ELSEVIER
SAUNDERS

Thorac Surg Clin 14 (2004) 61–69

THORACIC
SURGERY
CLINICS

Imaging for esophageal tumors

Robert J. Korst, MD, Nasser K. Altorki, MD*

Division of Thoracic Surgery, Department of Cardiothoracic Surgery, Weill Medical College, Cornell University, 525 E. 58th Street, New York, NY 10021, USA

Carcinoma of the esophagus comprises the vast majority of malignant esophageal tumors and represents the seventh most common malignancy worldwide, with its incidence reaching endemic proportions in specific geographic locations in Asia and Africa [1]. Although esophageal cancer is presently responsible for only approximately 13,000 deaths annually in the United States [2], the incidence of adenocarcinoma of the esophagus is rising faster than any other malignant tumor in the United States [3]. Because the majority of patients present with advanced disease, only roughly 12% of patients diagnosed with this tumor will survive more than 5 years after diagnosis [2].

The treatment of carcinoma of the esophagus is stage-dependent (Table 1). While patients who have widely metastatic disease are not treated with curative intent (ie, only palliative chemotherapy or supportive care), most clinicians would agree that patients who have early (superficial, node-negative) cancers should undergo surgical resection for cure; however, the ideal treatment of locally advanced (transmural, node-positive) disease remains controversial, with some clinicians advocating surgical resection alone, others supporting preoperative neoadjuvant therapy followed by surgery, and still others backing definitive chemoradiation without surgery.

Given the stage dependency of therapeutic options for patients who have esophageal cancer, it is essential to determine the extent of disease accurately before formulating the treatment plan. Imaging plays an integral role in guiding the clinician in this staging process, with specific imaging modalities being useful for the evaluation of distant disease, locoregional disease, or both. Certain imaging techniques have proven to be useful in guiding biopsy procedures, such as fine needle aspiration (FNA) of suspicious lesions; however, the accuracy of some of these techniques seems to rely, at least in part, upon the experience of the operator [4]. Finally, individual imaging algorithms and the preference of one modality versus another varies with device availability, individual experience, and geographic location.

Imaging of distant metastatic disease

In the United States, approximately 20% to 30% of patients who have carcinoma of the esophagus have distant metastatic disease at the time of presentation [2,5]. The most common visceral metastatic sites include, in decreasing order of prevalence, liver, lung, bone, and adrenal glands [5,6]. As a result, imaging for patients who have esophageal cancer should evaluate these sites. The brain is an uncommon site of metastases from esophageal cancer, occurring in less than 2% of patients who have metastatic disease [5,6]. Further, it is uncommon for patients who have carcinoma of the esophagus to present with solitary metastatic lesions; most possess multiple numbers of metastases, albeit usually in a single organ [5,6]. In these cases of metastatic disease in a pattern consistent with esophageal cancer, oftentimes histologic confirmation by means of biopsies is not necessary; however, a second, corroborating imaging study should be performed. In the uncommon situation in which a patient presents with a single metastatic lesion radiographically, or a pattern inconsistent with that typically seen with esophageal

* Corresponding author.
E-mail address: naltkori@med.cornell.edu (N.K. Altorki).

1547-4127/04/$ – see front matter
doi:10.1016/S1547-4127(04)00038-6

Table 1
Staging scheme for carcinoma of the esophagus

Stage	Characteristics
Primary tumor (T)	
TX	Tumor cannot be assessed
T0	No evidence of tumor
Tis	Carcinoma in situ/high grade dysplasia
T1	Confined to mucosa or submucosa, not into muscularis proporia
T2	Invades into muscularis propria
T3	Invades through muscularis propria but not into adjacent organs
T4	Invades adjacent structures/organs
Nodal status (N)	
NX	Regional nodes cannot be assessed
N0	No regional nodal metastases
N1	Regional nodal metastases
Distant metastases (M)	
MX	Distant metastases cannot be assessed
M1a	Metastatic cervical nodes/upper thoracic esophageal tumor Metastatic celiac nodes/lower thoracic esophageal tumor
M1b	Any tumor location with visceral/bony metastases Any tumor location with nodal metastases beyond N1 or M1a
Stage groupings	
0	TisN0M0
I	T1N0M0
IIA	T2-3N0M0
IIB	T1-2N1M0
III	T3N1M0 T4 Any N
IVA	Any T Any N M1a
IVB	Any T Any N M1b

cancer, confirmatory biopsy should be performed more routinely to ensure that the patient does not have potentially curable (resectable) disease or another distinct disease process. Nearly all potentially metastatic foci can technically be assessed cytologically by means of image-guided FNA [4].

Because carcinoma of the esophagus is still an uncommon disease relative to other tumor types in the United States, little published data exist regarding accuracy of many imaging modalities (eg, radionuclide bone scan) exclusively for the detection of distant metastases in patients who have esophageal cancer; however, multiple published reports concerning the accuracy of these imaging techniques exist for carcinomatous tumors in general. Intravenous contrast-enhanced CT remains the workhorse for imaging patients who have carcinoma of the esophagus to rule out distant metastatic lesions because it allows assessment of the three most common sites of distant metastases. Scans should be obtained from the base of the neck (thoracic inlet) through the liver and adrenal glands in the upper abdomen. Metastatic deposits in the liver usually appear as hypodense, ill-defined lesions on contrast-enhanced CT scans (Fig. 1) [7,8]. As with any liver imaging modality, the sensitivity of the CT scan for detecting metastatic liver disease depends on the size of the lesion [7,8]. While the vast majority of lesions larger than 1 cm are detected using CT scan, the sensitivity drops precipitously for metastatic deposits less than 1 cm in diameter or if the scan is performed without intravenous contrast. Similarly, if the lesions are of adequate size (>1 cm), CT is useful for distinguishing metastases from benign entities, most notably cysts and hemangiomas, with the former possessing the density of fluid and the latter demonstrating peripheral enhancement with delayed washout of intravenous contrast [7,8].

Other imaging modalities that are useful in assessing the status of the liver include ultrasound (US) and MRI. Although transabdominal US is inexpensive and distinguishes between cystic and solid liver lesions accurately, its sensitivity in detecting metastatic liver deposits in general is clearly inferior to that of CT [7,8]. Laparoscopic US is potentially more sensitive than the transcutaneous approach [9], but it is an invasive procedure that tends to be especially user-dependent, with published data suggesting only limited benefit for patients who have cancer of the esophageal body [9,10]. MRI can be beneficial when CT demonstrates liver lesions and further characteri-

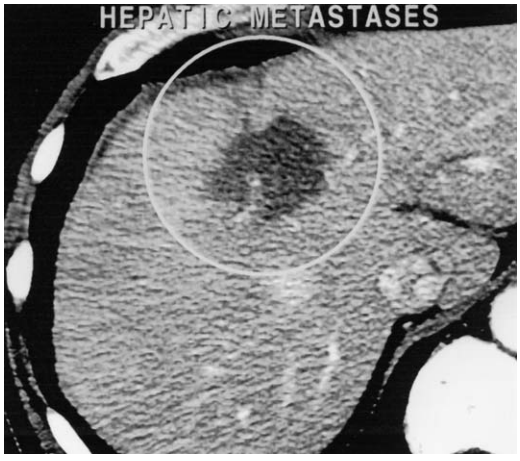

Fig. 1. Intravenous contrast-enhanced CT image of the liver of a patient who had carcinoma of the esophagus. The encircled region demonstrates a large, hypodense, irregularly bordered lesion representing the typical appearance of metastasis.

zation is needed. Gadolinium contrast agents might enhance the sensitivity of MRI, which is an effective modality for distinguishing metastases from benign liver lesions, including cysts and hemangiomas [7,8].

Pulmonary metastases are also seen in patients who have esophageal carcinoma. Suspicious pulmonary nodules are usually round, smooth-bordered, and noncalcified on CT scan. Given the high prevalence of incidental, benign pulmonary nodules seen in smokers over the age of 60 [11], any suspicious lung lesion should be biopsied using FNA or a thoracoscopic approach. Further, given the role of smoking in carcinogenesis of the lung and esophagus and the concept of field cancerization, primary lung cancer also needs to be ruled out in these situations, particularly if the pulmonary lesion is solitary [12].

Because bone is a common site for metastases from carcinoma of the esophagus, routine radionuclide bone scanning can be performed in these patients. In general, in patients who have cancer, a scan showing multiple areas of uptake strongly suggests metastases; however, only 50% of solitary foci represent metastases, even in patients who have a history of cancer [13]. Tracer accumulation can occur at any skeletal site with an elevated rate of bone turnover. As a result, corroborative studies are required in the majority of cases of a positive bone scan, which include MRI (which is especially useful for evaluation of the spine), plain radiographs, and even a CT scan. The radiographic evaluation of adrenal lesions has been the subject of many reported studies involving the use of CT and MRI. While primary malignant lesions of the adrenal glands are uncommon, the prevalence of benign adrenal adenomas in the general population is significant and might approach 7% by age 70 [14]. Because of the high intracellular lipid content in adenomas, thin-cut (3 mm), noncontrast CT and MRI have been reported to possess specificity rivaling that of FNA with cytologic examination for distinguishing metastases from adenomas [15].

Positron emission tomography ([18F]2-flouro2-deoxyglucose positron emission tomography [FDG]-PET) is a new imaging modality that is gaining popularity in staging patients who have many types of malignant disease. Based on the finding that malignant cells possess higher rates of glucose uptake compared with normal cells, several small studies have demonstrated that FDG-PET has been shown to radiographically detect occult distant metastatic disease in approximately 20% of patients who have esophageal cancer [16,17]. Given these encouraging preliminary findings, this concept is presently being evaluated in a large, multicenter, prospective study. Drawbacks of FDG-PET are related to its lack of sensitivity for detecting small (<1 cm) metastatic lesions and its relative lack of anatomic detail. The latter problem can be at least partially addressed by the advent of newer PET/CT fusion scanners, in which a composite image is generated incorporating FDG-PET and CT images. It is important to note that until larger, confirmatory studies are performed examining the utility of FDG-PET for detection of metastatic disease, FDG-PET findings in patients who have esophageal cancer should be confirmed with a second imaging technique or a biopsy depending on the individual clinical scenario. This guideline is especially true in the assessment of potentially metastatic pulmonary lesions because although the FDG-PET scan is frequently positive in pulmonary metastases, a number of benign pulmonary lesions (mainly inflammatory) can also be glucose avid [18].

Imaging of the primary tumor

Carcinoma of the esophagus originates in the epithelial lining and spreads into and through the wall of the esophagus and throughout the draining lymphatics to lymph nodes. Esophageal carcinoma readily disseminates hematogenously to distant sites. Published data have confirmed that the presence of lymph node metastases is a powerful predictor of prognosis in these patients and is a marker for systemic spread of the disease [19,20]. Similarly, the depth of penetration of the primary tumor into the esophageal wall predicts the presence or absence of lymph node metastases, with approximately 85% of T3 tumors being associated with lymphatic spread [1]. Accurate imaging of the primary tumor in patients who have esophageal carcinoma is therefore important, not only for determining resectability in patients who have locally advanced disease but also predicting prognosis in patients who have disease that appears to be limited to the esophagus.

In past decades, primary tumors of the esophagus were imaged using barium esophagography. Not only could the location and longitudinal extent of the tumor be determined, estimations of resectability could be made based on the esophagram. In this regard, Akiyama and colleagues found that 74% of transmural tumors caused distortion of the normal axis of the esophagus [21]. This distortion is caused by tethering of the esophagus in the region of the tumor.

The two most commonly used contemporary imaging procedures for assessing the primary tumor are CT and endoscopic ultrasound (EUS). Given its lack of anatomic detail, FDG-PET is unable to provide any definition of the esophageal wall or periesophageal

tissues, making it of limited utility in assessing the primary tumor (Fig. 2B). Similarly, CT does not provide adequate resolution in distinguishing the layers of the esophageal wall; however, information can be gained concerning neighboring organ involvement, or, more specifically, the lack thereof (Fig. 2A). Preservation of fat planes surrounding the tumor has been proposed and is supported as radiographic exclusion of a T4 tumor [22,23]. Conversely, loss of fat planes might indicate neighboring organ involvement. When the tumor compresses the membranous left main bronchus or trachea, bronchoscopy should be performed to definitively establish airway invasion. As with the airway, invasion of the descending thoracic aorta is difficult to predict using CT. Some published evidence suggests that the greater the circumference of the aorta abutted by the tumor, the more likely the tumor will be unresectable [24]. In summary, although T4 tumors can be excluded reliably by the preservation of peritumoral fat planes, the definitive establishment of neighboring organ invasion is difficult to predict with CT and on most occasions operative exploration is required.

EUS is an imaging modality that is gaining popularity in the preoperative assessment of patients who have esophageal tumors. The great strength of EUS lies in its ability to visualize the esophageal wall in greater detail than any other imaging modality. The esophageal wall is seen as four distinct layers using EUS: mucosa, muscularis mucosa, submucosa, and muscularis propria. A fifth layer corresponding to periesophageal fat is also readily discernable using EUS. A standard EUS examination usually involves evaluation of the tumor with 7.5 MHz and 12 MHz probes and is considered to be the most accurate means by which to estimate tumor invasion. In this regard, large review series place the accuracy of EUS in determining the depth of invasion of esophageal carcinoma at approximately 85% [25,26], with the identification of T2 tumors being the least accurate (Figs. 3, 4) [25,26].

Drawbacks of EUS include the relatively steep learning curve [27] and the inability to pass the transducer completely through the tumor in up to 50% of cases [25]. Newer probes are being developed continuously to address this problem, some being thin enough to pass through the instrument channel of the endoscope [28]. Other recent developments in EUS technology include probes that allow for helical scanning with subsequent three-dimensional reconstruction of EUS images [29] and the use of high-frequency transducers. These latter probes tend to be useful in imaging superficial tumors of the esophagus by providing more detail, and they can differentiate

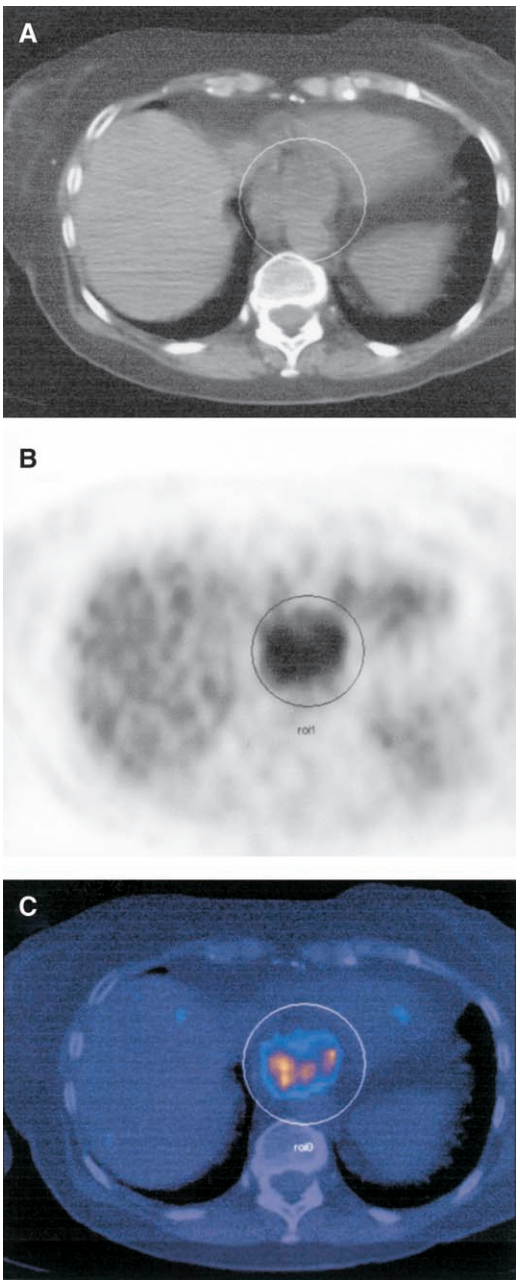

Fig. 2. CT/PET fusion study depicting esophageal carcinoma in the distal third of the esophagus. The lesion is encircled in each panel. (*A*) Noncontrast CT image. (*B*) FDG-PET image. (*C*) CT/PET fusion image.

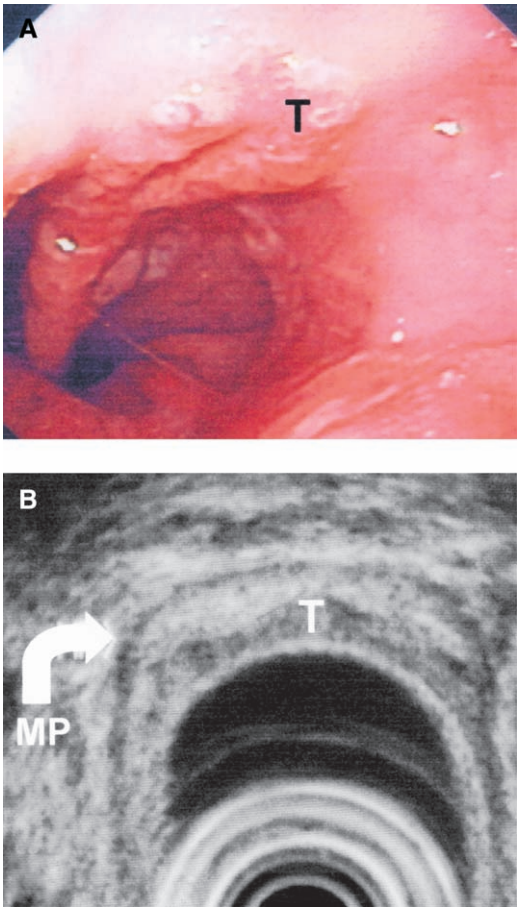

Fig. 3. Elderly patient who had T1 adenocarcinoma of the distal esophagus. (*A*) Endoscopic appearance. (*B*) EUS image demonstrating lack of penetration into the muscularis propria (MP).
Abbreviation: T, tumor.

between T1A and T1B successfully [30]. This distinction might be of importance in locations in which esophageal cancer screening is performed and lesions are detected at earlier stages more routinely.

Similar to EUS, preliminary data suggest that investigational techniques such as endoluminal MRI might be able to visualize the layers of the esophageal wall accurately [31]. Whether or not this technique will earn a role in the future of imaging for carcinoma of the esophagus requires further investigation.

Imaging of lymphatic metastases

It is generally agreed that the presence of lymph node metastases (N1 disease) associated with resectable carcinoma of the esophagus is the strongest known predictor of recurrence and mortality following definitive therapy for this disease [19,20]. As with some other types of malignancies, the degree of lymph node involvement might also be of prognostic value, with published studies demonstrating that patients who have less than three to five metastatic nodes survive appreciably longer than those who have more than 10 involved nodes following a potentially curative resection [19,32]. Given this information, the determination of lymph node status before definitive therapy might be of importance because patients who have more advanced locoregional disease could be enrolled in trials of novel or multimodal therapies.

Historically, clinicians have attempted to image lymph node metastases using multiple modalities with limited success. The accuracy of the CT scan for staging this aspect of the disease has been well described in multiple literature reports. Because the detection of metastatic nodes using CT depends primarily on size criteria, its sensitivity and specificity in detecting metastatic disease in the lymph nodes varies with the definition of an abnormally enlarged node. Sensitivity is enhanced if smaller size criteria are used, but specificity is sacrificed. Conversely, large lymph nodes on CT are more likely to be metastatic; however, many metastatic nodes are only minimally—if at all—enlarged, which hampers sensitivity. Using the common size criterion of 1 cm to define an enlarged node, most studies report that the sensitivity of CT is poor (30–60%) [17,33] and does not appear to be enhanced with helical scanning [34]. In contrast, specificity tends to be somewhat better, but still suboptimal (60–80%). In summary, if CT sug-

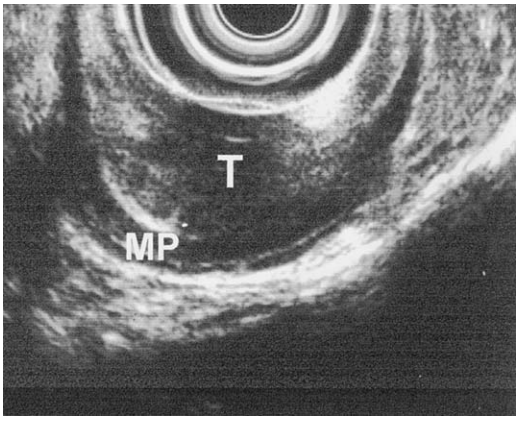

Fig. 4. EUS image of T2 squamous cell carcinoma of the esophagus. Note the tumor (T) is indistinguishable from the muscularis propria (MP).

gests the presence of metastatic lymph nodes, tissue confirmation should be obtained if the treatment plan will be affected.

In recent years the role of FDG-PET has been evaluated for the detection of lymph node metastases in patients who have esophageal cancer. FDG-PET is a physiologic examination that has poor anatomic definition, which severely affects its ability to predict N1 disease accurately in the peritumoral location [33,35]. In this regard, most esophageal tumors are intensely FDG avid, further inhibiting the resolution of the study and making it easy to miss metastatic nodes that are adjacent to the primary tumor. In contrast, when metastatic lymph nodes are located more remotely, the accuracy of FDG-PET increases [33,35]. The differentiation of FDG-avid peritumoral nodes from the primary tumor might be aided by the development of CT/PET fusion scanners (Fig. 5), in which the anatomic detail of CT is combined with the physiologic nature of FDG-PET, but this scenario remains to be seen.

Given these spatial limitations of FDG-PET, it is not surprising that the sensitivity of this modality in detecting peritumoral metastatic lymph nodes is poor (20–50%) in most contemporary series [17,33,35]; however, sensitivities as high as 90% have been reported in the detection of metastatic nodes in distant locations such as the abdomen and the neck [33,35]. In distinct contrast, the specificity of FDG-PET in lymph node evaluation tends to be high, exceeding 90% in many series [17,33,35].

US, transcutaneous and endoscopic, is used frequently to stage the N descriptor in patients who have esophageal carcinoma. US relies not only on size criteria to determine metastasis but also on the internal echo characteristics of individual nodes. Well-demarcated, larger, hypoechoic nodes with scattered large, internal echoes are more likely to represent metastases (Fig. 6) [36,37]. The use of transcutaneous US to image cervical and supraclavicular lymph nodes has become routine in some regions, especially in Asia, where reported accuracy is approximately 70% to 80% [36,38]; however, other reports have not been able to confirm these results [35].

The accuracy of EUS in detecting metastatic lymph nodes in patients who have esophageal carcinoma has also been investigated and reported in many series (Fig. 6). Wide variations of sensitivity and specificity have been reported in these series, ranging from 40% to 100% [39]. Similar to the ability to detect T stage, the ability of EUS to stage the N descriptor effectively is highly user-dependent. Centers that perform large numbers of procedures report higher accuracy rates [37], which have not been reproducible in other studies [35], which leads one to question the accuracy of EUS in routine practice settings. To address this issue, EUS has been combined with FNA of suspicious lymph nodes. The addition of FNA to EUS has been shown by some investigators to markedly enhance the specificity of EUS alone, especially in the region of the celiac axis [40,41]. Whether or not these excellent results can be

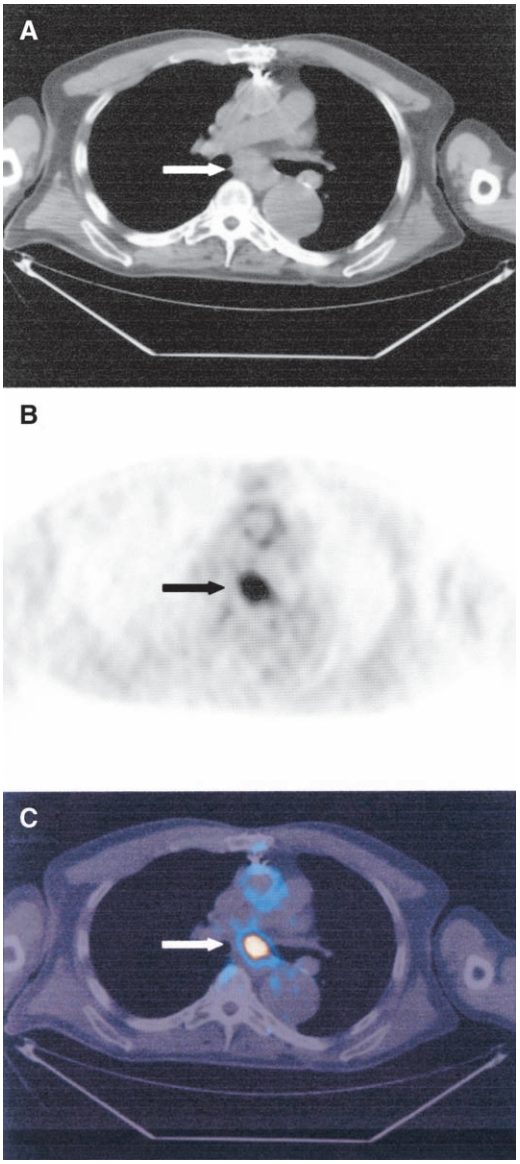

Fig. 5. CT/PET fusion study depicting malignant periesophageal lymph node. The *arrow* indicates the malignant node in each panel. (*A*) Noncontrast CT image. (*B*) FDG-PET image. (*C*) CT/PET fusion image.

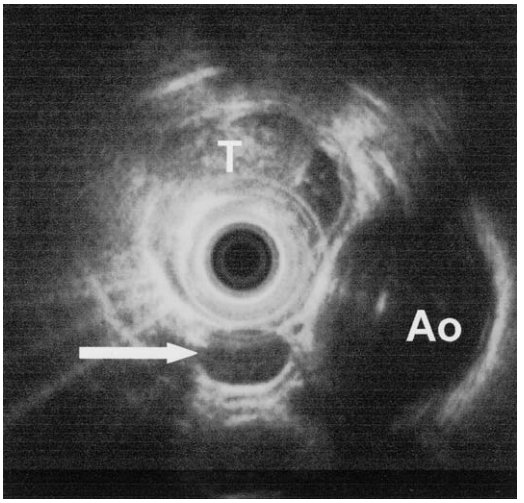

Fig. 6. EUS image of a typical metastatic lymph node in a patient who had carcinoma of the esophagus. The metastatic node is seen as a large, hypoechoic structure in the periesophageal location (*arrow*).
Abbreviations: Ao, descending thoracic aorta; T, tumor.

achieved and reproduced routinely remains to be determined and will influence the applicability of this technique in routine practice situations.

Assessment of response to therapy

Given the relatively poor prognosis of patients who have carcinoma of the esophagus who undergo surgical resection alone for locally advanced disease, preoperative (induction) chemotherapy or chemoradiotherapy are being investigated as means to obtain higher cure rates. Data from these clinical trials have suggested that patients who are complete pathologic responders to induction therapy seem to reap the most benefit from multimodal treatment protocols [42,43], so it might be advantageous to determine which patients would benefit most from surgery before resection. The accuracy of imaging modalities in this capacity is now being investigated, with some preliminary results published in recent literature.

Jones and colleagues compared the response to preoperative chemoradiation as determined by repeat CT scanning to pathological response rates prospectively in 50 patients [44]. Using standard radiographic response criteria, CT was found to be ineffective for determining pathologic tumor response or disease stage in this setting. Similarly, EUS was unable to stage patients accurately after induction therapy [45,46]; however, some evidence suggested that measurements of tumor size using EUS might correlate with response to chemoradiotherapy [47]. Some recent data suggest that a reduction in FDG uptake by esophageal tumors after induction chemoradiotherapy might correlate with pathologic response to therapy [48] and even improved survival in these patients [49]. The use of imaging studies to assess the response to therapy in patients who have esophageal carcinoma is an emerging field, and it requires extensive investigation in future studies.

Summary

Carcinoma of the esophagus must be staged accurately before a treatment plan is initiated, and imaging studies play a major role in this process. Imaging for esophageal carcinoma involves evaluation of the locoregional extent of the tumor and distant metastatic disease. A CT scan of the chest and upper abdomen provides the most comprehensive information about esophageal carcinoma; however, accurate assessment of the depth of primary tumor invasion and lymph node status remains limited, even with newer generation scanners. Endoscopic US is a user-dependent modality that has emerged as a highly accurate technique in experienced hands to evaluate the depth of penetration of esophageal tumors, but its ability to detect metastatic lymph nodes is less impressive, leading some investigators to perform confirmatory needle aspiration of suspicious nodes. FDG-PET is a physiologic examination that is the subject of intense investigation in patients who have esophageal carcinoma. Preliminary studies have suggested that FDG-PET can detect otherwise radiographically occult distant metastatic disease in these patients, and changes in FDG uptake might correlate with the response to therapy. These findings need to be confirmed in larger studies. More sophisticated technology continues to be developed for imaging carcinoma of the esophagus, which will more than likely affect staging algorithms in the future.

References

[1] Korst RJ, Altorki NK. Esophageal cancer. In: Winchester DP, Daly JM, Jones RS, Murphy GP, editors. Cancer surgery for the general surgeon. Philadelphia: Lippincott-Raven; 1999. p. 155–72.
[2] Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics, 2000. CA 2000;50:7–33.
[3] Devesa SS, Blot WJ, Fraumeni Jr JF. Changing pat-

terns in the incidence of esophageal and gastric carcinoma in the United States. Cancer 1998;83:2049–53.
[4] Long BW. Image-guided percutaneous needle biopsy: an overview. Radiol Technol 2000;71(4):335–59.
[5] Quint LE, Hepburn LM, Francis IR, Whyte RI, Orringer MB. Incidence and distribution of distant metastases from newly diagnosed esophageal carcinoma. Cancer 1995;76(7):1120–5.
[6] Christie NA, Rice TW, DeCamp MM, Goldblum JR, Adelstein DJ, Zuccaro Jr G, et al. M1a/M1b esophageal carcinoma: clinical relevance. J Thorac Cardiovasc Surg 1999;118(5):900–7.
[7] Paulson EK. Evaluation of the liver for metastatic disease. Semin Liver Dis 2001;21:225–36.
[8] Robinson PJA. Imaging liver metastases: current limitations and future prospects. Br J Radiol 2000;73: 234–41.
[9] Bemelman WA, van Delden OM, van Lanschot JJ, de Wit LT, Smits NJ, Fockens P, et al. Laparoscopy and laparoscopic ultrasonography in staging of carcinoma of the esophagus and gastric cardia. J Am Coll Surg 1995;181(5):421–5.
[10] van Dijkum EJ, de Wit LT, van Delden OM, Kruyt PM, van Lanschot JJ, Rauws EA, et al. Staging laparoscopy and laparoscopic ultrasonography in more than 400 patients with upper gastrointestinal carcinoma. J Am Coll Surg 1999;189(5):459–65.
[11] Henschke CI, McCauley DI, Yankelevitz DF, Naidich DP, McGuinness G, Miettinen OS, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. Lancet 1999;354(9173):99–105.
[12] Margolis ML, Howlett P, Bubanj R. Pulmonary nodules in patients with esophageal carcinoma. J Clin Gastroenterol 1998;26:245–8.
[13] Rosenthal DI. Radiologic diagnosis of bone metastases. Cancer 1997;80(8 Suppl):1595–607.
[14] Reincke M. Mutations in adrenocortical tumors. Horm Metab Res 1998;30(6–7):447–55.
[15] Lockhart ME, Smith JK, Kenney PJ. Imaging of adrenal masses. Eur J Radiol 2002;41(2):95–112.
[16] Luketich JD, Friedman DM, Weigel TL, Meehan MA, Keenan RJ, Townsend DW, et al. Evaluation of distant metastases in esophageal cancer: 100 consecutive positron emission tomography scans. Ann Thorac Surg 1999;68(4):1133–6.
[17] Block MI, Patterson GA, Sundaresan RS, Bailey MS, Flanagan FL, Dehdashti F, et al. Improvement in staging of esophageal cancer with the addition of positron emission tomography. Ann Thorac Surg 1997;64(3): 770–6.
[18] Croft DR, Trapp J, Kernstine K, Kirchner P, Mullan B, Galvin J, et al. FDG-PET imaging and the diagnosis of non-small cell lung cancer in a region of high histoplasmosis prevalence. Lung Cancer 2002;36(3):297–301.
[19] Korst RJ, Rusch VW, Venkatraman E, Bains MS, Burt ME, Downey RJ, et al. Proposed revision of the staging classification for esophageal cancer. J Thorac Cardiovasc Surg 1998;115(3):660–9.
[20] Altorki N, Kent M, Ferrara C, Port J. Three-field lymph node dissection for squamous cell and adenocarcinoma of the esophagus. Ann Surg 2002;236(2):177–83.
[21] Akiyama H, Kogure T, Itai Y. The esophageal axis and its relationship to the resectability of carcinoma of the esophagus. Ann Surg 1972;176:30–6.
[22] Rice TW. Clinical staging of esophageal carcinoma. CT, EUS, and PET. Chest Surg Clin N Am 2000; 10(3):471–85.
[23] Thompson WM, Halvorsen RA. Staging esophageal carcinoma II. CT and MRI. Semin Oncol 1994;21: 447–52.
[24] Picus D, Balfe DM, Koehler RE, Roper CL, Owen JW. Computed tomography in the staging of esophageal carcinoma. Radiology 1983;146(2):433–8.
[25] Lightdale CJ. Staging esophageal carcinoma I. Endoscopic ultrasonography. Semin Oncol 1994;21: 438–46.
[26] Rosch T. Endosonographic staging of esophageal cancer: a review of literature results. Gastrointest Endosc Clin N Am 1995;5:537–47.
[27] Schlick T, Heintz A, Junginger T. The examiner's learning effect and its influence on the quality of endoscopic ultrasonography in carcinoma of the esophagus and gastric cardia. Surg Endosc 1999;13:894–8.
[28] Silverstein FE, Martin RW, Kimmey MB, Jiranek GC, Franklin DW, Proctor A. Evaluation of an endoscopic ultrasound probe: in vitro and in vivo canine studies. Gastroenterology 1989;96:1058–62.
[29] Tokiyama H, Yanai H, Nakamura H, Takeo Y, Yoshida T, Okita K. Three-dimensional endoscopic ultrasonography of lesions of the upper gastrointestinal tract using a radial–linear switchable thin ultrasound probe. J Gastroenterol Hepatol 1999;14(12):1212–8.
[30] Waxman I. Endosonography in columnar-lined esophagus. Gastroenterol Clin N Am 1997;26(3):607–12.
[31] Ozawa S, Imai Y, Suwa T, Kitajima M. What's new in imaging? New magnetic resonance imaging of esophageal cancer using an endoluminal surface coil and antibody-coated magnetite particles. Recent Results Cancer Res 2000;155:73–87.
[32] Eloubeidi MA, Desmond R, Arguedas MR, Reed CE, Wilcox CM. Prognostic factors for the survival of patients with esophageal carcinoma in the US: the importance of tumor length and lymph node status. Cancer 2002;95(7):1434–43.
[33] Kato H, Kuwano H, Nakajima M, Miyazaki T, Yoshikawa M, Ojima H, et al. Comparison between positron emission tomography and computed tomography in the use of the assessment of esophageal carcinoma. Cancer 2002;94(4):921–8.
[34] Romagnuolo J, Scott J, Hawes RH, Hoffman BJ, Reed CE, Aithal GP, et al. Helical CT versus EUS with fine needle aspiration for celiac nodal assessment in patients with esophageal cancer. Gastrointest Endosc 2002; 55(6):648–54.
[35] Lerut T, Flamen P, Ectors N, Van Cutsem E, Peeters M, Hiele M, et al. Histopathologic validation of lymph node staging with FDG-PET scan in cancer of the esophagus and gastroesophageal junction: a prospec-

tive study based on primary surgery with extensive lymphadenectomy. Ann Surg 2000;232(6):743–52.
[36] Natsugoe S, Nakashima S, Matsumoto M, Sakita H, Sakamoto F, Okumura H, et al. Biologic and imaging diagnosis of lymph node metastasis in esophageal carcinoma. J Surg Oncol 2002;81(1):25–32.
[37] Catalano MF, Sivak Jr MV, Rice T, Gragg LA, Van Dam J. Endosonographic features predictive of lymph node metastasis. Gastrointest Endosc 1994;40(4):442–6.
[38] Natsugoe S, Yoshinaka H, Shimada M, Shirao K, Nakano S, Kusano C, et al. Assessment of cervical lymph node metastasis in esophageal carcinoma using ultrasonography. Ann Surg 1999;229(1):62–6.
[39] Kelly S, Harris KM, Berry E, Hutton J, Roderick P, Cullingworth J, et al. A systematic review of the staging performance of endoscopic ultrasound in gastro-oesophageal carcinoma. Gut 2001;49(4):534–9.
[40] Eloubeidi MA, Wallace MB, Reed CE, Hadzijahic N, Lewin DN, Van Velse A, et al. The utility of EUS and EUS-guided fine needle aspiration in detecting celiac lymph node metastasis in patients with esophageal cancer: a single-center experience. Gastrointest Endosc 2001;54(6):714–9.
[41] Parmar KS, Zwischenberger JB, Reeves AL, Waxman I. Clinical impact of endoscopic ultrasound-guided fine needle aspiration of celiac axis lymph nodes (M1a disease) in esophageal cancer. Ann Thorac Surg 2002; 73(3):916–20.
[42] Urba SG, Orringer MB, Turrisi A, Iannettoni M, Forastiere A, Strawderman M. Randomized trial of preoperative chemoradiation versus surgery alone in patients with locoregional esophageal carcinoma. J Clin Oncol 2001;19(2):305–13.
[43] Bosset JF, Gignoux M, Triboulet JP, Tiret E, Mantion G, Elias D, et al. Chemoradiotherapy followed by surgery compared with surgery alone in squamous-cell cancer of the esophagus. N Engl J Med 1997;337(3): 161–7.
[44] Jones DR, Parker Jr LA, Detterbeck FC, Egan TM. Inadequacy of computed tomography in assessing patients with esophageal carcinoma after induction chemoradiotherapy. Cancer 1999;85(5):1026–32.
[45] Beseth BD, Bedford R, Isacoff WH, Holmes EC, Cameron RB. Endoscopic ultrasound does not accurately assess pathologic stage of esophageal cancer after neoadjuvant chemoradiotherapy. Am Surg 2000; 66(9):827–31.
[46] Mallery S, DeCamp M, Bueno R, Mentzer SJ, Sugarbaker DJ, Swanson SJ, et al. Pretreatment staging by endoscopic ultrasonography does not predict complete response to neoadjuvant chemoradiation in patients with esophageal carcinoma. Cancer 1999;86(5): 764–9.
[47] Willis J, Cooper GS, Isenberg G, Sivak Jr MV, Levitan N, Clayman J, et al. Correlation of EUS measurement with pathologic assessment of neoadjuvant therapy response in esophageal carcinoma. Gastrointest Endosc 2002;55(6):655–61.
[48] Kato H, Kuwano H, Nakajima M, Miyazaki T, Yoshikawa M, Masuda N, et al. Usefulness of positron emission tomography for assessing the response of neoadjuvant chemoradiotherapy in patients with esophageal cancer. Am J Surg 2002;184(3):279–83.
[49] Downey RJ, Akhurst T, Ilson D, Ginsberg R, Bains MS, Gonen M, et al. Whole body 18FDG-PET and the response of esophageal cancer to induction therapy: results of a prospective trial. J Clin Oncol 2003; 21(3):428–32.