

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Prateek Sharma, MD

The Role of Endoscopic Ultrasound in Esophageal Cancer



Douglas O. Faigel, MD
 Chairman, Division of Gastroenterology and Hepatology
 Professor of Medicine
 Mayo Clinic
 Scottsdale, Arizona

G&H How common is esophageal cancer, and what are the main risk factors?

DF Esophageal cancer is not very common. Approximately 18,000 cases are diagnosed each year in the United States, with an incidence of 4 per 100,000. Two types of esophageal cancer exist: squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma is more common in people of color and makes up a little less than half of all cases of esophageal cancer. Risk factors include drinking and smoking. Adenocarcinoma is most commonly seen in white males and is associated with gastroesophageal reflux disease and obesity. Adenocarcinoma is increasing in incidence, whereas squamous cell carcinoma has been relatively stable if not slightly declining as fewer people smoke.

G&H When and how did endoscopic ultrasound emerge as a tool for evaluating and staging esophageal cancer?

DF Endoscopic ultrasound (EUS) was developed in the late 1980s and was introduced in the United States in the early 1990s. One of the first applications of this modality was to evaluate esophageal cancers. Prior to the use of EUS for staging cancer, computed tomography (CT) scan was the primary staging modality. However, CT scans were not as effective 30 to 40 years ago as

they are now, and clinicians realized that EUS allowed them to gather more information than they could with other existing techniques. EUS, being highly accurate in determining the stage of esophageal cancer, opened up this disease to stage-directed therapies.

G&H How does EUS compare to other imaging modalities or surgery for staging esophageal cancer?

DF The management of esophageal cancer is stage directed, meaning the appropriate therapy is chosen based on the patient's stage and other clinical characteristics. Surgery is the gold standard for staging esophageal cancer, but most patients are not sent directly to surgery without first undergoing preoperative therapy. When trying to determine the T stage (ie, the depth of tumor invasion), which is important for selecting therapy, EUS is the best local staging option. In terms of pretreatment staging, magnetic resonance imaging (MRI), CT scan, and positron emission tomography (PET) scan are all complementary to EUS. MRI does tend to have less of a role in the esophagus, however, and can be expensive and may display artifacts when assessing the lungs due to motion artifacts. CT scan has improved over the years, especially with the development of multidetector CT. CT scan is beneficial for identifying large masses and evaluating distant metastases in the liver and lungs, which

is an important feature as EUS cannot be used to look for lung metastases. PET scanning is also a very helpful modality. It may detect metastases that were subtle on CT scan, and can be useful in determining whether the

EUS allows clinicians to establish their patients' stage, which helps determine the type and order of treatment to pursue.

therapy seems to be working. PET scan works by detecting hypermetabolic tissue, which is usually indicative of cancer. If radiation or chemotherapy is effective, PET scan will show a decrease in hypermetabolism.

G&H What does the literature report regarding the use of EUS in staging superficial esophageal cancer?

DF Using EUS to stage superficial esophageal cancer is slightly controversial. EUS tends not to be able to discern the difference between the 2 earliest stages of esophageal cancer, T1a and T1b, but it does recognize when cancer is not at T2, T3, or T4 status. EUS is also useful when looking for lymph nodes. In my practice, I perform EUS before conducting endoscopic mucosal resection or endoscopic submucosal dissection for resection of superficial cancers just to confirm that the patient does actually have a superficial cancer, and not a cancer that is much deeper or that has metastasized to the lymph nodes.

G&H What is the role of EUS in the setting of advanced esophageal cancer?

DF It can be somewhat challenging to tell the difference between stages and to differentiate a T3 from a T4 cancer, clinically or with standard cross-sectional imaging such as CT scan. For example, I had a patient who had esophageal cancer that appeared to be resectable on CT scan but was shown to be clearly invading the aorta on EUS (T4). That made a major difference in the treatment decision, even though both imaging modalities displayed advanced, or at least locally advanced, cancer. On the other hand, if a patient has liver or other distant metastases, EUS is not needed as the patient is already stage IV.

The main limitation of EUS in larger tumors is that the malignant stricture may not allow the echoendoscope to be completely advanced through the tumor, resulting in incomplete staging. Dilation can be performed to allow complete staging, but it should be noted that aggressive dilation can result in an esophageal perforation, especially for more proximal tumors or squamous cell carcinomas. Thus, a careful approach is needed. For more advanced stages, clinicians should be cautious about using EUS and not causing more of a problem rather than helping.

G&H In which patients is the use of EUS indicated?

DF For the vast majority of patients who do not have metastatic disease, EUS is standard. EUS allows clinicians to establish their patients' stage, which helps determine the type and order of treatment to pursue. Treatment options may include chemotherapy, various types of radiation therapy, surgery, or endoscopic resection.

G&H What is the accuracy of EUS in evaluating lymph nodes? How does it compare to CT scan?

DF EUS is quite sensitive for detecting lymph nodes, and the sensitivity and specificity are higher when EUS is combined with fine-needle aspiration (FNA). Occasionally, patients will have enlarged lymph nodes that are benign because of inflammation, and FNA allows clinicians to determine more accurately whether those lymph nodes are malignant. The literature has reported that EUS-FNA also detects more adenopathy than what a CT scan shows.

Of note, FNA should not be used to evaluate the peritumoral nodes if the needle has to be passed through the tumor into the lymph node to sample it. The majority of clinicians are unwilling to do this, both out of concern for getting a false-positive by going through the tumor and for spreading the tumor to the lymph node if it is currently not in the lymph node.

Lymph nodes that cannot be aspirated should be regarded as malignant and treated accordingly by increasing therapy. For example, if a patient has a T2 tumor, he or she might undergo surgery without radiation or chemotherapy. However, if lymph nodes are seen behind the tumor and therefore cannot be aspirated, the lymph nodes should be regarded as positive and the patient should be given neoadjuvant therapy. A T2N0 tumor is stage I, but a T2N1 tumor is stage III. I would rather give the patient a little more therapy than not give the patient a therapy that he or she needs.

G&H Does EUS have value in postradiation and -chemotherapy staging?

DF Whether EUS can change the management in this setting can be debated, but EUS does have some value in determining whether a patient has responded to treatment, or if he or she has progressed through therapy and needs a different treatment. An EUS performed before and after therapy allows clinicians to compare certain aspects and identify changes. If the maximal thickness of the tumor dropped by at least half or is below 6 mm posttreatment, or if the cross-sectional area decreased by at least 50%, these are signs of downstaging and of response to therapy. On the other hand, it is difficult to tell whether a patient is a complete responder. There is a high false-negative rate with biopsies in the post-radiation therapy setting. If new nodes appear on EUS and are positive with FNA, that is a sign that the patient may need a change in therapy.

G&H What training is needed to perform EUS, and how significant is the learning curve?

DF EUS is a difficult technique to learn and comes with a significant learning curve. My institution offers a 1-year fellowship in advanced endoscopy that includes training in EUS as well as in endoscopic retrograde cholangiopancreatography. Someone seeking to perform EUS is best served by doing a fellowship where he or she can complete at least 300 EUSs supervised by an expert, especially if he or she is interested in performing all aspects of EUS, not just in the setting of esophageal cancer.

G&H What are the priorities of research in this area?

DF It is unclear whether or not patients who are thought to be complete responders need to undergo surgery. It would be beneficial to establish methods of identifying such patients who may not need surgery, and perhaps EUS could be used in this setting. There is interest in determining if there is a role for EUS with early esophageal cancer and if EUS can be used for treatment. Attempts have been made to use EUS-guided fine-needle injections to treat esophageal cancer, but the injections have not worked well thus far. Research is also needed to investigate the use of EUS to improve response to therapy by providing a local therapy.

Dr Faigel has no relevant conflicts of interest to disclose.

Suggested Reading

Attila T, Faigel DO. Role of endoscopic ultrasound in superficial esophageal cancer. *Dis Esophagus*. 2009;22(2):104-112.

DaVee T, Ajani JA, Lee JH. Is endoscopic ultrasound examination necessary in the management of esophageal cancer? *World J Gastroenterol*. 2017;23(5):751-762.

Krill T, Baliss M, Roark R, et al. Accuracy of endoscopic ultrasound in esophageal cancer staging. *J Thorac Dis*. 2019;11(suppl 12):S1602-S1609.

Lightdale CJ, Kulkarni KG. Role of endoscopic ultrasonography in the staging and follow-up of esophageal cancer. *J Clin Oncol*. 2005;23(20):4483-4489.

Misra S, Choi M, Livingstone AS, Franceschi D. The role of endoscopic ultrasound in assessing tumor response and staging after neoadjuvant chemotherapy for esophageal cancer. *Surg Endosc*. 2012;26(2):518-522.

Old OJ, Isabelle M, Barr H. Staging early esophageal cancer. *Adv Exp Med Biol*. 2016;908:161-181.

Zhang Y, He S, Dou L, et al. Esophageal cancer N staging study with endoscopic ultrasonography. *Oncol Lett*. 2019;17(1):863-870.