

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Stenting for Esophageal Cancer



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G&H What are the main symptoms and risk factors for esophageal cancer?

VK The typical symptom for patients who present with esophageal cancer is dysphagia or difficulty swallowing food. In some cases, they can present with upper gastrointestinal bleeding and/or anemia. The most common risk factors are male sex, Barrett esophagus (especially dysplastic Barrett esophagus), White race, cigarette smoking and/or tobacco use, and obesity. Other genetic and familial risk factors are still being investigated.

G&H Can you please provide a brief overview of how and when stenting is used in patients with esophageal cancer?

VK The goals of esophageal stenting are palliating dysphagia, improving nutrition, allowing weight gain, preventing complications of esophageal obstruction, and improving quality of life. This procedure is for patients with malignant dysphagia who are poor operative candidates regardless of stage or those who have incurable disease, either primary esophageal or metastatic disease from another etiology.

In addition, stenting may be used as a bridge to definitive surgery in certain cases. Stents may also be used for palliating dysphagia in patients with recurrent esophageal cancer who had previous surgery (or definitive chemoradiation). Less commonly, stenting is used for managing complications of esophageal cancer, such as tracheoesophageal fistulas. Occasionally, it has been described for bleeding control from an esophageal tumor and/or management of perforation in the setting of esophageal cancer.

The key in placing an esophageal stent is that it should be performed as part of a multidisciplinary approach with oncology and thoracic surgery colleagues, typically resulting from a tumor board–based treatment plan. Some centers have formal clinical or research protocols that guide this decision-making as well. When selecting patients for esophageal stenting for malignancy, indiscriminate use of esophageal stenting is strongly discouraged, so it should ideally not be offered without prior discussion with all of the stakeholders involved.

G&H How successful is the procedure in general?

VK Over the years, the devices and techniques for esophageal stenting have been refined significantly. The technical success rate of this procedure is quite high, in the mid to high 90% range. The procedure can be done safely and efficiently in the endoscopy unit on an outpatient basis. The clinical success rate remains somewhat of a challenge because these patients will universally have some degree of postprocedure discomfort/pain, and stent-related complications can occur in the 40% to 50% range.

G&H How does tumor location affect placement of the stent?

VK Tumor location is very important. The length of the tumor, tumor bulk, morphology, and location (whether it is a distal esophageal tumor or a proximal esophageal tumor, such as in squamous cell carcinoma) are important to note so that the appropriate type and length of stent can be selected. When a stent is placed for distal esophageal cancer, in many cases the tumor will traverse the

gastroesophageal junction, so stent placement will have to be planned accordingly to allow an open conduit into the stomach.

It is important to know the anatomic landmarks, where the tumor (stricture) starts and ends, and how much, if any, of the gastric cardia is involved. That allows the endoscopist to plan an adequate length of stent in the gastric lumen while similarly leaving an optimal length of stent in the esophagus, proximal to the tumor, for anchoring. Ideally, the epicenter of the tumor stricture should be seen at the middle portion of the stent on fluoroscopy.

G&H What are the potential adverse events after a stent procedure in patients with esophageal cancer?

VK The most common adverse events are chest pain and discomfort, which can start almost immediately in the recovery room, after the stent placement procedure. Although some patients may feel a foreign body sensation or pressure in the chest, others will have more significant chest pain. This discomfort may evolve in the first 24 to 48 hours as the stent will expand radially over time to its maximal diameter. The discomfort may crescendo during the next 3 to 5 days as the stent expands fully and seeks to restore luminal patency within the obstructed esophagus. Additional issues that may arise relate to free reflux of content from the stomach into the esophagus, and this is particularly true when the stent crosses the gastroesophageal junction, as now there is no mechanical antireflux barrier present.

Migration of esophageal stents, especially in patients who subsequently undergo radiation, is an issue. Bleeding can be a catastrophic and potentially fatal complication, especially if it occurs from penetration of the stent flanges into any major mediastinal vessels (eg, the aorta). More commonly, occlusion of the stent by tumor ingrowth or food impaction can occur and require re-intervention. Fistula formation or tracheal compression may occur, resulting in respiratory distress and stridor.

G&H How effective is liquid nitrogen spray cryotherapy as an alternative to stenting in patients with esophageal cancer?

VK Liquid nitrogen spray cryotherapy has emerged as a very effective alternative modality for palliation of malignant esophageal dysphagia. It has been used for this application for more than a decade, as in the study by Kachaamy and colleagues in *Gastrointestinal Endoscopy*, as well as by our group and other colleagues across the country. The main goals of spray cryotherapy treatment are to palliate dysphagia and debulk the endoluminal

tumor, restore esophageal patency, and retard further luminal tumor growth. Stent placement can be avoided in some cases. Endoscopic cryotherapy typically has no effect on the ability of an invasive tumor to metastasize; it is intended primarily for local (endoluminal) palliation.

A few cryotherapy studies have been published, including those by Kachaamy and colleagues, Hanada and colleagues, and Eluri and colleagues. I was fortunate to be part of the national registry study by Eluri and colleagues that has been reported in abstract form. In this study, in 49 patients with esophageal cancer across 10 sites, esophageal stenting was avoided in approximately

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two-thirds of the group for the duration of the follow-up. Approximately 30% of the patients still needed a stent eventually, but a majority (89%) of patients either maintained or improved their mean dysphagia scores after the first cryotherapy treatment itself. Almost all of the patients had significant improvement in their social functioning, oral intake, and global health status.

Hanada and colleagues also reported that a certain percentage of patients will avoid stent placement if they undergo palliative cryotherapy. In this study, the average delay in stenting while patients were undergoing cryotherapy was more than a year. Spray cryotherapy has definitely emerged as an alternative, and a certain percentage of patients will be able to avoid or delay esophageal stenting with concomitant improvement in their global health status and social functioning.

G&H Are there other treatment options available in patients with esophageal cancer who may not be candidates for stenting?

VK Yes. In the past, endoscopic laser therapy was used. It has fallen out of favor owing to the tedium associated with it and the relatively few centers and providers who are able to offer it anymore. Photodynamic therapy also was used in the past, but again is much less commonly

used now owing to the cost and patient inconvenience related to light exposure posttreatment. For smaller tumors, argon plasma coagulation can be used, but it is relatively ineffective for larger bulkier tumors. As previously mentioned, spray cryotherapy definitely is an option as well. A lot of patients will undergo definitive chemoradiation or just radiation alone, especially when dealing with squamous cell carcinoma, which tends to be more responsive to radiotherapy.

G&H What type of follow-up, including dietary recommendations, is needed in patients after stent placement?

VK This is a very important aspect of this intervention that providers, patients, and their family need to pay very careful attention to. Once the stent has been placed, patient education and adherence to post-stent dietary and lifestyle modifications are very important. Despite restoration of endoluminal patency, patients need to be on a liquid or puree diet on the day of the procedure as the stent expands radially, and this process may take up to 24 to 48 hours depending on the degree of obstruction.

Patients should avoid alcohol or other irritants. Typically, soft foods can be consumed on the second day, and patients should chew the foods properly, eat in an upright position, and drink liquids to help the passage of solid foods. Under no circumstances should patients be reclining or eating large amounts of food at one time. Even though the endoluminal patency has been restored, it is an artificial mechanical conduit that has been created and has its own limitations. Patients should also drink at least 4 ounces of water with pills and stay in an upright or sitting position for a couple of hours after each major meal. Finally, to mitigate the effects of reflux, patients should sleep with the head of the bed raised at a 30° to 45° angle. Providers are encouraged to spend time educating patients on these aspects to ensure the best outcome with stent placement and prevent complications (food impaction, aspiration).

G&H What areas of esophageal cancer need further research?

VK In medicine, particularly when dealing with cancer, research is the gateway to real progress. We have come a long way in our understanding of the medical-surgical aspects of esophageal cancer treatment, as well as overall patient well-being and quality-of-life aspects. Research in a few different areas is gaining traction. A lot of time, effort, and money have been invested in developing new technology and modalities for screening and surveillance of Barrett esophagus and early esophageal cancer. For

example, adjunctive tissue sampling modalities are now available, such as the wide-area transepithelial brush biopsy with 3-dimensional computer-assisted analysis, also known as the WATS^{3D} device (CDx Diagnostics), which enhances the yield of Barrett esophagus and dysplasia/neoplasia detection at endoscopy.

Additionally, a predictive analytics–based test is now commercially available (TissueCypher, Castle Biosciences) in which the tissue sample is used to assess for genetic mutations that may be able to predict the probability of neoplasia in a patient during a 5-year future time frame. There are new devices that are available commercially and also in clinical trials (Cytosponge, Medtronic; EsoCheck, Lucid Diagnostics) in which sponges or small capsules are swallowed by the patient and the sample obtained is checked for dysplasia, neoplasia, and so forth.

The second area that has received a lot of interest is improvement of the quality of surveillance in patients with Barrett esophagus, with an eye to improve the quality and diagnostic yield of surveillance as well as help reduce or eliminate the chances of interval cancer. Interval cancer is a malignancy that develops between 2 timed endoscopic surveillance events and generally reflects poor examination quality and lack of adherence to established guidelines and best practice. One recent area of research in patients with advanced malignancy has evaluated the

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role of spray cryotherapy as a neoadjuvant prelude to chemoradiation or as a combined modality with ongoing chemoradiation, with treatment sessions separated by defined time intervals, as reported by Shah and colleagues as well as in an oral presentation by Kachaamy. In the latter, patients received the established standard of care (such as chemoradiation) but also intermittently received liquid nitrogen spray cryotherapy. This pilot study was presented at Digestive Disease Week 2022 and received a lot of attention. This will be an area of increased interest going forward (ie, combining systemic therapy with local [endoluminal] tumor ablation), whether it is cryotherapy or other endoscopic therapies.

In the realm of oncology, recently the US Food and Drug Administration approved 2 immunotherapy agents

(pembrolizumab [Keytruda, Merck] and nivolumab [Opdivo, Bristol Myers Squibb]) for esophageal cancer, and they can be combined with standard chemotherapy and/or are being investigated as stand-alone treatments. The National Comprehensive Cancer Network also recommended immunotherapy in its revised treatment guidelines (April 2022), thus endorsing this major advance in esophageal cancer treatment.

On the surgical side, progress has been made in offering minimally invasive surgery techniques with or without robotics that minimize the amount of chest trauma and allow for a more complete resection with less morbidity compared with traditional surgery. There is a lot of interest in molecular profiling of cancer and developing personalized targeted therapies for each individual cancer, which will be the trend of the future. Other areas that require further research include the best approach to managing early invasive cancer (ie, T1b pathology), as well as evaluating quality-of-life issues, patient wellness, and treating patients using holistic therapies, above and beyond traditional medical-surgical options.

The treatment paradigm for esophageal cancer has shifted to a true multimodality approach in which it is not just the endoscopists, surgeons, or the gastrointestinal oncologists who work alone, but they all come together

and try to provide the best treatment paradigm for a particular patient. That is where the key to success lies in this field. It is an extremely important concept to ensure that the best quality, evidence-driven care is delivered to the patient in an attempt to ensure the best outcomes.

Disclosures

Dr Kaul has been a consultant for Steris, CDx Diagnostics, Cook Medical, Motus GI, and Ambu.

Suggested Reading

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