

# How to reduce fistula formation after self-expandable metallic stent insertion for treating malignant esophageal stricture?

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See “Self-expandable metallic stent-induced esophagorespiratory fistulas in patients with advanced esophageal cancer” by Iatagan R. Josino, Bruno C. Martins, Andressa A. Machado, et al., Clin Endosc 2023;56:761–768.

Esophageal cancer is a common cause of malignant esophageal obstruction and often diagnosed at an advanced stage. The clinical presentation for esophageal cancer is diverse; however, many patients present with dysphagia due to obstruction, ongoing malnutrition, weight loss, and poor health-related quality of life.<sup>1</sup> Although palliative surgery may be considered in patients with good performance, patients with unresectable or medically poor performance require nonsurgical methods to treat dysphagia. For most patients with malignant unresectable esophageal obstruction, treatment options include self-expandable metallic stent (SEMS) insertion, radiotherapy, and chemotherapy. Each of these can be administered as a single or combination therapy.<sup>1</sup>

Endoscopic SEMS insertion is a nonsurgical treatment modality for the palliation of malignant obstructions. Dysphagia can be resolved through SEMS insertion, and nutritional status can be improved. Nevertheless, appropriate stent selection is still under consideration. An important consideration is select-

ing a stent with approximately 2 cm remaining both proximally and distally from the stricture site. A study comparing large (20–23 mm) and small (16–18 mm) diameter stents demonstrated no significant difference in dysphagia relief. However, patients with smaller diameter stents have increased risk of recurrent dysphagia, tissue overgrowth, and food bolus obstruction. Conversely, patients with large-diameter stents experience increased adverse events, such as hemorrhage, perforation, fistula formation, and fever.<sup>2</sup>

Although an early randomized controlled study comparing covered SEMS with uncovered SEMS revealed no significant difference in initial dysphagia improvement,<sup>3</sup> the application of partially covered stents has demonstrated superiority over uncovered stents, resulting in a decreased incidence of tumor infiltration through the stent mesh.<sup>3</sup> However, it is worth noting that the proximal and distal flares of partially covered stents still have the potential for tumor ingrowth. Conversely, fully covered stents may mitigate tumor ingrowth, albeit with a potential increase in the risk of stent migration.<sup>4</sup> Another study, which compared fully covered stents with partially covered stents, found no significant differences regarding stent migration and dysphagia relief.<sup>5</sup> Consequently, fully covered stents remain a viable and optional therapeutic approach for malignant esophageal obstruction.

The axial and radial forces of the stent are important in determining its characteristics.<sup>6,7</sup> The pressure applied to the esophageal wall is primarily influenced by the radial force of the stent.

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While a higher radial force can enhance stable stent position, it may also lead to potential adverse events, such as perforation and bleeding.<sup>4</sup> In a recent study comparing stents with low radial force to those with high radial force, severe adverse events occurred more frequently in the high-radial-force group compared to the low-radial-force group (14% vs. 2%,  $p=0.03$ ).<sup>8</sup> In patients with a history of radiotherapy, the high-radial-force group exhibited a higher incidence of severe adverse events compared to the low-radial-force group (36% vs. 0%,  $p=0.03$ ).<sup>8</sup> Therefore, selecting a low-radial-force stent may reduce the risk of severe adverse events following stent placement without compromising its effectiveness, making it a preferred choice for individuals with malignant dysphagia, especially those who have undergone radiotherapy.<sup>4</sup> Esophago-respiratory fistula (ERF) is an expected adverse event in the palliative treatment of dysphagia by SEMS. If the axial force of the protruding part of the SEMS exerts continuous pressure on one point of the esophagus and adjacent trachea, ischemic changes occur at the contact sites, and the protruding part of the SEMS may penetrate the adjacent trachea.<sup>9</sup>

In the current issue of *Clinical Endoscopy*, Josino et al.<sup>10</sup> reported a retrospective study of SEMS-induced ERF in patients with advanced esophageal cancer. They documented an incidence of SEMS-induced ERF of 11%, affecting 37 out of 335 patients, occurring at a median time of 129 days post-SEMS placement. Risk factors for SEMS-induced ERF included a stent flare of 28 mm (hazard ratio [HR], 2.05; 95% confidence interval [CI], 1.15–5.51;  $p=0.02$ ) and administration of post-stent chemotherapy (HR, 2.0; 95% CI, 1.01–4.00;  $p=0.05$ ). Conversely, lower-third tumors exhibited a protective effect against SEMS-induced ERF (HR, 0.5; 95% CI, 0.26–0.85;  $p=0.01$ ). There was no difference in the overall survival rates. The tumor location appeared to be more important in the occurrence of SEMS-induced ERF. Cancer of the upper two-thirds of the esophagus was identified as a risk factor for the development of SEMS-induced ERF. Most cases occurred in patients with squamous cell carcinoma (SCC). SCC can occur in the upper to mid-esophagus, which is anatomically adjacent to the trachea; therefore, SCC might develop into SEMS-induced ERF. A large flange was found to be another risk factor for SEMS-induced ERF. It appears to be more likely to cause damage to the esophageal mucosa and adjacent trachea because the axial force is concentrated on the most protruding part of the stent. Additionally, post-SEMS placement chemotherapy was associated with SEMS-induced ERF (HR, 2.0; 95% CI, 1.01–4.00;  $p=0.05$ ).

There may be a relation between the impact of concomitant chemotherapy and development of SEMS-related adverse events.<sup>11,12</sup> Therefore, a recent European Society of Gastrointestinal Endoscopy guideline recommended against stent placement concomitant with radiotherapy.<sup>13</sup> Although there are various limitations, such as a single-center retrospective study and biases due to the large heterogeneity (stents of various types, sizes, and manufacturers), this study offers a valuable message to clinicians about stent selection based on deeper comprehension of SEMS. Furthermore, these findings may serve as valuable resources for clinicians in making stent choices tailored to individual cases.

### Conflicts of Interest

The author has no potential conflicts of interest.

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