note, we recommend against the use of dual chemoradiation therapy as a means to mitigate dysphagia in patients with metastatic disease. We feel the toxicity of this approach cannot be justified in a purely palliative setting, given the poor overall prognosis of this disease, and certainly not when several other effective and less toxic options are available. We also recommend against "double palliation," in which patients receive two palliative therapies simultaneously. This would include maneuvers such as SEMS placement followed by EBRT/BT, as well as EBRT followed by additional BT. The rationale for combining techniques is compelling: to provide more durable management of dysphagia. We would argue, however, that most patients treated with a single technique (EBRT for example) would never need additional local therapy. Furthermore, there is likely no harm in delaying Page 8 of 9 Annals of Esophagus, 2018

additional local therapy, in the few patients who will eventually require such treatment, to the time of recurrent symptoms.

Overall, decisions regarding management of malignant dysphagia should be individualized to consider the severity of the obstruction, the need for systemic therapy, prior therapy received, and finally the patient's life expectancy and personal wishes. With careful consideration of these factors, and with an understanding of the various available therapies, we can reliably, easily, and safely provide relief of dysphagia and improved QOL for most patients.

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Footnote

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