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The Role of Integrated Computed Tomography Positron-Emission Tomography in Esophageal Cancer: Staging and Assessment of Therapeutic Response

Jeremy J. Erasmus, MD, and Reginald F. Munden, DMD, MD

Computed tomography (CT) and endoscopy/endoscopic ultrasonography are usually performed to initially stage patients with esophageal cancer, to determine primary tumor response, and to detect nodal and distant metastases after preoperative therapy. Positron-emission tomography (PET) with [18F]-fluoro-2-deoxy-D-glucose and integrated CT-PET are useful in the initial staging of patients with esophageal cancer as well as in the prediction of pathologic response, disease-free interval, and overall survival after preoperative therapy. Importantly, integrated CT-PET imaging decreases the number of futile attempts at surgical resection, mainly because of the detection of occult distant metastases. The following sections review the use of integrated CT-PET imaging in determining the T, N, and M descriptors of the American Joint Commission on Cancer's 2002 guidelines for pathologic and clinical staging at initial diagnosis and after chemoradiation therapy in those patients being considered for surgical resection.

KEYWORDS esophageal cancer, staging, induction therapy, response assessment, computer tomography, positron emission tomography

Clinical staging of esophageal cancer is usually performed by using a combination of endoscopy and imaging studies. Endoscopy/endoscopic ultrasonography (EUS) and computed tomography (CT) are usually performed to initially stage patients with esophageal cancer and to determine primary tumor response and detect nodal and distant metastases after preoperative therapy.[1-12] Positron emission tomography (PET) with [^{18}F]-fluoro-2-deoxy-D-glucose (FDG) has been reported to be useful in the initial staging of patients with esophageal cancer as well as in the prediction of pathologic response, disease-free interval, and overall survival after preoperative therapy.[10,13-20] Small studies have reported a 3% to 20% change in management of patients with esophageal cancer because of the addition of FDG-PET to the preoperative assessment.[4,5,21-24] However, the poor spatial resolution of PET when compared with CT often precludes accurate assessment of the primary tumor and localization of nodal metastases as well as detection of small pulmonary metastases. The recent use of integrated CT-PET imaging with coregistration of anatomic and functional imaging data may improve the localization of regions of increased FDG uptake and the accuracy of staging in patients with esophageal cancer.[25,26]

This article reviews the initial staging and the determination of response to preoperative chemoradiation therapy in patients with esophageal cancer and will emphasize the appropriate role of CT-PET imaging in patient management.

Staging

Patients with esophageal cancer are typically staged before therapy according to the recommendations of the American Joint Commission on Cancer's 2002 guidelines for pathologic and clinical staging[27] (Table 1). FDG-PET imaging followed by EUS has been proposed as the most cost-effective strategy in the preoperative staging and management of patients with esophageal cancer.[6,28,29] However, the precise role of FDG-PET and CT-PET in the staging algorithm of patients

Division of Diagnostic Imaging, The University of Texas M. D. Anderson Cancer Center, Houston, TX

Address reprint requests to Jeremy J. Erasmus, MD, Department of Diagnostic Radiology, Unit 0371, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030. E-mail: jerasmus@di.mdacc.tmc.edu

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Table 1 American Joint Committee on Cancer (AJCC) Cancer Staging Manual, Sixth Edition Esophagus (TNM) (Sarcomas are not included.)[27]

Primary Tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*
T1	Tumor invades lamina propria or submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
Regional Lymph Nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
Distant Metastasis (M)	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
Tumors of the lower thoracic esophagus:	
M1a	Metastasis in celiac lymph nodes
M1b	Other distant metastasis
Tumors of the midthoracic esophagus:	
M1a	Not applicable*
M1b	Nonregional lymph nodes and/or other distant metastasis
Tumors of the upper thoracic esophagus:	
M1a	Metastasis in cervical nodes
M1b	Other distant metastasis

*For tumors of midthoracic esophagus, use only M1b because these tumors with metastasis in nonregional lymph nodes have an equally poor prognosis as those with metastasis in other distant sites. (Reprinted with permission.[27])

with potentially resectable esophageal cancer has not been definitively defined. Although not useful as a single-imaging modality in staging patients with esophageal cancer, the CT component of integrated CT-PET is an indispensable complementary modality. As integrated CT-PET becomes more widely available, it has the potential to be the imaging modality of choice in the staging of esophageal cancer, especially because of the ability to detect nonregional metastases. However, a caveat to this statement is that the CT component of CT-PET imaging, performed in many institutions without the use of intravenous contrast material and in partial or complete expiration, precludes the optimal detection of small lung metastases and hepatic metastases. In our experience, the optimal imaging/staging strategy is a combination of EUS, contrast-enhanced CT of the chest and abdomen, and integrated CT-PET imaging. The following sections review the use of integrated CT-PET imaging in determining the T, N, and M descriptors of the American Joint Commission on Cancer's 2002 guidelines for pathologic and clinical staging at initial diagnosis and after chemoradiation therapy in those patients being considered for surgical resection.

Primary Tumor

The extent of the primary tumor is categorized as T1 through T4 according to the depth of tumor penetration into the esophageal wall and is important in determining therapy with curative resection precluded when there is invasion of adjacent structures (Fig 1) (Table 1). EUS is the preferred method of evaluating the T component of esophageal carcinoma, and in a meta-analysis by Rosch,[30] EUS had an accuracy of 89% for T staging. However, accuracy is reported to be lower in tumors greater than 5 cm in diameter, stenotic tumors, and tumors located at the esophagogastric junction.[31,32]

CT-PET has a limited role in evaluating the T descriptor because of the inability to differentiate between T1, T2, and T3 parameters and in the identification of nonresectable invasion of adjacent structures (T4 disease) (Fig 2).[33-35] In this regard, Lowe and coworkers[35] have reported that local tumor staging (T) was done correctly by CT and PET in only 42% of patients with esophageal cancer (compared with 71% with EUS).

Regional Lymph Nodes

EUS and CT are almost uniformly used to evaluate the presence and location of regional nodal metastases (ie, paraesophageal and abdominal nodes cephalad to the celiac axis) (Table 1). Although CT is accurate in showing enlarged nodes, the sensitivity and specificity for the detection of N1 disease nodal involvement has been reported to be only 84% and 67%, respectively.[35] The limitations of anatomic imaging in N1 nodal staging have not been significantly improved by the addition of FDG-PET to the imaging algorithm because the high FDG uptake in the primary esophageal malignancy often obscures increased FDG uptake in locoregional nodes.[36] The sensitivity of PET in the detection of nodal metastatic disease is overall poor and has been reported to be in the range of 22% to 82%.[3,35,37,38] In a recent meta-analysis of 12 studies con-

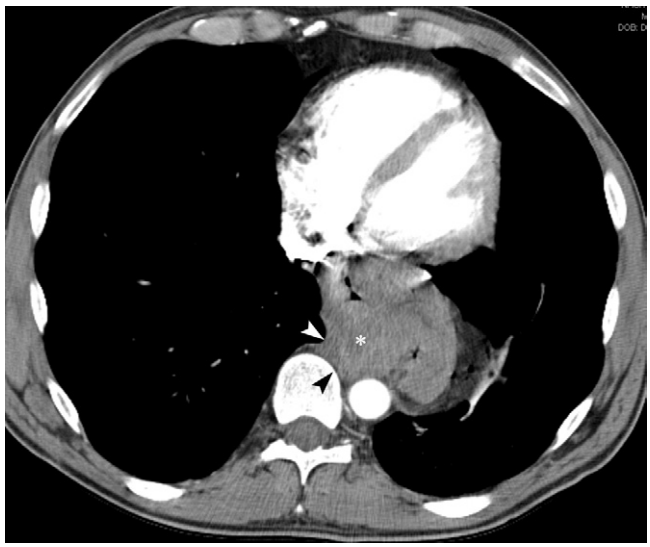

Figure 1 Contrast-enhanced CT in a 43-year-old man with esophageal cancer shows large esophageal mass (*) with extension into the adjacent paraspinal tissue (arrowheads) (T4 disease). In the absence of gross invasion, accurate assessment of locoregional invasion by CT is inaccurate. Note the adjacent hiatal hernia.