

Esophageal stenting for benign and malignant disease: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline



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Bibliography

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This Guideline is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE), endorsed by the European Society for Radiotherapy and Oncology (ESTRO), the European Society of Digestive Endoscopy (ESDO), and the European Society for Clinical Nutrition and Metabolism (ESPEN). The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was adopted to define the strength of recommendations and the quality of evidence.

Main recommendations for malignant disease

- ESGE recommends placement of partially or fully covered self-expandable metal stents (SEMSs) for palliative treatment of malignant dysphagia over laser therapy, photodynamic therapy, and esophageal bypass (strong recommendation, high quality evidence).
 - For patients with longer life expectancy, ESGE recommends brachytherapy as a valid alternative or in addition to stenting in esophageal cancer patients with malignant dysphagia. Brachytherapy may provide a survival advantage and possibly a better quality of life compared to SEMS placement alone. (Strong recommendation, high quality evidence.)
 - ESGE recommends esophageal SEMS placement as the preferred treatment for sealing malignant tracheoesophageal or bronchoesophageal fistula (strong recommendation, low quality evidence).
 - ESGE does not recommend the use of concurrent external radiotherapy and esophageal stent treatment. SEMS placement is also not recommended as a bridge to surgery or prior to preoperative chemoradiotherapy. It is associated with a high incidence of adverse events and alternative satisfactory options such as placement of a feeding tube are available. (Strong recommendation, low quality evidence.)
- ## Main recommendations for benign disease
- ESGE recommends against the use of self-expandable stents (SEMSs) as first-line therapy for the management of benign esophageal strictures because of the potential for adverse events, the availability of alternative therapies, and costs (strong recommendation, low quality evidence).
 - ESGE suggests consideration of temporary placement of SEMSs as therapy for refractory benign esophageal strictures (weak recommendation, moderate evidence).
Stents should usually be removed at a maximum of 3 months (strong recommendation, weak quality evidence).
 - ESGE suggests that fully covered SEMSs be preferred over partially covered SEMSs for the treatment of refractory benign esophageal strictures, because of their lack of embedment and ease of removability (weak recommendation, low quality evidence).
 - For the removal of partially covered esophageal SEMSs that are embedded, ESGE recommends the stent-in-stent technique (strong recommendation, low quality evidence).
 - ESGE recommends that temporary stent placement can be considered for treating esophageal leaks, fistulas, and perforations. The optimal stenting duration remains unclear and should be individualized. (Strong recommendation, low quality evidence.)
 - ESGE recommends placement of a SEMS for the treatment of esophageal variceal bleeding refractory to medical, endoscopic, and/or radiological therapy, or as initial therapy for patients with massive esophageal variceal bleeding (strong recommendation, moderate quality evidence).

Abbreviations

BMI	body mass index
CI	confidence interval
CSEMS	covered self-expandable metal stent
ESDO	European Society of Digestive Oncology
ESGE	European Society of Gastrointestinal Endoscopy
ESPEN	European Society for Clinical Nutrition and Metabolism
ESTRO	European Society for Radiotherapy and Oncology
FCSEMS	fully covered self-expandable metal stent
GEJ	gastroesophageal junction
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HR	hazard ratio
PCSEMS	partially covered self-expandable metal stent
PEG	percutaneous endoscopic gastrostomy
PDT	photodynamic therapy
RBES	refractory benign esophageal stricture
RR	risk ratio or relative risk
RCT	randomized controlled trial
RTCT	radiotherapy combined with chemotherapy
SEMS	self-expandable metal stent
SEPS	self-expandable plastic stent
TIPS	transjugular intrahepatic portosystemic shunt
QoL	quality of life

Introduction

Esophageal cancer is the eighth most common cancer worldwide with an estimated 456 000 new cases and 400 000 deaths in 2012 [1]. More than 50% of patients with esophageal carcinoma have metastatic disease at the time of diagnosis. Dysphagia is the most common symptom of incurable obstructive esophageal cancer and can be treated by esophageal stent placement. In recent years different designs of esophageal stents have emerged for improving dysphagia and quality of life in patients with malignant esophageal tumor, malignant fistula, or extrinsic compression [2,3]. Esophageal stent placement in patients with incurable esophageal cancer is aimed at maintaining oral intake and improving quality of life, but it carries a risk of adverse events such as hemorrhage, pain, and fistula [4]. The current variety of commercially available stents for malignant disease comprises uncovered self-expandable metal stents (SEMSs); fully covered self-expandable metal stents (FCSEMSs), in which the entire length of the stent is covered; partially covered self-expandable metal stents (PCSEMSs), in which the proximal and distal ends of the stent are devoid of a covering; and fully covered self-expandable plastic stents (SEPSs). All currently available SEMSs are made of nitinol, a nickel and titanium alloy. In Europe, the types of stents that are predominately used in the treatment of malignant dysphagia are PCSEMSs and FCSEMSs.

Esophageal stents are also commonly used for the treatment of benign esophageal diseases, albeit most stents are not officially approved for this indication. Common and investigative indications include treatment of refractory benign esophageal stricture (RBES), sealing of perforations, leaks, and treatment of acute esophageal variceal bleeding. FCSEMS and PCSEMS as well as SEPS are used for this indication, but only the latter has formal approval for RBES. All stents used for benign esophageal conditions should be removed, except for the self-expandable biodegradable stents that have recently become available in Europe.

This clinical Guideline aims to describe the role of esophageal stents in patients with malignant or benign esophageal disease and makes recommendations on circumstances that warrant their use.

Methods

The European Society of Gastrointestinal Endoscopy (ESGE) commissioned this Guideline and appointed a Guideline leader (M.J.B.) who invited the listed authors. The key questions were prepared by the coordinating team (M.C.W.S., J.-M.D., C.H., M.J.B.) and then approved by the other members (see **Appendix e1**, available online). The coordinating team established task force subgroups, each with a leader (P.D.S. for malignant disease and T.H.B. for benign disease), and divided the key topics among these task forces.

Each task force performed a systematic literature search to prepare evidence-based and well-balanced statements on their assigned key questions. All selected articles were graded for the level of evidence and strength of recommendation according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [5]. The numbers of articles retrieved and selected by each task force are indicated in the evidence tables (see **Tables e1 – e6** in **Appendix e2**, available online).

Each task force proposed statements for their assigned key questions, which were discussed during a meeting in Amsterdam (April 2015). In August 2015, a draft prepared by the coordinating team was sent to all group members. It was also sent for review and endorsement to the European Society for Radiotherapy and Oncology (ESTRO), the European Society of Digestive Oncology (ESDO), and the European Society for Clinical Nutrition and Metabolism (ESPEN). The manuscript was reviewed by two members of the ESGE Governing Board and sent for further comments to the National Societies and ESGE Individual Members. After agreement on a final version, the manuscript was submitted to *Endoscopy* for publication. All authors agreed on the final revised manuscript.

This Guideline was issued in 2016 and will be considered for review and update in 2021 or sooner if new and relevant evidence becomes available. Any updates to the Guideline in the interim will be noted on the ESGE website: <http://www.esge.com/esge-guidelines.html>.

Recommendations and statements

ESOPHAGEAL STENTS IN MALIGNANT DISEASE

ESGE recommends placement of partially or fully covered self-expanding metal stents (SEMSs) for palliation of malignant dysphagia over laser therapy, photodynamic therapy, and esophageal bypass (strong recommendation, high quality evidence).

ESGE recommends against the placement of nonexpandable and expandable plastic stents for the palliation of malignant esophageal strictures (strong recommendation, high quality evidence).

Efficacy

Photodynamic therapy (PDT), laser therapy, and esophageal bypass have not been shown to be superior to SEMS placement for the palliation of malignant dysphagia in several randomized con-

trolled trials (RCTs) [6–11]. From 1993 up to 2005 several RCTs have compared SEMs versus rigid plastic stents [12–18]. One of the largest published RCTs including 217 patients [17] showed a better improvement in dysphagia score at 1 and 6 weeks with SEMs compared to rigid plastic stents and fewer late adverse events. Systematic reviews and meta-analyses showed that SEMs insertion was superior to rigid plastic stents in terms of improvement and recurrence of dysphagia, as well as occurrence of adverse events including perforation and migration [19,20]. Multiple types of self-expandable stents are available. They differ in terms of design, luminal diameter, radial force, flexibility, and degree of shortening after deployment. In Europe, partially or fully covered SEMs are used for the treatment of malignant dysphagia because recurrent dysphagia due to tumor ingrowth has been a major drawback of uncovered SEMs [21]. In most cases a 100% technical success rate of stent placement has been reported with an improvement in dysphagia score of at least 2 points (from 3 [liquids only] to 1 [almost all solids]) within 1–2 days [20]. Most new stent designs have been evaluated in single-arm prospective or retrospective series. SEPS are similar to SEMs with regard to relief of dysphagia in the short term, but adverse events occurred more often with SEPS, especially migration, making SEMs preferable over SEPS for malignant dysphagia [22].

Safety

The most prevalent adverse events following stent placement are shown in [Table e7 \(Appendix e3, available online\)](#) and details are also presented in [Appendix e3](#). Analysis of pooled data from RCTs and prospective and retrospective studies showed that major adverse events occur in 18%, 21%, and 10% of patients with PCSEMS, FCSEMS, and SEPS, respectively, while recurrent dysphagia develops in 41%, 29%, and 37% of these patients, respectively [22–39]. Stent insertion-related mortality is 0%–2% [23, 40].

For patients with longer life expectancy, ESGE recommends brachytherapy as a valid alternative or in addition to stenting in esophageal cancer patients with malignant dysphagia. Brachytherapy may provide a survival advantage and possibly a better quality of life compared to SEMs placement alone. (Strong recommendation, high quality evidence.)

Two RCTs have compared SEMs versus brachytherapy. One RCT compared a PCSEMS (Ultraflex) with single-dose intraluminal brachytherapy in 202 patients with incurable esophageal cancer [4]. Compared to SEMs placement, brachytherapy improved dysphagia less rapidly, but after 1 month from treatment, dysphagia score improvement no longer differed significantly between stent placement and brachytherapy. With respect to survival, patients treated by brachytherapy had more days with almost no dysphagia during follow-up than those treated by stent placement. In addition, major complications (i.e., perforation, hemorrhage) occurred more frequently after stent placement than after brachytherapy. There was no difference in recurrent dysphagia and median survival. Quality-of-life (QoL) scores significantly favored brachytherapy, whereas total costs were similar across the two groups. In the other RCT (n=65), insertion of SEMs offered a more immediate relief of dysphagia compared to brachytherapy, but quality of life was better with brachytherapy for patients with longer survival [41]. The main limitations of brachytherapy include limited availability, technical difficulty, and need for dedicated logistics and expertise. Therefore this treatment can only be considered in dedicated centers.

Esophageal stent placement for malignant tracheoesophageal or bronchoesophageal fistula

Esophageal SEMs placement is recommended as the preferred treatment for sealing malignant tracheoesophageal or bronchoesophageal fistula (strong recommendation, low quality evidence).

Application of double stenting (esophagus and airways) can be considered when fistula occlusion is not achieved by esophageal or airway prosthesis alone (strong recommendation, low quality evidence).

Malignant tracheoesophageal or bronchoesophageal fistula develops in 5% to 15% of patients with esophageal cancer and in less than 1% of patients with lung carcinoma [42,43]. Because of advances in palliative treatment, the incidence has increased over the last 30 years to above 10% among all nonresected esophageal cancers [44].

Tracheoesophageal or bronchoesophageal fistulas are usually late developments of advanced cancer of the esophagus, lung, or mediastinum, caused by tumoral invasion or as an adverse event of cancer therapies, in particular chemoradiotherapy [45–47]. Importantly, the condition of such patients has often already significantly deteriorated when they develop a fistula and the remaining life expectancy is short (weeks to months). Rapid relief of disabling symptoms due to the fistula, preferably by minimally invasive treatment, is thus of pivotal importance in order to improve quality of life.

Esophageal stenting is the most widely used approach [48]. Multiple studies using SEMs for sealing off esophageal – airway fistulas have reported improvement in symptoms and sealing of the fistula in 75%–100% of patients [2,42,43,49–55]. Application of double stenting (esophagus and airways) can be considered when fistula occlusion is not achieved by esophageal or airway prosthesis alone [51,56–58]. In the largest prospective series, Shin et al. successfully placed SEMs in 61 patients with malignant esophageal – airway fistulas, sealing off the fistula in 49 patients (80%), while 10 patients (16%) required concomitant airway stents [42]. Re-opening of the fistula occurred in 17 patients (35%); of these, 8 were successfully re-treated with SEMs, in 2 patients the fistula was closed spontaneously, and 7 patients did not undergo further treatment [42].

Procedure-related complications are reported in 0%–27% of patients with a mortality rate of 0%–12% [42,43,49,50,52,54].

In another study that compared quality of life following placement of a SEMs versus gastrostomy or jejunostomy or best supportive care, quality of life improved more with SEMs placement, particularly for symptoms of dyspnea, dysphagia, other eating problems, dry mouth, cough, and hypersalivation [59]. In three large retrospective studies, esophageal stent placement was associated with a significant improvement in survival compared with no sealing of the fistula, a feeding gastrostomy or jejunostomy, or best supportive care [42,43,50].

Stent placement for malignant dysphagia as a bridge to surgery

ESGE does not recommend SEMs placement as a bridge to surgery or prior to preoperative chemoradiotherapy. It is associated with a high incidence of adverse events, and other satisfactory options such as placement of a feeding tube are preferable. (Strong recommendation, low quality evidence.)

It is now accepted that neoadjuvant chemotherapy or chemoradiotherapy should be administered to all patients with a resectable esophageal cancer, except for cancers staged 0–IIA [60–62]. In a systematic review and meta-analysis of 9 studies (n = 180 patients) on esophageal stenting preceding or concomitant with neoadjuvant chemotherapy for esophageal cancer, the procedural success rate was 95% (95% confidence interval [95%CI] 90%–98%) [63]. There was a significant decrease in dysphagia score and a nonsignificant increase in patient weight (0.6 kg) and serum albumin. However, major adverse events were extremely frequent, including stent migration (incidence 32%, 95%CI 26%–40%) and chest discomfort (incidence 51.4%, 95%CI 21%–81%). SEPS were used in 5 of the 9 studies (41% of patients). The negative impact on oncologic outcome of SEMs placement as bridge to surgery was also confirmed in a large European cohort of 2944 patients [64]. This study showed an in-hospital postoperative mortality and morbidity rate for the SEMs versus control groups of 13.2% versus 8.6% and 63.2% versus 59.2%, respectively. In addition, significant differences in R0 resection (71.0% vs. 85.5%), median time to recurrence (6.5 vs. 9.0 months), and 3-year overall survival (25% vs. 44%) were found, to the disadvantage of the SEMs group. The results remained significant after excluding SEMs-related esophageal perforations and after adjusting for confounding factors. Similar unfavorable results have been reported with biodegradable stents as a bridge to surgery [65]. Profound weight loss and malnutrition as a consequence of severe dysphagia and cancer cachexia are cardinal symptoms in esophageal cancer [66,67]. To detect nutritional disturbances at an early stage, the European Society for Clinical Nutrition and Metabolism (ESPEN) recommends regular evaluation of nutritional intake, weight change, and body mass index (BMI), at the time of cancer diagnosis and repeated according to the stability of the clinical situation [68]. In patients with digestive cancer, body composition may be quite easily assessed from computed tomography scans [69]. ESPEN recommends nutritional support prior to major surgery in patients with severe nutritional risk (e.g., those with weight loss > 10–15% within 6 months) as a grade A recommendation [70]. If oral feed intake is inadequate despite counseling and oral nutritional supplements, supplemental enteral nutrition or, if the latter is not sufficient or possible, parenteral nutrition is recommended [68,71]. In patients with severe dysphagia, this can be achieved through nasogastric tube placement, percutaneous feeding tube placement, or parenteral nutrition. Percutaneous endoscopic gastrostomy (PEG) or endoscopic jejunostomy is recommended by ESPEN in place of nasogastric tube placement if enteral feeding is scheduled to last more than 2–3 weeks [72,73]. Furthermore, a Cochrane review of RCTs showed that intervention failure (e.g., feeding interruption, blocking or leakage of the tube, no adherence to treatment) was more frequent with nasogastric tube placement compared with PEG feeding (risk ratio [RR] 0.24, 95%CI 0.08–0.76) [74]. However, in esophageal cancer patients who are scheduled to undergo a gastric tube reconstruction a PEG placement may be contraindicated, in which case a feeding tube is the preferred treatment. The proportion of patients who refuse placement of a feeding tube in the setting of head and neck cancer patients treated with (chemo)radiation has been found to be very low (4% in an RCT) [75].

Esophageal stents and concomitant palliative treatment with radiotherapy

ESGE does not recommend the concurrent use of radiotherapy if an esophageal stent is present (strong recommendation, low quality evidence).

ESGE suggests that SEMs placement with concurrent single-dose brachytherapy is safe and effective for relief of dysphagia (weak recommendation, low quality evidence).

In contrast to the rapid improvement in dysphagia by stent placement, palliative radiotherapy improves dysphagia after 4 to 6 weeks [76]. Temporary and permanent placement of retrievable metallic stents with concurrent radiotherapy has been suggested as an effective method for increasing survival, immediately improving dysphagia and dietary intake in the period before the effects of radiotherapy become apparent [77–80]. However, a higher risk of life-threatening adverse events has been reported, suggesting that palliative stenting should be delayed until radiotherapy has failed [81–83].

Potential scattering from the metal material in SEMs may complicate radiation dosimetry. In a simulated clinical protocol measuring the effects of esophageal stents of various materials and designs on radiation effects on tissue adjacent to the stent in the radiation field, a dose enhancement was seen with SEPSs and stainless steel stents, and not with nitinol stents [84]. In another study, dose perturbation by SEMs was related to the density of the mesh, with a higher density having greater effect, while SEPS and biodegradable stents had minimal-to-no dose effects outside of the radiopaque markers [85].

In contrast to external radiotherapy, the combination of SEMs and single-dose brachytherapy has been reported to be feasible and safe as a palliative treatment in patients with advanced esophageal cancer [77,86]. In an RCT that included 53 patients, Guo et al. compared conventional SEMs treatment with SEMs loaded with iodine-125 seeds for brachytherapy; these authors reported a significantly longer dysphagia-free period and longer survival in the irradiation stent group [25,87].

Data on the use of biodegradable stents in patients receiving brachytherapy are limited, but a high rate of major stent-related complications has been described and a normal diet could not be tolerated because of retrosternal pain and vomiting in more than one third of patients [78].

Esophageal stent placement after palliative chemotherapy and radiotherapy

Data are contradictory with respect to the risk of major adverse events in patients receiving a stent for recurrent malignancy following radiotherapy alone or combined with chemotherapy (RTCT). Some studies show an increased risk while other studies, including a meta-analysis, do not report any relationship between SEMs placement after RTCT and the incidence of life-threatening adverse events or survival; only minor adverse events such as chest pain are associated, suggesting stenting is safe in these patients [18,22,32,88–94]. In detail, the reported rate of life-threatening adverse events ranged from 16% to 77% in patients treated with stents after RTCT compared to 0% to 45% in patients without previous treatment [18,22,32,88–91]. Reported stent-related mortality ranged from 0% to 54% in patients with prior RTCT compared to 0% to 6% in patients without prior RTCT.

It has been suggested that the increased risk, if any, of developing life-threatening adverse events, in patients with prior RTCT may be related to the radiation-induced damage on the esophageal wall, potentiated by chemotherapy. However, it is difficult to discern whether such stent-related adverse events are due to stents and radiation effects, the advanced nature of the disease process, or both. Radiotherapy can cause esophagitis, ulcerations, submucosal fibrosis, and vasculitis, with ischemic damage of the esophageal wall causing esophageal perforations and esophageal–respiratory fistulas via local hypoxemia. Although SEMs placement is effective for short-term palliation of malignant dysphagia, stent pressure on a damaged esophageal wall increases the risk of necrosis [89,95–99]. The effect of radiation on the esophageal wall is dose-dependent, with serious damage especially when doses greater than 6Gy have been administered [97,99]. The risks of sudden fatal hemorrhage and formation of a respiratory fistula are relatively high in patients with invasive (T4) cancer [47,96].

ESOPHAGEAL STENTS IN BENIGN DISEASE

Refractory benign strictures

ESGE recommends against the use of SEMs as first-line therapy for the management of benign esophageal strictures because of the potential for adverse events, the availability of alternative therapies, and costs (strong recommendation, low quality evidence).

Most studies have used expandable stents for treatment of refractory or recurrent esophageal strictures as defined by Kochman: generally when more than 3 to 5 dilations (either mechanical or pneumatic) have been performed without clinical and endoscopic response or when it was impossible to achieve a 14-mm lumen over 3 dilation sessions [100]. No studies have compared the clinical efficacy of different initial strategies (i.e., dilation vs. stent placement). Therefore, algorithms are mainly based on the experience of tertiary referral centers [101]. Most experts agree that stent placement should be considered when other treatment options (dilation with or without intralesional triamcinolone acetate injections and/or incisional therapy) have failed, though a clear definition of clinical failure has not been uniformly adopted.

ESGE suggests consideration of temporary placement of self-expandable stents for refractory benign esophageal strictures (weak recommendation moderate quality evidence).

ESGE does not recommend a specific type of expandable stent (covered metal, plastic, biodegradable) because none has been shown to be superior to any other for this indication (strong recommendation, moderate quality evidence).

A recent systematic review and meta-analysis (10 prospective and 8 retrospective studies; 444 patients) evaluated the clinical outcome of stent placement for refractory benign esophageal stricture (RBES) [102]. FCSEMS were used in 9 studies (227 patients), 8 trials used SEPS (140 patients) and 4 studies used biodegradable stents (77 patients). Overall, the pooled clinical success rate was 40.5% (95%CI 31.5%–49.5%). Patients treated with SEPS and SEMs did not have significantly different success rates compared with patients treated with biodegradable stents. The overall migration rate was 28.6% (95%CI 21.9%–37.1%). Stent removal was successful in 99% of cases. Finally, the overall adverse event rate was 20.6% (95%CI, 15.3%–28.1%) with no significant difference between the three types of stents. Only one patient died; this was due to massive bleeding.

Factors predicting successful stent treatment

A systematic review demonstrated that the clinical success of stenting in RBES was significantly lower in patients with cervical strictures and for strictures longer than 2 cm [100]. The latter finding was confirmed by a prospective study showing stricture length as the only factor associated with success, with longer strictures being at higher risk of recurrence (hazard ratio [HR] 1.37, 95%CI 1.08–1.75) [103]. The previously mentioned review and meta-analysis by Fuccio et al. [102] showed that the etiology of the stricture might influence outcome, with esophageal strictures that had developed after surgical resection or radiation therapy being potentially more responsive to stent treatment. However, no firm conclusion can be drawn because many etiologies of stricture were under-represented and, in many studies, the results were not stratified according to the stricture etiology.

ESGE does not recommend permanent stent placement for refractory benign esophageal stricture; stents should usually be removed at a maximum of 3 months (strong recommendation, weak quality evidence).

No studies have compared different strategies in terms of stenting duration. It is generally accepted that FCSEMS or SEPS should remain in place for at least 6–8 weeks and no more than 12 weeks, to maximize success and to minimize the risk of hyperplastic tissue reaction and stent embedment. Indeed, a large multicenter study that specifically addressed the safety of endoscopic removal of self-expandable stents inserted to treat RBES found no association between indwelling time and the risk of major adverse events [104].

ESGE suggests that FCSEMS be preferred over PCSEMS for the treatment of refractory benign esophageal stricture, because of their lack of embedment and ease of removability (weak recommendation, low quality evidence).

The use of partially covered or uncovered SEMs in benign strictures should be avoided because the hyperplastic tissue reaction of the esophageal mucosa to the bare metal mesh often results in recurrent dysphagia. Furthermore, complete embedding of the uncovered metal wires in the esophageal wall may preclude safe stent removal [105,106].

ESGE recommends the stent-in-stent technique to remove PCSEMS that are embedded in the esophageal wall (strong recommendation, low quality evidence).

In the case of embedded PCSEMS, temporary placement of a second, fully covered, stent in the first stent (“stent-in-stent” technique) has been shown to facilitate safe removal of the embedded stent, by induction of pressure necrosis of the overgrowing and ingrowing mucosa [103,107–110]. Stents used for the stent-in-stent technique should have a fully covered design and a diameter at least equal to that of the partially covered embedded stent in order to provide sufficient pressure at the site of embedment. In addition, the fully covered stent needs to overlap completely tissue ingrowth inside the lumen of the partially covered stent. The second stent is left in place for 10–14 days, before it is retrieved and removal of the embedded PCSEMS is attempted. The success rate of the stent-in-stent technique is above 90%; in the case of failure, a second FCSEMS should be placed and left in place for 10–14 days before a second attempt to remove the stent is performed [103].

Esophageal stent placement in combination with other dilation approaches

ESGE suggests that a combined approach of stent placement with additional techniques (e.g., corticosteroid injection, chemotherapeutic topical application) should not be used in an attempt to improve the long-term benefit of temporary stenting (weak recommendation, very low quality evidence).

Endoscopic incisional therapy has been proposed as either an alternative or additional treatment to endoscopic dilation. Initially proposed for the treatment of recurrent Schatzki rings, it has also been used for the treatment of anastomotic strictures. To our knowledge there have been no studies that have reported using a combined or sequential approach with incisional therapy followed by stent placement.

In order to prevent stricture recurrence, corticosteroid injection into the stricture followed by dilation was proposed more than 10 years ago [111]. Small retrospective studies reporting corticosteroid injection before stent placement do not allow conclusions to be drawn on the additional clinical value for prolonging efficacy following temporary stent placement [112].

Topical application of mitomycin-C has been proposed for refractory corrosive esophageal strictures. Mitomycin-C is a chemotherapeutic agent that inhibits the proliferation of fibroblasts and collagen synthesis and has been proposed to prevent stricture relapse. There are few available studies, mainly case reports and small series, to support its use, and no studies of this treatment combined with stent placement [113, 114].

Treatment options after stent failure for refractory benign esophageal stricture

If refractory benign esophageal stricture has not satisfactorily improved after 2 separate treatments with temporary stenting, ESGE suggests alternative treatment strategies such as self-dilation or surgical treatment (weak recommendation, low quality evidence).

In poor surgical candidates, ESGE recommends self-dilation with rigid dilators (strong recommendation, low quality evidence).

Stent placement for treatment of RBES may be repeated although the majority of studies have demonstrated that additional stent placement does not produce significant incremental benefit [106, 115]. If sustained stricture resolution is not obtained after temporary stenting on two occasions, the suggested treatment options are self-dilation and surgery. Surgery is advised when possible according to anatomical extent as well as patient condition and willingness to undergo such a complex surgical procedure. The best candidates for self-dilation are those who are self-motivated, compliant, and poor surgical candidates [116, 117]. Based on two retrospective studies, esophageal self-dilation was successful in treating 90% of patients, with significant improvement in global dysphagia scores and overall quality of life [116, 117].

Benign esophageal leaks, fistulas, and perforations

ESGE recommends that temporary stent placement can be considered for treatment of leaks, fistulas, and perforations. No specific type of stent can be recommended and the duration of stenting should be individualized. (Strong recommendation, low quality of evidence).

SEMSs have been used for management of perforations and leaks [118, 119]. Closure of an iatrogenic perforation can also be performed by other endoscopic methods [120]. **Table e5 (Appendix e2, available online)** shows the results of the published stud-

ies on the efficacy and safety of SEMS placement for benign rupture and leakage. In two systematic reviews, the clinical success after placement of temporary stents (FCSEMSs, PCSEMSs, and SEPSs) for benign rupture and anastomotic leaks of the esophagus was similar with different stent types (FSEMS 85%, PSEMS 86%, SEPS 84% [121, 122]. The mean duration of stenting was 7 weeks. Stent migration occurred in 25%, and it occurred more often with SEPS (26%) and FCSEMS (26%).

Data on the use of biodegradable stents are limited. In a small study, 4 of 5 patients with an esophageal leak or anastomotic perforation achieved long-term leak sealing after placement of a covered biodegradable stent [123].

The optimal duration of stenting remains unknown. In most studies stent removal was performed 6–8 weeks (range 4–10 weeks) after insertion. Stent-associated esophagorespiratory fistula is a serious adverse event that may occur as a consequence of SEMS placement for benign disease. In one retrospective study of 397 patients, 20 patients developed esophagorespiratory fistulas after a median of 5 months following stent placement [124]. Most fistulas occurred at the proximal edge of the stent and in the setting of prior external radiation therapy; thus the cause may have been ischemic pressure necrosis.

Acute variceal bleeding

ESGE recommends considering placement of a SEMS for the treatment of esophageal variceal bleeding refractory to medical, endoscopic, and/or radiological therapy, or as initial therapy for patients with massive bleeding (strong recommendation, moderate quality evidence).

Table e6 (Appendix e2, available online) shows the results of the published studies to date on the applicability, efficacy and safety of covered SEMS for acute esophageal variceal bleeding [125–131]. Most published studies are observational studies [125–131]. Results from these studies are in agreement with a recently published systematic review and meta-analysis showing that treatment with SEMSs is successful in controlling severe or refractory acute variceal bleeding, without the occurrence of severe adverse events and with a 1-month survival of more than 60%; these findings confirmed that this therapy can be used as a bridge to transjugular intrahepatic portosystemic shunt (TIPS) or liver transplantation in a significant proportion of patients [132]. An RCT compared patient outcome after SEMS placement (SX-Ella Danis stent; n=13) versus balloon tamponade (Sengstaken-Blakemore tube; n=15) in patients with esophageal variceal bleeding refractory to medical and endoscopic treatment [133]. Successful therapy was significantly more frequent in the stent than in the balloon tamponade group (66% vs. 20%) with a significantly higher rate for control of bleeding (85% vs. 47%), lower transfusion requirements (3 ± 3.4 vs. 6 ± 4.8 packed red blood cell units), and a lower incidence of serious adverse events (15% vs. 47%), mainly due to differences in aspiration pneumonia (0 vs. 5) and esophageal tear (1 patient in the balloon tamponade group). No significant difference in 6-week survival was observed (54% vs. 40%).

Despite the efficacy of stent placement in controlling acute variceal bleeding, a mortality rate of 25% has been described in these patients, reflecting the seriousness of the underlying condition of the patient in the case of refractory acute variceal bleeding [129]. In published studies SEMSs have remained in place for up to 2 weeks [125, 131, 134, 135]. When a dedicated SEMS is used retrieval is done using a specifically designed system (PEX-Ella or extractor for SX-Ella Stent Danis).

This Guideline, produced by ESGE and endorsed by the European Society for Radiotherapy and Oncology (ESTRO), the European Society of Digestive Oncology (ESDO), and the European Society for Clinical Nutrition and Metabolism (ESPEN), represents a consensus of best practice based on the available evidence at the time of preparation. The Guideline may not apply in all situations and should be interpreted in the light of specific clinical situations and resource availability. Further controlled clinical studies may be needed to clarify aspects of the statements, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to the recommendations. The Guidelines is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. It is not a set of rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.

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Appendix e1, e2, e3

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