Esophageal Cancer
Tumor-Node-Metastasis Staging

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KEYWORDS

• Esophageal cancer • TNM staging system • Endoscopic ultrasound • Computed tomography
• FDG positron emission tomography/computed tomography

KEY POINTS

- Squamous cell carcinoma and adenocarcinoma represent more than 90% of cases of esophageal cancer, the latter of which is the most prevalent histologic subtype in North America.
- The most commonly used scheme for staging esophageal cancer is the eighth edition of the American Joint Committee on Cancer/The International Union for Cancer Control TNM system.
- The T category ranges from Tis (high-grade dysplasia) to T4 (invasion of the primary tumor into adjacent structures).
- The N category is subdivided into the following components based on the number of involved regional lymph nodes: N1—1 to 2 lymph node metastases, N2—3 to 6 lymph node metastases, and N3—greater than 6 lymph node metastases.
- The M category includes M0 (no metastasis) and M1 (nonregional lymph nodal metastasis and distant visceral metastasis) subcategories.

INTRODUCTION

Esophageal cancer is a relatively uncommon malignancy in the United States, although its incidence has been increasing since the 1980s. It currently ranks seventh in terms of incidence and sixth in overall mortality worldwide.[1] The 2 most common histologic types of esophageal cancer are squamous cell carcinoma (SCC) and adenocarcinoma (AC), representing more than 90% of all cases.[2] SCC accounts for more than 80% of all cases worldwide and is the predominant histologic type in less developed countries. In contrast, AC represents more than 60% of all cases in North American, Australia, and Europe.[3,4]

The treatment of esophageal cancer is stage-specific in order to ensure the best possible clinical outcomes. The treatment plan typically includes surgical resection for early disease, multimodality treatment with neoadjuvant chemotherapy, or combined chemoradiotherapy followed by surgery for patients with locally advanced cancer and systemic therapy for patients with metastatic disease. Accordingly, accurate pretreatment staging is important to ensure the development of appropriate treatment plans. The most commonly used staging for esophageal cancer is the eighth edition of the American Joint Committee on Cancer (AJCC)/The international Union for Cancer Control (UICC) TNM system. TNM staging includes determination of the depth of local invasion by the primary tumor (T), the presence and number of regional lymph nodes involved (N), and the presence or absence of distant metastasis (M). Because of differences in epidemiology, pathogenesis, location, and

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outcomes of the major histologic subtypes, TNM staging is separate for AC and SCC and takes into account the differences in prognosis between clinically and pathologically staged patients. In this regard, clinical (cTNM) staging before treatment and pathologic (pTNM) staging after surgical resection are used. The eighth edition of the TNM system also includes an additional stage grouping for patients who have undergone neoadjuvant therapy and surgical resection (ypTNM).[4–6]

Tumor-Node-Metastasis Staging System

Categories and subcategories are used in cTNM, pTNM, and ypTNM staging.[4–6] The T category represents the primary tumor, and the subcategories describe the depth of local invasion (T1–T4). Lymph node metastasis is designated by the N category, and the subcategories (N0–N3) describe the number of regional lymph nodes. The M category represents distant metastatic disease and includes subcategories describing its absence (M0) or presence (M1) (**Fig. 1**). Nonanatomic categories comprise histologic cell type, grade of differentiation (G), and location (L) of the primary tumor. Categories G and L are used only for pTNM. These anatomic and nonanatomic categories and subcategories are used to determine cTNM (based on imaging studies and histology obtained by biopsies) (**Table 1**) and pTNM (**Table 2**) and ypTNM (both based on pathology of the resected specimen) (**Table 3**).

ANATOMIC CATEGORIES

Clinical TNM

Currently, clinical staging of patients with esophageal cancer includes multimodality evaluation using a combination of esophagogastroduodenoscopy/endoscopic ultrasound (EUS); EUS–fine-needle aspiration (FNA); computed tomography (CT) of the chest, abdomen, and pelvis; and fluorodeoxyglucose (FDG) PET/CT. CT and FDG PET/CT complement each other in the evaluation of esophageal cancer cases. Conventional contrast-enhanced CT generally provides higher-quality images, particularly of the lungs, whereas FDG PET/CT provides functional and anatomic information useful in baseline staging and the evaluation of therapeutic response.

Primary Tumor (cT)

The esophageal wall is composed of 3 distinct layers—mucosa, submucosa, and muscularis propria. There is no serosa, and the muscularis

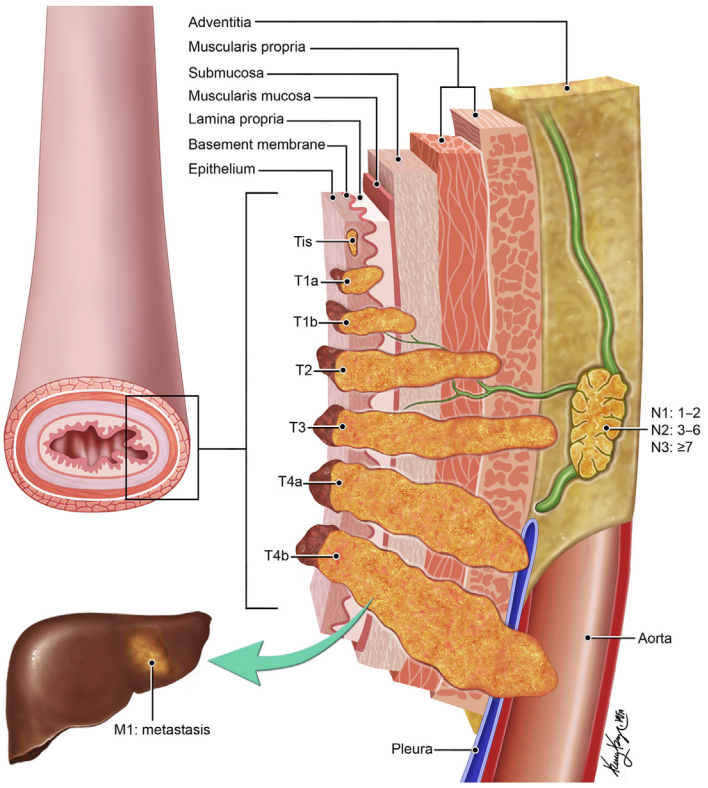

Fig. 1. TNM anatomic categories include the primary tumor (T), regional lymph node (N), and distant metastases (M). The T category provides information regarding the extension of tumor invasion into the esophageal wall. The N category represents regional lymph node involvement, and the M category represents metastasis to distant organ/s.

Table 1
Clinical TNM stage groups

Clinical TNM Adenocarcinoma

Stage	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
IIA	T1	N1	M0
IIB	T2	N0	M0
III	T2–3	N1	M0
	T3–4a	N0–1	M0
IVA	T1–4a	N2	M0
	T4b	N0–2	M0
	T1–4	N3	M0
IVB	Any T	Any N	M1

Clinical TNM Squamous Cell Carcinoma

Stage	T	N	M
0	Tis	N0	M0
I	T1	N0–1	M0
II	T2	N0–1	M0
	T3	N0	M0
III	T3	N1	M0
	T1–3	N2	M0
IV	T4	N0–2	M0
IIIA	T1–T2	N2	M0
	T1–4	N3	M0
IVA	T4	N0–2	M0
IVB	Any T	Any N	M1

The cTNM is separate for AC and SCC, given the differences in epidemiology, pathogenesis, location and outcomes of both subtypes. cTNM is based on imaging and biopsy specimens.

propria is contiguous with the periesophageal connective tissue or adventitia. The depth of local tumor invasion (T) is determined by the involvement of each of these histologic layers and adjacent structures. The absence of a serosa facilitates local tumor invasion into the pleura, pericardium, diaphragm, and peritoneum.[7] The T subcategory ranges from Tis (high-grade dysplasia) to T4 (tumor invasion into adjacent structures) (see **Fig. 1**). Malignant cells in the epithelium confined by the basement membrane are categorized as Tis. T1 tumors are subdivided into T1a (tumor confined to the submucosa) and T1b (invasion of the submucosa) components. T2 lesions invade the muscularis propria and T3 tumors invade the adventitia. T4 lesions invade adjacent structures and are subdivided into T4a (potentially resectable invasion of the pleura, pericardium or diaphragm) and T4b (typically unresectable invasion of other

Table 2
Pathologic TNM stage groups

Pathologic TNM Adenocarcinoma

Stage	T	N	M	G
0	Tis	N0	M0	N/A
IA	T1a	N0	M0	G, X
IB	T1a	N0	M0	G2
	T1b	N0	M0	G1–2, X
IC	T1	N0	M0	G3
	T2	N0	M0	G1–2
IIA	T2	N0	M0	G3, X
IIB	T1	N1	M0	Any
	T3	N1	M0	Any
IIIA	T1	N2	M0	Any
	T2	N0–1	M0	Any
IIIB	T4a	N1–2	M0	Any
	T3	N1	M0	Any
	T2–3	N2	M0	Any
IVA	T4a	N2	M0	Any
	T4b	N0–2	M0	Any
	T1–4	N3	M0	Any
	T1–4	N0–3	M1	Any

Pathologic TNM Squamous Cell Carcinoma

Stage	T	N	M	G	Location
0	Tis	N0	M0	1, X	Any
IA	T1a	N0	M0	G1, X	Any
IB	T1b	N0	M0	G1, X	Any
	T1	N0	M0	G2–3	Any
	T2	N0	M0	G1	Any
IIA	T2	N0	M0	G2–3, X	Any
	T3	N0	M0	G1	Upper/ middle
IIB	T3	N0	M0	G2–3	Upper/ middle
	T3	N0	M0	X	Any
	T3	N1	M0	Any	X
	T1	N1	M0	Any	Any
IIIA	T1	N2	M0	Any	Any
	T2	N1	M0	Any	Any
IIIB	T4a	N0–1	M0	Any	Any
	T3	N1	M0	Any	Any
	T2–3	N2	M1	Any	Any
IVA	T4a	N2	M0	Any	Any
	T4b	N0–2	M0	Any	Any
	T1–4	N3	M0	Any	Any
IVB	T1–4	N0–3	M1	Any	Any

The pTNM is based on pathologic findings after esophagectomy. Differences in survival profiles make it necessary to separate stage groups for AC and SCC.

Table 3
Postneoadjuvant pathologic TNM stage groups

Stage	T	N	M
I	T0–2	N0	M0
II	T3	N0	M0
IIIA	T0–2	N1	M0
IIIB	T4a	N0	M0
III	T3	N1–2	M0
	T0–3	N2	M0
IVA	T4a	N1–2, X	M0
	T4b	N0–2	M0
	T1–4	N3	M0
IVB	T1–4	N0–3	M1

ypTNM is identical for both AC and SCC and is based on the pathologic review of the resected specimen in patients who have had neoadjuvant therapy.

adjacent structures, such as aorta, vertebral body or trachea) components.[4–6]

EUS is considered the imaging modality of choice for determining cT, because it provides a detailed view of the esophageal wall layers and is the most accurate modality for assessing the depth of tumor invasion, with an overall accuracy of 71% to 92%[8,9] (**Fig. 2**). Because of differences in treatment and prognosis, accurate determination of the depth of invasion is important. In this regard, Tis and T1a lesions can be treated with endoscopic resection whereas T1b tumors require esophagectomy.[9–11] The accuracy of EUS, however, in differentiating between superficial tumors (cTis, cT1a, and cT1b) is limited. A meta-analysis evaluating the accuracy of EUS in determining cTis, cT1a, and cT1b compared with specimens obtained after endoscopic and surgical resection found a cT-stage concordance of only 65%. The investigators concluded that EUS is not sufficiently accurate in differentiating high-grade dysplasia and superficial ACs.[12] In another meta-analysis, however, EUS had sensitivity of 85% and specificity of 87% for cT1a and had sensitivity and specificity of 86% for cT1b. In this study, the investigators concluded that EUS has high accuracy for staging of superficial tumors.[13] Although the literature is unclear regarding the adequacy of EUS in the staging of superficial esophageal cancer, endoscopic mucosal resection and endoscopic submucosal dissection are alternative options and provide accurate differentiation of superficial tumors as well as treatment.[14–16] The accuracy of EUS for staging cT increases in advanced tumors (cT2 and greater), with a reported accuracy of 100% in cT3.[17] EUS also can be limited, however, in the evaluation of advanced disease. In this regard, the presence of malignant strictures in 20% to 36% of these cases can mechanically preclude optimal scope placement. Additionally, the small field of view with EUS potentially can limit accurate evaluation of the depth of invasion of large T4 tumors.[9,18]

CT cannot differentiate between the histologic layers of the esophageal wall and has a relatively poor sensitivity for determining cT (approximately 67%) (**Fig. 3**).[19] CT is the most accurate imaging modality, however, for identifying the invasion of adjacent structures (cT4). The loss of the fat plane between the tumor and adjacent structures in the mediastinum is highly suggestive of local invasion. Similarly, pleural or pericardial invasion is likely when there is loss of the fat plane between the tumor and the pleura/pericardium and the presence of an effusion and/or thickening.[18] Aortic invasion is suggested if there is an area of contact between

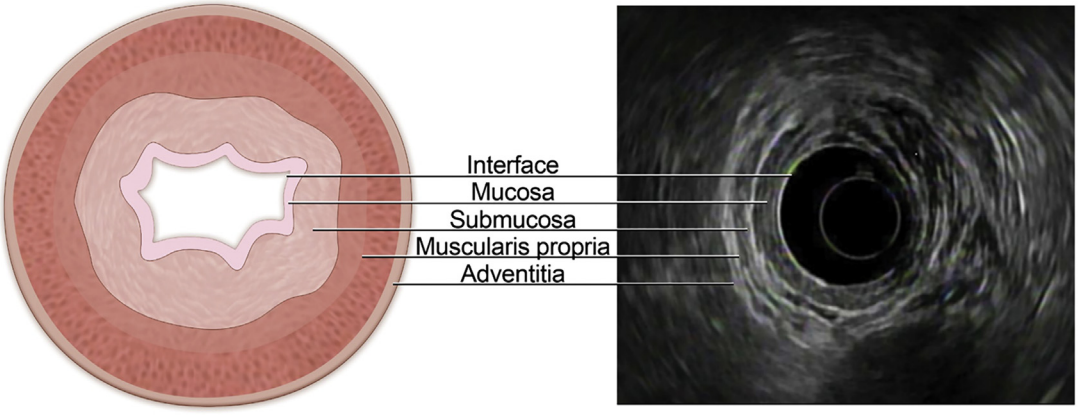

Fig. 2. EUS provides a detailed view of the esophageal wall layers and is the most accurate modality for assessing the T subcategories.

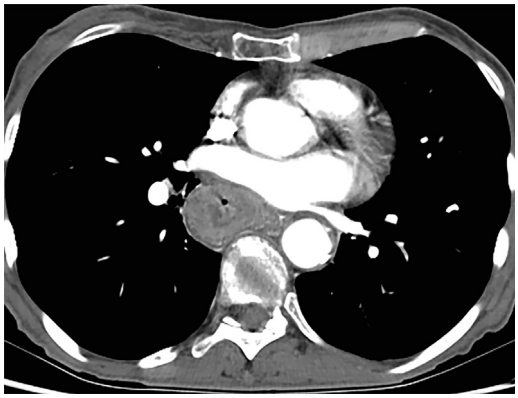

Fig. 3. Contrast-enhanced axial CT of the chest at the level of the left inferior pulmonary vein shows circumferential thickening of the esophageal wall consistent with malignancy. The precise extension of tumor invasion into the esophageal wall, however, cannot be accurately determined by CT.

the tumor and the aorta greater than 90o or if there is obliteration of the fat plane between the esophagus, aorta, and spine adjacent to the tumor.[20,21] Gross invasion of adjacent structures, including extension of the primary tumor into the lumen of the trachea, local destruction of an adjacent vertebral body, and extension of the primary malignancy, into the spinal canal are diagnostic of cT4 (Fig. 4).[22,23]

Similar to CT, the determination of the cT by FDG PET/CT is limited by poor spatial resolution. Increased FDG in the primary tumor, however, can allow detection and localization of those tumors that are not visualized anatomically. Although superficial esophageal cancer confined to the mucosa (cT1) typically is not visualized due to tumors having volumes below the resolution of FDG PET/CT, visualization increases as cT stage increases. In a study by Kato and colleagues,[24] 43% of T1 tumors, 83% of T2 tumors, 97% of T3 tumors, and 100% of T4 tumors were detected on PET imaging due to increased FDG uptake. Focal FDG uptake in the esophagus also can occur secondary to additional factors, such as esophagitis or mucosal ulceration.[14] Another cause of false-positive FDG uptake in the esophagus is inflammation after endoscopic biopsy of the mucosa.[25] For these reasons, focal increased FDG uptake in the esophagus should be correlated with the recent clinical history and findings at endoscopy.

Regional Lymph Nodes (cN)

The cN subcategory ranges from N0 to N3 and describes the number of regional lymph node metastases.[6] Regional lymph nodes are defined as any periesophageal lymph node from the upper esophageal sphincter to the celiac axis.[26] These include extrathoracic lymph nodes in the lower cervical periesophageal region, periesophageal intrathoracic lymph nodes, bilateral paratracheal and subcarinal nodes, diaphragmatic lymph nodes adjacent to the crura, paracardial lymph nodes, and upper abdominal lymph nodes (left gastric, common hepatic, splenic, and celiac lymph nodes). Lymph nodes outside these regions are considered distant metastatic disease.[26] Supraclavicular lymph nodes not located in the periesophageal region are considered M1 disease.

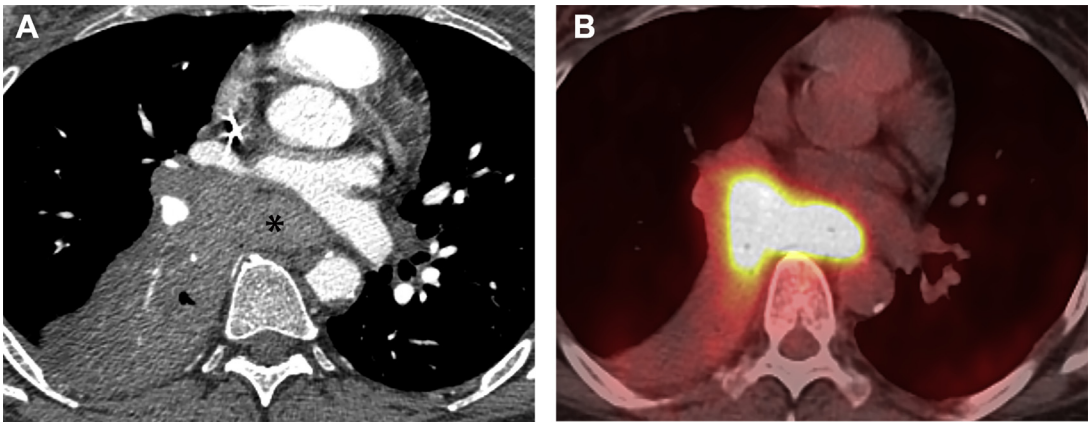

Fig. 4. (*A*) Contrast-enhanced axial CT of the chest at the level of the left inferior pulmonary vein shows a poorly marginated esophageal mass (*asterisk*) extending into the azygoesophageal recess. The mass occludes the bronchus intermedius and results in atelectasis of the right lower lobe. (*B*) Fused axial FDG PET/CT at the same level confirms the findings on CT. CT is the optimal modality for detecting gross extension of the primary tumor into the adjacent structures. (*Courtesy of* Kelly Kage, MFA, CMI, UT MD Anderson Cancer Center, Houston, TX; with permission.)

The esophagus has a rich lymph-capillary system. Most of the lymphatics are concentrated in the submucosa, although they also are present in the lamina propria. These lymphatics connect to periesophageal lymph node stations and with the thoracic duct. Lymphatic channels run radially (penetrating the esophageal wall transversally) and longitudinally (upward and downward).[27] Longitudinal lymphatic spread occurs in an expected way: tumors located in the cervical and upper thoracic esophagus drain preferentially in a cranial direction to cervical lymph nodes; tumors in the distal esophagus and gastroesophageal junction drain caudally to intra-abdominal lymph nodes; and tumors in the midthoracic esophagus can drain in either direction. Lymphatic spread is not limited, however, to these pathways. For instance, lymph node metastases along the recurrent laryngeal nerves in the neck still can occur with distal esophageal tumors.[27] Furthermore, because of the rich submucosal lymphatic plexus, metastases to distant lymph node stations can occur while bypassing regional lymph nodes. Such skip metastases are found in 10% to 20% of resected tumors.[28]

The number of involved lymph nodes has been shown to have an influence on survival, and this is reflected in the subdivision of the N category into N1 (1–2 lymph nodes involved), N2 (3–6 lymph nodes involved), and N3 (>6 lymph nodes involved) subcategories (see **Fig. 1**).[26] An important consideration is that the probability of lymph node metastases increases with greater local tumor invasion. For instances, lymph node metastases occur in up to 35% of T1b patients and up to 80% of T3 patients.[29,30]

EUS has been reported as an accurate imaging modality for determining cN. EUS assesses the size, shape, and the echogenicity pattern of the lymph nodes and is useful in determining the presence of metastasis. For instance, a rounded lymph node greater than 1 cm in short-axis diameter with well-demarcated borders and central hypoechoic area (indicating loss of the fatty hilum) is strongly suggestive of nodal disease[31] (**Fig. 5**). Because EUS and EUS-FNA have sensitivities of 85% and 97%, respectively, the AJCC strongly recommends that the latter be performed for accurate cN staging.[6] EUS-FNA diagnosis of metastasis in lymph nodes adjacent to the primary malignancy can be limited due to the passage of the biopsy needle through the primary malignancy, which can result in contamination and false-positive results.[32]

CT has a relatively low diagnostic performance for the identification of lymph node metastasis, with reported sensitivity of 50% and specificity of 83% when using a criteria of greater than 1 cm in short-axis diameter.[33] False-negative and false positive results occur because normal-sized lymph nodes can have microscopic metastatic disease that cannot be identified by CT, and inflammatory/infectious processes can result in hyperplasia and enlarged lymph nodes, respectively.[34] Another potential limitation of CT is in the evaluation of lymph nodes abutting or in close proximity to the primary tumor. These lymph nodes can be difficult to separate from the primary tumor and cN can be difficult to determine accurately.[31]

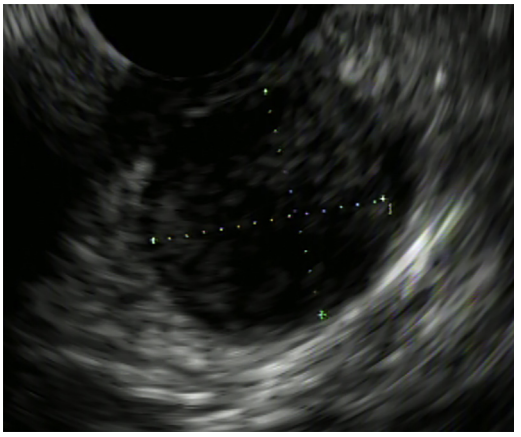

Fig. 5. EUS shows a rounded lymph node with well-defined borders and hypoechogenicity, findings suspicious for lymph node metastasis, the presence of which was confirmed by FNA biopsy.

FDG PET/CT combines anatomic and metabolic activity in detecting lymph node metastasis (**Fig. 6**). The accuracy in determining cN is highly variable, ranging from 35% to 90%.[35] False-negative results occur because of microscopic disease below the resolution of PET/CT, and false-positive results occur in inflammatory or reactive lymph nodes. Additionally, it can be difficult to differentiate peritumoral lymph nodes from the primary tumor because intense FDG uptake by the tumor can obscure the adjacent lymph nodes. Because the reported FDG PET/CT sensitivity for cN ranges from 43% to 70% and the specificity from 76% to 95%, the role of PET/CT is limited in the evaluation of cN.[33]

Distant Metastases (cM)

In the eighth edition of the TNM staging system, the M category is subcategorized as M0 (indicating the absence of metastasis) and M1 (representing the presence of distant metastasis). Distant metastases occur in 18% to 30% of patients at the time of presentation and are an

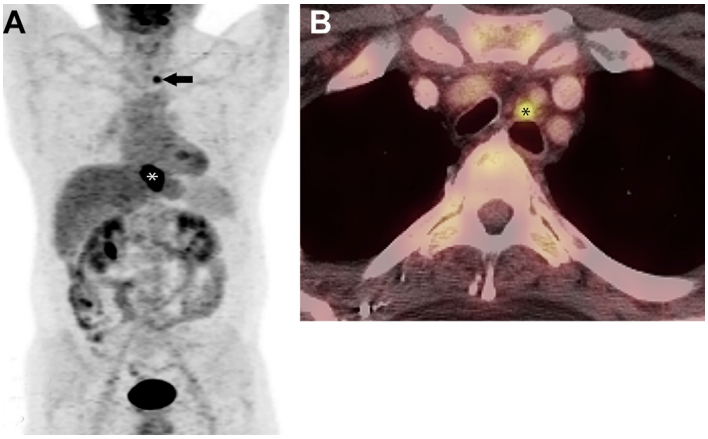

Fig. 6. (*A*) Coronal WB–FDG PET shows increased FDG uptake within the distal esophagus (*asterisk*) consistent with esophageal cancer and a smaller focus of increased FDG uptake more cephalad in the mediastinum (*arrow*). (*B*) Fused axial FDG PET/CT shows increased FDG uptake in a mediastinal lymph node (*asterisk*) adjacent to the esophagus suspicious for lymph node disease. cN1 was confirmed by EUS-FNA biopsy.

important factor in determining resectability.[36] The risk of hematogenous spread of the primary tumor increases with advanced local tumor invasion and lymph node involvement but also can occur early with small primary tumors and no apparent nodal metastases. The most common sites of distant metastasis include nonregional lymph nodes, liver, bone, lung, and adrenal glands.[37] Metastases in unusual sites (brain, skeletal muscle, subcutaneous fat, and thyroid gland) are considerations and occur in up to 7.7% of patients.[18,38]

CT has a reported sensitivity of 66% to 81% for the identification of distant metastases and is the ideal imaging modality detecting pulmonary metastases. A diagnostic CT using breath-hold techniques is the optimal modality to detect small lung metastases. In this regard, the imaged lungs on FDG PET/CT typically are suboptimal because they often are acquired while a patient is breathing or during partial breath-held inspiration. The resulting degradation of image quality can make detection of small nodules difficult, especially adjacent to the hemidiaphragms.[39,40]

FDG PET/CT is the imaging modality with the highest sensitivity and specificity for the detection of distant metastases (83.3% and 98.4%, respectively).[41] Several comparative studies have shown that FDG PET/CT is more accurate than CT in detecting distant metastases. FDG PET/CT increases the accuracy of clinical staging and can avoid futile surgery in patients considered for resection.[41,42] Changes in stage and treatment have been reported in approximately 30% of patients after performing FDG PET/CT imaging. In addition, synchronous tumors have been identified in 2% of patients on FDG PET/CT.[43] The high sensitivity and specificity of FDG PET/CT over other imaging modalities for the detection of distant metastases make it important in the staging of patients with newly diagnosed esophageal cancer. Because the detection of a metastasis has a major impact on clinical management, cytologic or histopathologic confirmation of a suspected lesions identified on FDG PET/CT is strongly recommended (**Fig. 7**).

Early studies showed poor performance of MR imaging in the evaluation of cT and cN, mainly due to technical issues resulting in image quality degradation (swallowing, respiratory, and cardiac motion). In addition, long scan times historically have prevented more widespread use of MR imaging. Recently, studies combining T2-weighted sequences and diffusion-weighted imaging (DWI) have had shorter time duration and may be useful in determining cT and cN (**Figs. 8** and **9**). Gao and colleagues[44] reported an overall accuracy of MR imaging in determining the T category of 63.2% and of 50.1% for N category when combining T2-weighted sequences and DWI. An apparent diffusion coefficient (ADC) map can be derived from DWI to quantify the restricted diffusion and differentiate benign from malignant lesions. ADC can increase the detection of the primary malignancy and metastatic lymph nodes. Additionally, higher ADC values are associated with greater invasiveness and less differentiation of the primary tumor and worse overall patient prognosis. Whole-body (WB)–MR imaging, including DWI, has been reported to have accuracy similar to FDG PET/CT in detecting the primary tumor and lymph node and distant metastases.[45] In a recent study, WB–MR imaging and FDG PET/CT identified the primary tumor in 98% and 94% patients, respectively. The sensitivity and specificity for the identification of lymph node metastases were 30% and 100%, respectively, for WB–MR imaging and 27% and 100%, respectively, for FDG PET/CT. In 2 of the 49 patients, distant metastases were identified

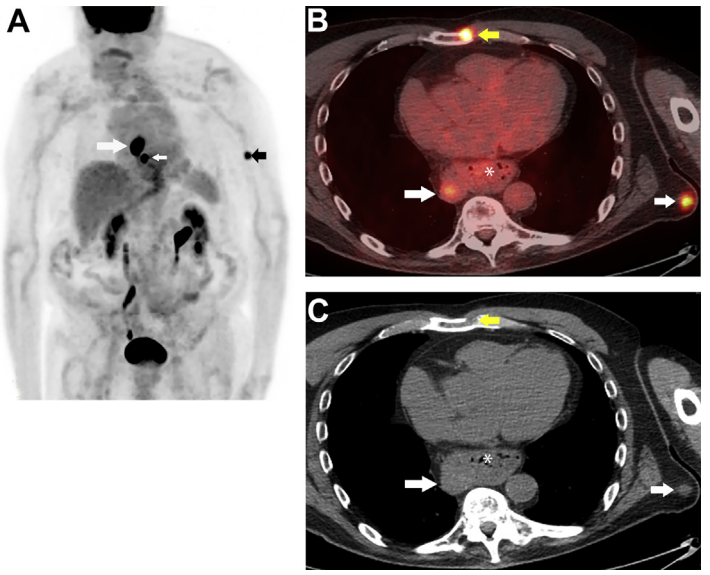

Fig. 7. (*A*) Coronal WB–FDG PET demonstrates multiple regions of focal increased FDG uptake in the mediastinum (*white arrows*) and the left chest wall (*black arrow*). (*B*) Fused axial FDG PET/CT and (*C*) CT show the FDG-avid primary tumor (*large arrow*), lytic sternal metastasis (*yellow arrow*), and a soft tissue nodule in the chest wall (*short arrow*). Subsequent biopsy of the chest wall nodule confirmed metastatic disease. *, hiatal hernia.

by both modalities. High-resolution (1-mm slice thickness), delayed-phase MR imaging can be used in conjunction with conventional MR imaging to further evaluate the primary tumor and has an accuracy range of 89% to 96% in determining the T subcategories.[46] A potential limitation of this technique, however, is that the small field of view can result in incomplete evaluation of large or multifocal tumors.

The potential of FDG PET/MR imaging in the preoperative staging of esophageal carcinoma has been evaluated. Lee and colleagues[45] compared the diagnostic efficacy of EUS, CT, FDG PET/CT, and FDG PET/MR imaging for the preoperative local and regional staging of esophageal cancer. For T subcategory assessment, EUS showed the highest accuracy followed by FDG PET/MR imaging and CT (86.7%, 66.7%, and 33.3%, respectively). For the N subcategory, FDG PET/MR imaging showed the highest diagnostic accuracy followed by EUS, FDG PET/CT, and CT (83%, 75%, 66.7%, and 50%,

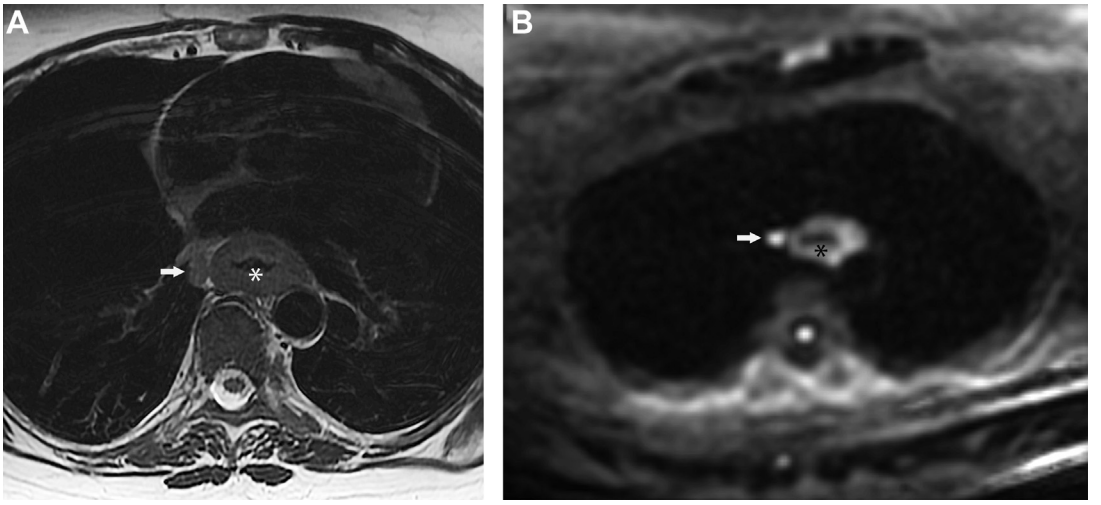

Fig. 8. (*A*) Axial T2-weighted MR image shows diffuse thickening of the distal esophagus consistent with a primary malignancy (*asterisk*). There is an adjacent enlarged lymph node (*arrow*) suspicious for lymph node metastasis. (*B*) Axial DWI at the same level shows high signal intensity within the esophageal wall (*asterisk*) and an adjacent lymph node (*arrow*), consistent with malignancy.

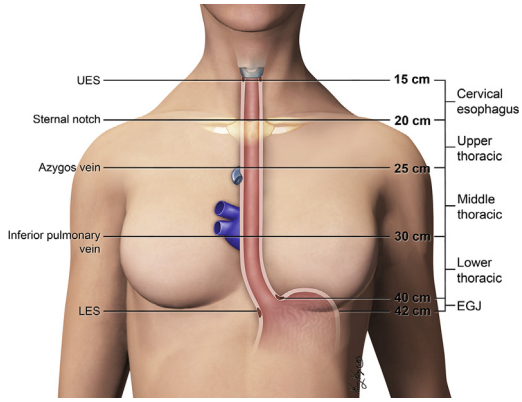

Fig. 9. Location of the primary esophageal cancer based on endoscopic measurements from the incisors. The esophagus is divided into 4 distinct anatomic regions. The cervical esophagus extends from the cricopharyngeus muscle to the suprasternal notch (15–20 cm from the incisors); the upper thoracic esophagus extends from the suprasternal notch to the lower border of the azygos vein (20–25 cm from the incisors); the midthoracic esophagus extends from the lower border of the azygos vein to the inferior pulmonary veins (25–30 cm from the incisors); and the lower thoracic esophagus extends from the inferior pulmonary veins to the stomach, including the intra-abdominal esophagus and the esophago-gastric junction (EGJ) (30–40 cm from the incisors). LES, lower esophageal sphincter; UES, upper esophageal sphincter. (*Courtesy of* Kelly Kage, MFA, CMI, UT MD Anderson Cancer Center, Houston, TX; with permission.)

respectively), respectively. Although FDG PET/MR imaging had an acceptable accuracy for T assessment and higher accuracy than EUS and FDG PET/CT for prediction of the N subcategory, improvements in FDG PET/MR imaging are required for it to become a routine modality in cTNM determination.

NONANATOMIC CATEGORIES

Histologic Cell Type

SCC usually occurs in the middle or upper one-third of the esophagus whereas AC is found most commonly in the distal esophagus and esophagogastric junction. The histologic cell type affects survival of cTNM-staged patients. For example, the survival of patients with early-stage and intermediate-stage SCC is worse than those with AC. Accordingly, SCC and AC have separate stage groupings, specifically for stage I and stage II cancers[6] (see **Table 1**).

Grade

Histologic grade (G) reflects the biologic activity of the tumor and is subcategorized as well-differentiated (G1), moderately differentiated (G2), and poorly differentiated (G3). If the G is undifferentiated, the tumor is considered G3. Histologic G affects the survival of patients with early-stage cancers (pT1–2NOMO AC and pT2N0M0 SCC)[6] (see **Table 2**).

Location

The location of the primary tumor optimally is determined by esophagoscopy and is divided into 4 distinct anatomic regions that are measured from the incisors during EUS. The cervical esophagus extends from the cricopharyngeus muscle to the suprasternal notch and is 15 cm to 20 cm from the incisors by endoscopy; the upper thoracic esophagus extends from the suprasternal notch to the lower border of the azygos vein and is 20 cm to 25 cm from the incisors; the midthoracic esophagus extends from the lower border of the azygos vein to the inferior pulmonary veins and is 25 cm to 30 cm from the incisors; and the lower thoracic esophagus extends from the inferior pulmonary veins to the stomach (including the intra-abdominal esophagus and the gastroesophageal junction) and is 30 cm to 40 cm from the incisors (see **Fig. 8**). ACs with an epicenter less than or equal to 2 cm into the gastric cardia are considered esophageal cancers and those with greater than 2-cm involvement of the gastric cardia are staged as gastric cancers.[6,26] The L of the primary tumor only affects outcome in patients with SCC with stage IIA and stage IIB disease (see **Table 2**).

SUMMARY

The incidence of esophageal cancer continues to increase, and appropriate treatment requires accurate determination of the extent of disease. In this regard, the most commonly used staging for esophageal cancer is the eighth edition of the TNM staging system. Currently, clinical staging of patients with esophageal cancer includes evaluation with EUS, CT, FDG PET/CT, MR imaging, and FDG PET/MR imaging. EUS is the best modality for determining the depth of tumor invasion (cT) and the presence of regional lymph node (cN) metastasis. CT usually is performed to evaluate whether the primary tumor invades adjacent structures as well for the detection of regional and nonregional nodal metastases and distant systemic metastases. FDG PET/CT improves the accuracy of staging and is particularly useful in the preoperative assessment of patients with esophageal cancer. Knowledge of the eighth edition TNM staging system and the appropriate use of imaging are important in ensuring appropriate patient management.

CLINICS CARE POINTS

- The most commonly used method of staging esophageal cancer is the eighth edition of the AJCC/UICC TNM system.
- The T category represents the depth of invasion of the primary tumor into the esophageal wall. The N category represents the number of regional lymph node metastasis, and the M category represents metastasis to nonregional nodes and distant organ/s.
- EUS is the best imaging modality for determining the depth of tumor invasion (cT) and the presence of regional lymph node metastasis (cN).
- CT is used to evaluate invasion of adjacent structures and to detect regional and nonregional nodal metastasis and distant systemic metastasis.
- FDG PET/CT is useful particularly in identification of distant and unusual metastasis.

DISCLOSURE

The authors declare that there are no conflicts of interest regarding the publication of this article.

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