# The Role of EUS in Esophageal Cancer

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*Abstract*

Esophageal cancer is the fifth most common gastrointestinal cancer and the ninth leading cause of cancer death in the United States. The incidence of esophageal adenocarcinoma is on the rise. Accurate staging of esophageal cancer is critical for the selection of appropriate treatment. Endoscopic ultrasound (EUS) plays an important role in the staging of esophageal cancer. EUS provides a detailed view of the esophageal wall, helps determine tumor depth of infiltration, and can

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characterize lymph nodes as malignant or benign. As such, EUS is the most accurate modality for regional staging of esophageal cancer and is more accurate than computed tomography and positron emission tomography scan for the characterization of nodal status. EUS plays a limited role in the detection of metastatic disease and restaging after neoadjuvant therapy. This chapter elaborates on the role of EUS in the care of patients with esophageal cancer.

**Key Words:** EUS, Esophageal cancer, Staging, Barrett's esophagus

## INTRODUCTION

Esophageal cancer is the fifth most common gastrointestinal cancer and the ninth leading cause of cancer death in the United States. Every year, there are ~14,000 new cases of esophageal cancer diagnosed, of which ~8,000 are adenocarcinoma and 6,000 are squamous cell cancers. Adenocarcinoma of the esophagus has one of the fastest rising incidence rates of any malignancy in the United States (1). The outcome of esophageal cancer is strongly linked to its stage at diagnosis and the overall 5-year survival rate remains less than 20% (2). Accurate staging of esophageal cancer is critical for the selection of appropriate treatment. Endoscopic ultrasound (EUS) plays a central role in the staging of esophageal cancer and may also be important in detecting disease recurrence.

## DIAGNOSIS

The role of EUS in the initial diagnosis of esophageal cancer is limited to cases in which routine endoscopy has failed to make a diagnosis (3). Specifically, if biopsies or brush cytology during endoscopy are nondiagnostic and the clinical suspicion remains high for malignancy, then EUS can be performed with or without fine needle aspiration (FNA) for a definitive diagnosis (4).

## STAGING ESOPHAGEAL CANCER

Esophageal cancer is staged according to the TNM system established by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) (Tables 1–3) (5, 6). This system incorporates the depth of invasion of the primary tumor (T classification), the status of regional lymph nodes (N classification) and the presence or absence of distant metastases (M classification). The TNM classifications are then grouped into stages according to prognosis (Tables 2 and 3). The 5-year survival rate is more than 95%

**Table 1**
**TNM classification of esophageal cancer**

| | |
|---|---|
| T | Primary tumor |
| Tx | Tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| Tis | High-grade dysplasia |
| T1 | Tumor invades the lamina propria, muscularis mucosae (T1a) or submucosa (T1b), but does not breach the submucosa |
| T2 | Tumor invades the muscularis propria, but does not breach the muscularis propria |
| T3 | Tumor invades the adventitia |
| T4 | Tumor invades adjacent structures; T4a: resectable tumor invading the pleura, pericardium, or diaphragm, T4b: unresectable tumor invading other adjacent structures, such as aorta, vertebral body, trachea, etc. |
| N | Regional lymph nodes |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Metastasis in 1–2 regional lymph nodes |
| N2 | Metastasis in 3–6 regional lymph nodes |
| N3 | Metastasis in seven or more regional lymph nodes |
| M | Distant metastasis |
| M0 | No distant metastasis |
| M1 | Distant metastasis |



**Table 2**
**Anatomic stage/prognostic groups squamous cell carcinoma[a]**

| *Stage* | *T* | *N* | *M* | *Grade* | *Tumor location* |
|---|---|---|---|---|---|
| 0 | Tis (HGD) | N0 | M0 | 1, X | Any |
| IA | T1 | N0 | M0 | 1, X | Any |
| IB | T1 | N0 | M0 | 2–3 | Any |
| | T2-3 | N0 | M0 | 1, X | Lower, X |

[a] Or mixed histology including a squamous component or NOS

(continued)

**Table 2**
**(continued)**

| *Stage* | *T* | *N* | *M* | *Grade* | *Tumor location* |
|---|---|---|---|---|---|
| IIA | T2-3 | N0 | M0 | 1,X | Upper, middle |
| | T2-3 | N0 | M0 | 2–3 | Lower, X |
| IIB | T2-3 | N0 | M0 | 2–3 | Upper, middle |
| | T1-2 | N1 | M0 | Any | Any |
| IIIA | T1-2 | N2 | M0 | Any | Any |
| | T3 | N1 | M0 | Any | Any |
| | T4a | N0 | M0 | Any | Any |
| IIIB | T3 | N2 | M0 | Any | Any |
| IIIC | T4a | N1-2 | M0 | Any | Any |
| | T4b | Any | M0 | Any | Any |
| | Any | N3 | M0 | Any | Any |
| IV | Any | Any | M1 | Any | Any |

[b]Location of the primary cancer site is defined by the position of the upper (proximal) edge of the tumor in the esophagus

**Table 3**
**Anatomic stage/prognostic groups adenocarcinoma**

| *Stage* | *T* | *N* | *M* | *Grade* |
|---|---|---|---|---|
| 0 | Tis (HGD) | N0 | M0 | 1,X |
| 1A | T1 | N0 | M0 | 1–2, X |
| 1B | T1 | N0 | M0 | 3 |
| | T2 | N0 | M0 | 1–2, X |
| IIA | T2 | N0 | M0 | 3 |
| IIB | T3 | N0 | M0 | Any |
| | T1-2 | N1 | M0 | Any |
| IIIA | T1-2 | N2 | M0 | Any |
| | T3 | N1 | M0 | Any |
| | T4a | N0 | M0 | Any |
| IIIB | T3 | N2 | M0 | Any |
| IIIC | T4a | N1-2 | M0 | Any |
| | T4b | Any | M0 | Any |
| | Any | N3 | M0 | Any |
| IV | Any | Any | M1 | Any |

for stage 0 disease, 50–80% for stage I disease, 30–40% for stage IIA disease, 10–30% for stage IIB disease and 10–15% for Stage III disease (7). The median survival for patients with metastatic disease treated with palliative chemotherapy is less than 1 year (8).

Accurate staging is therefore important for determining prognosis, guiding appropriate therapy, and allowing the evaluation of treatment protocols. Increasing T classification itself corresponds to worsening 5-year survival rates. The 5 year-survival rate is 46, 30, 22, and 7% for T1, T2, T3, and T4 tumors, respectively (9). By guiding appropriate therapy and avoiding unnecessary treatment, accurate staging may also reduce the costs of care of esophageal cancer. A retrospective review of cases of esophageal cancer referred for preoperative staging identified 26% of patients with stage I and stage IV tumors that could be spared neoadjuvant chemoradiotherapy and surgery, respectively for an average cost savings of $3443 per patient (10).

## T STAGING

EUS is the most accurate modality for regional staging of esophageal cancer. It provides a detailed view of the esophageal wall and helps determine tumor depth of infiltration.

Standard endoscopes operating at frequencies of 7.5 and 12 MHz are able to visualize the esophageal wall as a five-layered structure. Understanding the ultrasound appearance of the five layers of the normal esophagus allows us to recognize the degree of tumor infiltration into the wall layers and thus stage the primary lesion. The first hyperechoic layer of the esophagus seen on EUS corresponds to the superficial mucosa, the second hypoechoic layer corresponds to the deep mucosa, the third hyperechoic layer corresponds to the submucosa, the fourth hypoechoic layer to the muscularis propria, and the fifth hyperechoic layer corresponds to the adventitia (11). T1a lesions invade the lamina propria or muscularis mucosae, while T1b lesions invade the submucosa. By EUS, this appears as a hypodense lesion that extends into the second or third layer, but not through the third layer (Fig. 1). T2 lesions invade but do not breach the muscularis propria, which corresponds to the invasion of the fourth ultrasound layer (Fig. 2). T3 lesions invade the periesophageal tissue, but do not invade adjacent structures. By EUS, this corresponds to invasion beyond the fourth echolayer (Fig. 3). Lastly, T4a lesions are generally considered resectable and invade the pleura, pericardium, or diaphragm while T4b lesions are considered unresectable lesions that invade other adjacent structures such as the aorta, vertebral body, trachea, etc. (Fig. 4).

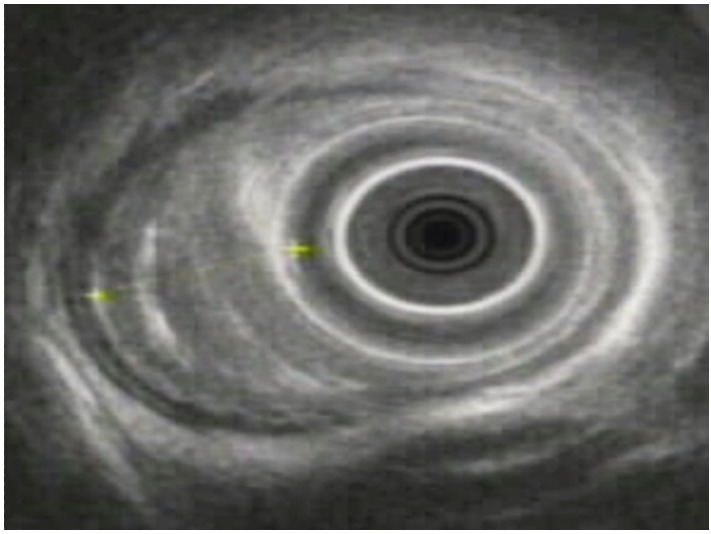

**Fig. 1.** T1b mass invading the submucosa but sparing the hypoechoic muscularis propria.

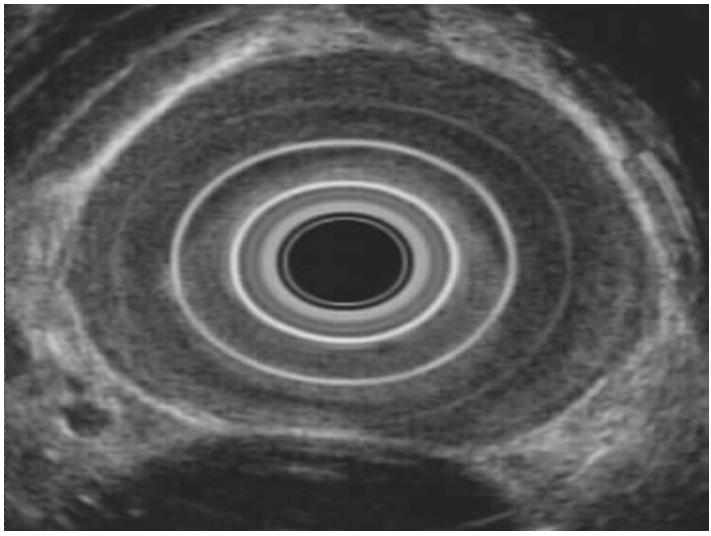

**Fig. 2.** A T2 cancer. The muscularis propria is involved, but the surrounding adventitia is not invaded.

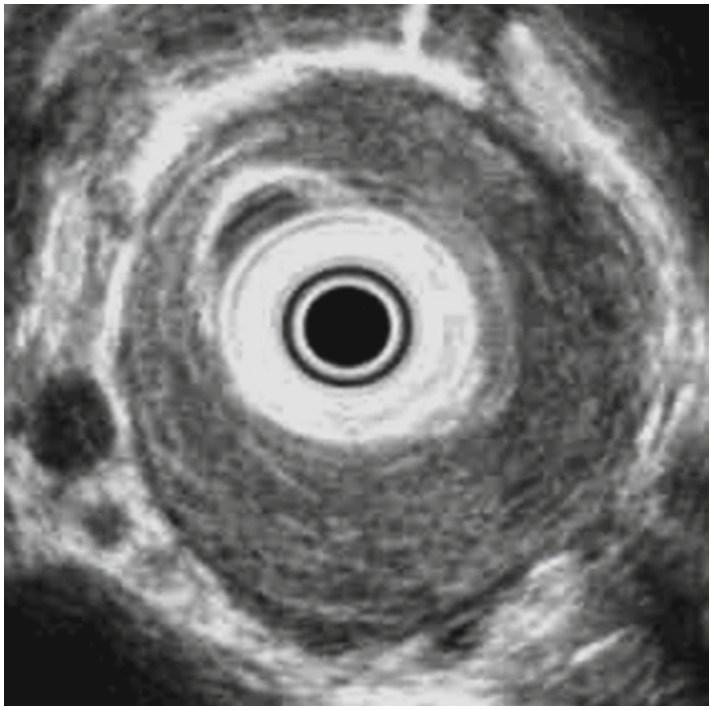

**Fig. 3.** A T3 tumor. The outer border of the tumor is irregular with pseudopod-like extension of tumor noted at the 6 o'clock position.

The choice of using either a transverse- or linear-array echoendoscope for esophageal cancer staging is likely influenced more by operator experience than superiority of one instrument over the other. One prospective study with 43 patients compared staging of esophageal and gastric cancers using transverse-array and linear-array echoendoscopes (12). Both instrument types provided similar T classifications; however, transverse-array instruments yielded better detection of lymph nodes. Another prospective study with 104 patients found excellent agreement in TNM staging between linear and radial endoscopes with similar accuracy stage for stage (13). Overall, the choice of echoendoscope should be tailored to each patient's clinical scenario and ideally, one should maintain efficiency while maximizing the quality of the exam (14). For example, a T3 tumor with suspected celiac nodes based on computed tomography (CT) may be best staged with only a linear-array echoendoscope to permit both T staging and FNA of the celiac nodes. A suspected T1 lesion without nodes on CT may be better staged with a transverse-array or radial echoendoscope.

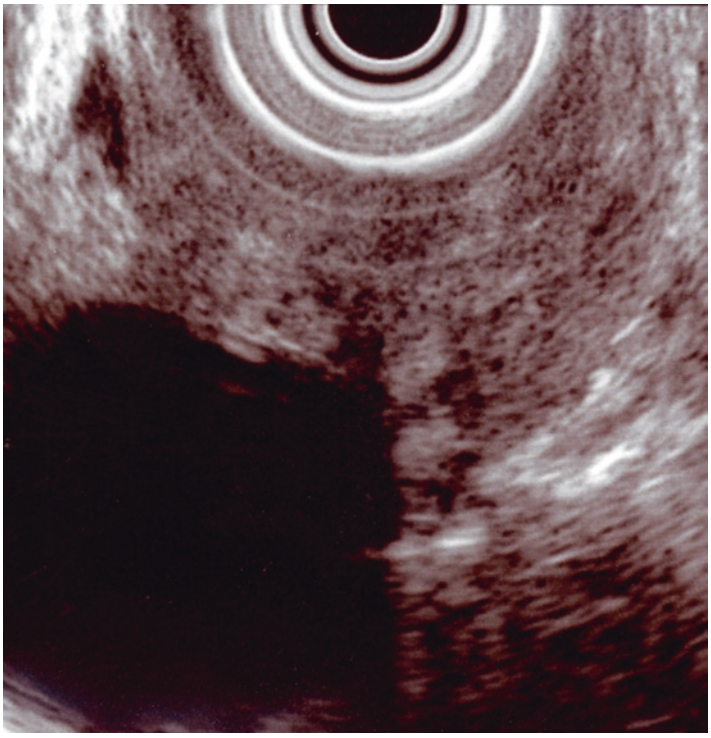

**Fig. 4.** A T4b tumor with invasion into the aorta noted by the loss of interface between the tumor and the great vessel.

A large body of literature supports EUS as the most accurate modality for local staging of esophageal cancer when compared to direct visualization endoscopy, CT, and positron emission tomography (PET) scanning. A review of 21 series found that EUS was 84% accurate for the prediction of T class (15). Other studies have found that the accuracy of EUS for T staging with most radial scanning 7.5–12 MHz transducers is between 75 and 92% compared to CT which has an accuracy of 42–60% (16–20).

However, the accuracy of EUS for staging of esophageal cancer varies by T classification (21). EUS is more reliable for staging T3 and T4 tumors, with accuracies of 89–94% and 88–100%, respectively, than it is for T1 and T2 tumors, with accuracies of 75–84% and 64–85%, respectively (16, 22). In particular, T2 lesions appear to be the most challenging because they are subject to overstaging (22, 23). EUS can differentiate T1 and T2 lesions from T3 or T4 lesions with 87% accuracy, 82% sensitivity, and 91% specificity (24).

High frequency miniprobe catheters (15–30 MHz) provide a more detailed visualization of the mucosa and submucosa, and their use therefore increases the accuracy of staging T1 and T2 tumors to 83–94% (25). One study of 22 patients compared preoperative staging by miniprobe with EUS, using surgical pathology as the gold standard. The accuracy of T staging was 86% for mucosal carcinoma and 94% for submucosal carcinoma using the miniprobe compared to 71% for mucosal carcinoma and 78% for submucosal carcinoma using standard frequency echoendoscopes (26). Therefore, miniprobes play an important role in the evaluation of superficial lesions being considered for nonsurgical treatment, including endoscopic mucosal resection (EMR) or photodynamic therapy (PDT). If disease is limited to the mucosa by EUS, EMR may be undertaken to provide pathologic staging useful in the management of early cancer or high grade dysplasia (27).

## N STAGING

The TNM system for nodal staging of esophageal cancer has recently changed with an emphasis on both the location of lymph nodes as well as the number of lymph nodes since the data demonstrate that the number of regional lymph nodes containing metastases is the most important prognostic factor (Fig. 5). Regional lymph nodes extend from

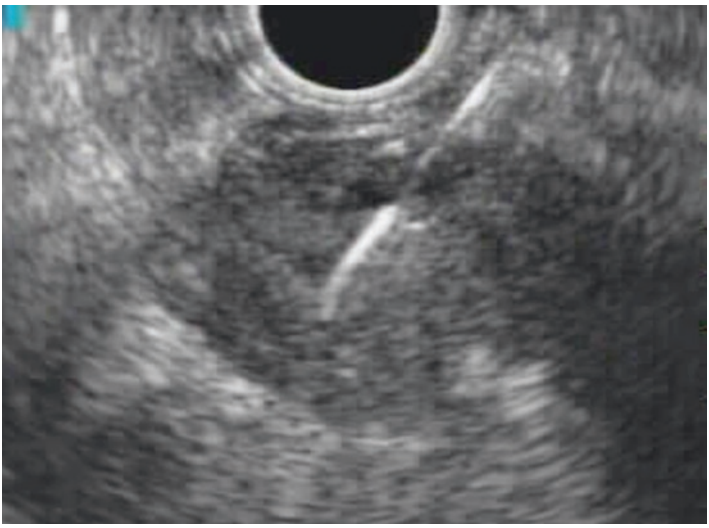

**Fig. 5.** FNA of a subcarinal lymph node. The needle is the white line entering the hypoechoic node at the 1 o'clock position lymph node.

periesophageal cervical nodes to celiac nodes. A major difference between the old and new (as of 2010) staging system is that the involvement of a celiac lymph node is considered regional (N) and no longer metastatic disease (M1a).

An increasing number of malignant regional lymph nodes detected by EUS are associated with poorer survival in patients with esophageal cancer. In a retrospective case series of 85 patients with esophageal adenocarcinoma, those with 0, 1–2, and >2 malignant-appearing lymph nodes had median survivals of 66, 14.5, and 6.5 months, respectively (28).

EUS is one of the most accurate modalities available for the staging of regional lymph nodes. When examining lymph nodes by EUS, there are several features that can help predict malignancy. Size greater than 1 cm, round shape, sharply demarcated borders, and hypoechoic echotexture are all suggestive of malignancy. When all four features are present, the accuracy of these predictors is 80%; however, only a minority of lymph nodes will have all four features present at once (29, 30). The overall accuracy of EUS for N staging is 75–80% compared to CT scan, which has an overall accuracy of 51–74% (15, 17–19, 22). EUS is also superior to PET scan, which has an accuracy of 37–90% (31–34). In a prospective study of 75 patients with newly diagnosed esophageal cancer, the sensitivity and specificity for nodal involvement by modality were 86 and 67% for EUS, 84 and 67% for CT, and 82 and 60% for PET (20).

There are subtle differences in the ability of EUS to differentiate benign from malignant lymph nodes based on location. For example, EUS is more accurate when staging celiac lymph nodes than mediastinal lymph nodes. EUS has a sensitivity of 83%, specificity of 98%, and an accuracy of 95% for celiac lymph nodes compared to mediastinal lymph nodes, for which EUS has a sensitivity of 79%, specificity of 63% and an accuracy of 73% (35). The accuracy of N1 classification is higher than for N0 (89% vs. 69%) (15).

The use of FNA improves the ability of EUS to confirm malignant adenopathy. In a large multicenter trial of 171 patients with upper GI lesions, EUS with FNA for N classification was found to have a sensitivity of 92%, specificity of 92%, positive predictive value of 100%, and a negative predictive value of 86% with an overall accuracy of 92% (36). EUS with FNA has a superior accuracy to EUS alone with a rate of 87% compared to 74%, respectively in one series (37). In patients who have already undergone CT scan for staging of their esophageal cancer, EUS with FNA may change the tumor stage in a significant number of cases (38% in one series) (37). When performing FNA, at least three passes should be made to maximize sensitivity (38).

One limitation of FNA is the inability to aspirate lymph nodes that are located behind the primary tumor. Passage of a needle through the tumor to access the lymph node for aspiration can lead to contamination of the specimen with malignant cells from the primary tumor itself. Complications from FNA for staging of esophageal cancer are rare (39).

A selective approach to EUS-FNA for preoperative nodal staging of esophageal cancer has been evaluated in an attempt to minimize cost and address situations in which EUS-FNA is not technically feasible. Vazquez-Sequeiros et al. performed a prospective study of 144 patients with esophageal cancer who were evaluated with EUS. They found that a modified set of criteria, including the four standard criteria for malignant adenopathy (size, shape, borders, echotexture) helped predict malignancy (20, 40). The additional features included in their prediction model were the presence or absence of celiac lymph nodes, the number of lymph nodes (>5 vs. ≤5) and EUS T stage (T3/T4 vs. T1/T2). When the presence of at least one criterion was used as indicating N1 stage, sensitivity approached 100%, and when the presence of ≥6 criteria was used to indicate N1 stage, specificity approached 100%. In this study, the investigators found that a selective use of FNA might have avoided performing FNA in 42% of patients. These modified criteria may help the endosonographer better select which lymph nodes to target in order to enhance the diagnostic yield of EUS-FNA. The current standard of care is to perform EUS-FNA whenever feasible to maximize staging accuracy (41, 42).

In addition to FNA, elastography is emerging as another technique with the potential to improve staging. Elastography uses concepts similar to ultrasonography to convey information about the firmness of a tissue in response to compression (43). The clinical utility of elastography is based on the fact that malignant tissues are typically harder than benign tissues. Elastography software can be incorporated into EUS processors, making it an adjunctive technique during EUS, just as Doppler has become integrated into endosonography. Elastography may help distinguish benign from malignant lymph nodes, thereby allowing the endoscopist to select which nodes should be preferentially aspirated. It may also prove useful when staging nodes deemed inaccessible due to intervening vessels or adjacent tumor (44).

One study using EUS-elastography to distinguish benign from malignant nodes found a sensitivity and specificity of 100 and 50%, respectively (45). In another study with 78 lymph nodes (cervical, mediastinal, and abdominal), investigators found a sensitivity of 85%, specificity of 92%, and an accuracy of 88.5% (46). Before elastography becomes universally accepted, technical improvements must be made and reliable diagnostic algorithms will need to be established.

### *Staging in the Setting of Malignant Strictures*

Complete assessment by EUS may be limited in the setting of esophageal obstruction. The incidence of malignant strictures that restrict the passage of an echoendoscope is ~30% (47). Studies suggest that failure to traverse such a stricture results in significantly decreased accuracy for both T and N staging (48, 49). Similarly, failure to pass an echoendoscope beyond a malignant stricture is an accurate predictor of advanced T classification and poorer survival. More than 90% of patients with a nontraversable stricture have stage III or IV disease (49). Median survival in patients with a nontraversable stricture is ~10 months compared to those without a stenosis, who have a median survival of ~20 months (50).

When faced with an obstructing malignant stricture, the endosonographer can choose to limit the EUS exam to the proximal tumor margin, perform esophageal dilation to permit passage of the echoendoscope, or attempt staging with a miniprobe (under direct visualization if a standard endoscope can traverse the stricture or blindly through the stricture). Stricture dilation may permit complete cancer staging, including the evaluation of the celiac axis, but it carries a risk of perforation estimated to range from 0 to 24% (48, 49, 51–53). Esophageal dilation may be performed using Savary-type wire-guided dilators or through-the-scope (TTS) balloon dilators.

In one study of 267 EUS examinations, 81 patients (30%) required dilation. Dilation was performed using Savary-Guillard wire-guided dilators in a gradual, step-wise fashion to a diameter of 9–18 mm. Successful dilation allowing the passage of the echoendoscope was accomplished in 85% of all patients and 94% of cases where the stricture was dilated to ≥14 mm (52). There were no complications. The accuracy of T staging after dilation, however, was only 61% which may indicate that trauma from the procedure disrupted normal tissue planes. In another study with 42 cases, Savary wire-guided dilations were carried out without fluoroscopy to a maximum diameter of 16 mm and no complications occurred (53). Dilation provided critical staging information in 19% of cases, including the detection of metastases (seven cases) and upstaging of a T3 tumor to T4 (one case). In 45% of these cases, celiac or retroperitoneal lymph nodes were found. Dilation to at least 14 mm diameter provided complete staging in 87% of patients. Dilation to 12.8 mm was insufficient to complete EUS with a 74% failure rate.

TTS balloon dilators may help complete staging in up to 95% of patients. In a multicenter retrospective study with 272 cases, 28% of cases required dilation (54). EUS was performed with a radial echoendoscope and FNA was then performed with a curved linear echoendoscope where

appropriate. Dilation was performed through at least two balloon sizes, but usually through three sizes of a single balloon without fluoroscopy. In this series, there were two perforations, one during EUS with dilation, and one during EUS without dilation. The perforation associated with dilation occurred when a TTS balloon was inflated directly to 16.5 mm. Nineteen percent of patients who required dilation had celiac adenopathy (previously considered M1a disease), and the authors concluded these nodes would have been missed had dilation not been undertaken. TTS balloon dilators may have advantages over bougienage because it does not require repeated esophageal intubations or fluoroscopy.

An alternative to dilation is to use either catheter miniprobes or, when available, a 7.5 MHz nonoptical, wire-guided esophagoprobe made by Olympus (MH908; Olympus America, Melville, NY). Mallery and Van Dam compared EUS outcomes at one institution before and after the introduction of the wire-guided MH908 esophagoprobe (47). They found the rate of complete staging increased from 60 up to 90% with an increased detection rate for metastatic disease (34% vs. 11%). One drawback of the use of such radial-array EUS probes in this setting is the inability to perform FNA of any visualized lymph nodes.

## M STAGING

Patients with distant metastasis are not amenable to surgical resection and are candidates for palliative treatment only. Distant metastases from esophageal cancer occur in nonregional lymph nodes, the liver (35%), the lungs (20%), bone (9%), adrenal glands (2%), the brain (2%), and the spleen, pancreas, stomach, and pericardium (1%) (55).

The AJCC TNM M classification is characterized by the presence (M1) or absence (M0) of metastases. With the new classification, M1 is no longer further subdivided into distant lymph node metastases (M1a) and other metastases (M1b) as this was not found to be useful (Table 1). In the past, this distinction between M1a and M1b was felt to be clinically relevant as the treatment may differ between the two. In many tertiary care centers, M1a disease is treated with induction chemoradiotherapy followed by surgery with the goal of cure, whereas M1b stage is treated with palliative measures only. M1a tumors have a better 5-year survival than M1b disease (6 vs. 2%) (56). In the new classification system, celiac lymph node involvement is considered regional nodal disease (N), while all distant disease is considered metastatic (M1).

Radiological imaging, with PET or CT scanning, is superior to EUS when screening for M1 disease. PET scan may be the most accurate tool

in this setting. In one study of 100 patients with esophageal cancer, PET scanning had a sensitivity of 69%, and an accuracy of 84% compared with CT scanning which had a sensitivity of 45% and an accuracy of 63% (57). A recent prospective study of 75 patients with newly diagnosed esophageal cancer evaluated by PET, CT, and EUS found similar performance for the detection of metastatic disease with PET and CT scan, which were both superior to EUS (20). PET scanning and CT scanning had sensitivity of 81% and specificity of 91 and 82%, respectively, for the detection of metastatic disease compared to sensitivity of 73% and specificity of 86% with EUS.

Some data suggests that EUS may be useful in screening for occult liver metastasis, which when small (<1 cm), can be missed by CT and even PET. Detection of occult liver metastases may help avoid unnecessary surgery. EUS, however, can only adequately assess the left hepatic lobe.

In a retrospective study of 98 patients with cancer of the esophagus or cardia, EUS found lesions suspicious for metastases in 7% of cases (58). FNA confirmed metastatic disease in four patients, while the fifth patient had a liver metastasis missed because of a falsely negative fine needle aspirate. The median size of the metastatic liver lesions was 5 mm, and they were all missed by CT or PET. Another study found that EUS detected metastatic liver lesions overlooked by conventional, cross-sectional CT imaging in 2% of cases (59).

## RESTAGING

Tumor restaging by EUS after neoadjuvant chemoradiotherapy may help identify patients whose tumors have progressed in stage to T4 or M1, and who are thus no longer surgical candidates. However, PET scan is emerging as the most accurate modality for predicting pathologic tumor response and serves as an independent predictor of survival. The accuracy of PET and integrated PET/CT in this setting ranges from 76 to 89% (60, 61).

EUS is inaccurate for restaging after neoadjuvant therapy as chemotherapy and radiation result in significant inflammation and fibrosis that can have the same sonographic appearance as tumor. The inflammatory response and necrosis within the esophageal wall may be most pronounced within 2 weeks of completing neoadjuvant therapy, making this a particularly inaccurate period for EUS. In one retrospective study of 97 patients treated with neoadjuvant chemoradiotherapy, posttreatment EUS was only 27% accurate in predicting stage (62). Downstaging by EUS did not predict the absence of residual tumor at surgery. In another

retrospective study of 49 patients with stage II or III esophageal cancer, EUS was able to distinguish T1/T2 tumors from T3 tumors in only 26% of cases (63). The authors found that using the criterion of a greater than 50% reduction in tumor thickness by EUS was only 44% sensitive and 75% specific to predict down staging (63). A second limitation of EUS after neoadjuvant therapy is that lymph nodes may shrink in size but still contain micrometastases that will be missed by endosonography. In one study, the accuracy of EUS without FNA for detecting malignant adenopathy after chemotherapy was only 64% (62).

Some have hoped that EUS after neoadjuvant treatment might at least help predict survival. For example, Chak et al. evaluated the change in maximal cross-sectional area of a tumor as measured by EUS before and after chemoradiotherapy in 59 patients (64). They considered a 50% reduction in area as a response. They then followed patients for a median of 19 months and found a significant difference in survival between responders, whose median survival was 17.6 months, and nonresponders, whose median survival was 14.5 months. In another prospective study of 41 patients, a 50% reduction in maximal tumor cross-sectional area correlated with pathologic tumor regression (65). EUS correctly predicted a positive response in 87% of patients and correctly predicted failure to respond in 77% of patients. However, the clinical utility of this information may be limited, and the routine measuring of tumor cross-sectional area has not become a widespread practice.

## DETECTING TUMOR RECURRENCE

Tumor recurrence is the most common cause of mortality in patients who have undergone resection. Approximately 50% of patients develop recurrent disease within 2 years of surgery. Postsurgery surveillance with EUS, or even standard endoscopy, is not part of routine follow-up care. However, studies have shown that EUS can detect cancer recurrence with a positive predictive value of 75–100% (66, 67). EUS is more sensitive than endoscopy in detecting locoregional recurrence, as recurrent disease is often extramucosal. In addition, fibrosis may be misinterpreted as recurrent cancer on CT, leading to misdiagnosis. In a study of 40 patients who underwent surgical resection of esophageal cancer, 10% had an unsuspected anastamotic recurrence diagnosed by EUS despite a negative CT (66). Similarly, in a study of 43 patients undergoing routine surveillance EUS every 6 months for at least 2 years after surgery, two-thirds did not have symptoms when recurrent disease was found (67). Whether or not the early detection of cancer recurrence after surgery impacts survival remains unknown.

## BARRETT'S ESOPHAGUS

Barrett's esophagus is the most important risk factor for the development of adenocarcinoma of the esophagus. Patients with high-grade dysplasia or early adenocarcinoma are candidates for local endoscopic therapy with EMR or PDT. The role of EUS in Barrett's esophagus is to accurately diagnose superficial lesions in order to guide local, organ-sparing therapy and to exclude those with lymph node involvement that warrant surgical treatment.

Buskens et al. retrospectively examined preoperative EUS results from 77 patients who underwent subtotal esophagectomy for high-grade dysplasia or T1 adenocarcinoma (68). The authors found that EUS correctly predicted the absence of lymph node metastases in 93% of patients. Tumors that did not penetrate beyond the first third of the submucosal layer (m1, m2, m3, or sm1) did not have lymph node metastases. The negative predictive value of EUS for submucosal invasion and lymph node metastases was 95 and 93%, respectively. Infiltration of the tumor beyond the first third of the submucosal layer on EUS was a significant predictor of the presence of lymph node metastases. A study of 22 patients with Barrett's esophagus complicated by high-grade dysplasia or intramucosal carcinoma compared preoperative EUS findings to surgical pathologic evaluation (69). The authors found that preoperative EUS had 100% sensitivity, 94% specificity, and 100% negative predictive value for submucosal invasion and 100% sensitivity, 81% specificity, and 100% negative predictive value for lymph node involvement. EUS has also been shown to be superior to CT scan for T and N staging in early Barrett's cancers (70). EUS has not been shown to be effective for surveillance in Barrett's esophagus with high grade dysplasia or early carcinoma after the treatment with PDT (71).

## QUALITY INDICATORS

The combined American Society of Gastrointestinal Endoscopy/American College of Gastroenterology Taskforce on Quality in Endoscopy developed several quality indicators specifically related to EUS in the setting of esophageal cancer staging (42). These include (1) using the AJCC/UICC TNM staging system when describing tumor and node findings, (2) documentation of celiac axis visualization in cases without obstruction, and (3) performing EUS-guided FNA of suspicious celiac lymph nodes when staging an intrathoracic tumor.

## CONCLUSION

EUS plays an important role in the care of patients with esophageal cancer. In particular, EUS is essential in staging of the primary esophageal tumor and its nodal status. Although there is no consensus on an optimal staging strategy, EUS, CT scan, and PET scan should be considered complimentary modalities in the accurate staging of esophageal cancer. EUS in this setting is safe, with risks similar to standard upper endoscopy. Advancements in technology, such as elastography, may help further enhance the accuracy and efficiency of EUS. Future studies should address the impact of EUS on patient outcomes.

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