Radiologic Assessment of Esophageal Cancer

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Introduction

Esophageal cancer represents the third most common gastrointestinal tract malignancy and sixth most common cause of cancer death worldwide [1, 2]. About 17,290 new cases of esophageal cancer will be diagnosed in the United States in 2018 (13,480 in men and 3810 in women) and about 15,850 deaths from esophageal cancer are estimated by the American Cancer Society [3]. The majority of esophageal cancers are either squamous cell carcinoma (SCC) or adenocarcinomas [1, 2]. SCC is the most common pathologic subtype with a higher incidence in developing countries [1, 2, 4]. Esophageal adenocarcinomas comprise 15% of all esophageal cancers [4]. Other malignant tumors such as sarcomas, lymphoma, and small cell carcinoma (neuroendocrine tumor) are rather rare [4]. Accurate initial staging of esophageal cancer is required to guide treatment protocols and to estimate prognosis [1, 2, 4–6].

Diagnosis

For many developing countries, barium esophagogram remains the primary diagnostic test for esophageal cancer [5]. The most common radiographic appearance is the presence of an abrupt irregular narrowing with an ulcerated surface in a stricture [5, 7] (Fig. 7.1). Modern barium esophagogram detects a lesion in 98% of studies of patients

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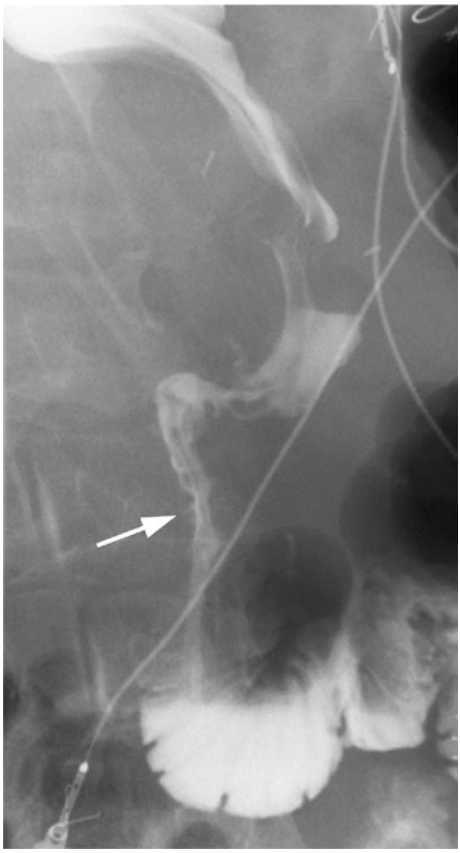

Fig. 7.1 Barium esophagogram of a patient with esophageal cancer shows abrupt narrowing of esophagus and focal areas of ulceration (arrow) with stricture

with esophageal cancer and is suggestive of esophageal cancer in 96%, with an estimated positive predictive value of 42% [5, 8]. As clinical diagnosis of esophageal cancer requires tissue confirmation, most centers in developed countries perform esophagoscopy with tissue sampling instead of esophagogram. Although the flexible fiberoptic system is most commonly utilized, in cases with severe stricture, esophagoscopy may not be possible. In these circumstances, endoscopic esophageal ultrasound (EUS) and EUS fine-needle aspiration (EUS FNA) are the procedures of choice. FNA with biopsy of suspicious findings is an important step during the staging process [5].

Staging

Clinical staging tools include esophagoscopy with biopsy, EUS, EUS-FNA, CT, and FDG positron emission tomography/computed tomography (PET/CT). Bronchoscopy, cervical lymph node biopsy, endoscopic bronchial ultrasound (EBUS) and EBUS-FNA, ultrasound, or CT-directed biopsies can be used in specific cases [1, 2, 4, 5, 7].

CT [9] and EUS have been the mainstay imaging modalities for initial staging; however, these modalities may over- or understage as many as 30–40% of cases [10]. PET/CT demonstrates superiority to other modalities especially given its effectiveness in the detection of distant metastatic disease [10]. Wallace et al. examined multiple imaging modalities for staging and concluded that the preferred staging procedure was PET/CT followed by EUS in cases where no evidence of metastasis was observed by PET/CT [10, 11].

Staging of esophageal cancer has been updated in the eighth edition of the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) cancer staging manuals [12]. This new edition includes separate clinical (CTNM), pathologic (pTNM), and postneoadjuvant therapy (ypTNM) staging groupings [12]. It is relevant to acknowledge that clinical staging is in general limited by the resolution of the imaging methods used for such staging. The limitations and strengths of each modality should, therefore, be taken into consideration.

Depth of invasion defines the T staging of primary cancer. T *is* (in situ) tumors are intra-epithelial without invasion of the basal membrane, currently termed high-grade dysplasia. T1 cancers extend beyond the basal membrane and invade the lamina propria, muscularis mucosa, or submucosa. T1 cancers can be classified as mucosal (T1a) or submucosal (T1b). T2 cancers breach into but not beyond the muscularis propria. T3 cancers invade beyond the esophageal wall without invading adjacent structures. T4 cancers invade structures adjacent to the esophagus. T4a cancers are still resectable, invading adjacent structures like the pleura, pericardium, and diaphragm. T4b tumors are unresectable due to invasion of other adjacent structures like the aorta, vertebral bodies, or trachea [2, 4, 5, 13].

A regional lymph node is defined as any paraesophageal lymph node extending from cervical nodes to celiac nodes. N classification includes N0 (no cancer-positive nodes), N1 (1 or 2 nodes), N2 (3–6 nodes), and N3 (7 or more) [2, 4, 5].

Distant metastasis is classified as either M0, no distant metastasis, or M1, distant metastasis. Histopathologic cell type is either squamous cell carcinoma or adenocarcinoma as AJCC/UICC staging is based on cancers arising from the esophageal epithelium. Histologic grade is categorized as G1 well differentiated, G2 moderately differentiated, G3 poorly differentiated, and G4 undifferentiated [4, 5, 13]. The histologic grade has been eliminated from the AJCC/UICC eighth edition, with the expectation for it to be considered for the ninth edition.

In this new edition, cancer location is expressed as the distance of the epicenter of the cancer from the incisors. Upper and lower border of the tumor and cancer length are needed to provide the epicenter. This is new compared to the prior determination of tumor location in the seventh edition, which was the proximal end of the cancer from the incisors. This location can be correlated with anatomic imaging. If the tumor is above the sternal notch, the esophageal cancer is located in the cervical esophagus. An upper thoracic location on CT corresponds to the region between the sternal notch and lower border of the azygos vein. Middle thoracic tumors are located between the azygos vein and inferior pulmonary vein. The lower thoracic region is below the inferior pulmonary vein to the stomach or gastroesophageal junction (Fig. 7.2) [4, 5, 11]. Adenocarcinomas with epicenter no more than 2 cm

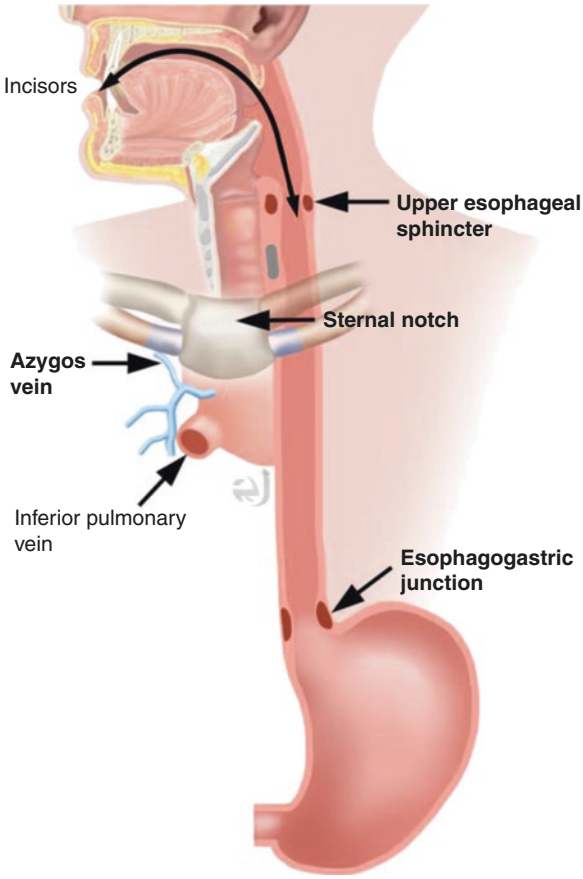

Fig. 7.2 Anatomic localization of esophageal cancer

into the gastric cardia are staged as esophageal adenocarcinomas, and those extending further are staged as stomach cancers.

T Staging

T1 and T2 tumors are generally treated with surgery, whereas patients with T3 and T4 tumors are frequently offered preoperative chemotherapy and/or radiation therapy. Hence, the detection of depth of invasion for proper T staging becomes crucial [1, 2, 4, 5, 7].

EUS

EUS is the most accurate imaging tool that provides information about involvement of the esophageal wall that is necessary to define T stage. EUS may detect the involvement of adjacent structures, specifically the invasion through the muscularis

propria layer, so that it may upstage a cancer to T4 in the presence of invasion [6]. The performance of EUS has been shown to improve as the T stage increases [2, 7]. The distinction between T1 or T2 and T2 or T3 cancers is essential for decision making because the former are typically N0, requiring resection alone, while T3–4 cancers have a higher probability of N1 disease requiring neoadjuvant therapy [12, 14].

EUS is not accurate in differentiating T *is* from T1. However, US performed with high-frequency probes showed very good results in distinguishing mucosal versus submucosal invasion [1]. In comparison to CT, EUS is more accurate in differentiating between T1, T2, and T3 tumors [2]. However, there are shortcomings of EUS. Like any other sonographic examination, it is operator dependent, and in cases where the esophageal lumen is narrowed, it may be impossible to pass the endoscope through the stricture [2, 4]. In these cases, mechanical dilatation can be performed; however, there is increased risk of esophageal perforation [1, 4].

The appropriate therapy for esophageal cancer partly relies on the accurate assessment of disease extent. This information is often acquired from PET/CT and EUS. The length of disease (LoD) is an important measurement that can influence therapy decisions. The results from a recent study showed that PET/CT tends to under-measure LoD compared to EUS [15].

Evaluation of depth of invasion for superficial esophageal cancer is generally performed by white light imaging (WLI) and EUS. Recent advances in magnifying endoscopy and narrow band imaging (M-NBI) enabled the assessment of the pattern of intra-epithelial papillary capillary loops and avascular area to predict the histology and cancer invasion depth. As the classification method for M-NBI is complicated, it is not widely used in clinical practice. Recently, a simplified method of classification was suggested by the Japanese Esophageal Society. A study by Wang et al. confirmed that a training program for this new simplified method improved the diagnostic accuracy of cancer invasion depth [16].

CT and MRI

Assessment of the esophagus by CT can be challenging especially for T1 and T2 esophageal cancers, as the detection of a small tumor in a poorly distended tubular structure is quite difficult. Usually, the esophageal wall measures less than 3 mm on CT of a distended esophagus [2, 4]. A wall thickness more than 5 mm is considered abnormal [4]. Asymmetric thickening of the esophageal wall is a primary but nonspecific finding [4] for esophageal cancer. CT assessment is less accurate for the detection and staging of esophageal cancer compared to EUS [1, 2, 4] (Fig. 7.3).

In circumstances when esophagoscopy is not possible, mostly due to the presence of a marked stricture, CT may provide information about the location of the tumor.

The most useful aspect of CT in T staging is to evaluate for the presence of invasion of adjacent soft tissues. Direct invasion or obliteration of the fat plane between the tumor and the anatomic structure may indicate local invasion [1, 2, 4, 7]. However caution is advised in cachectic patients and in patients with prior history of radiation therapy or surgery as fat planes on CT may not be clearly depicted [1, 2, 7].

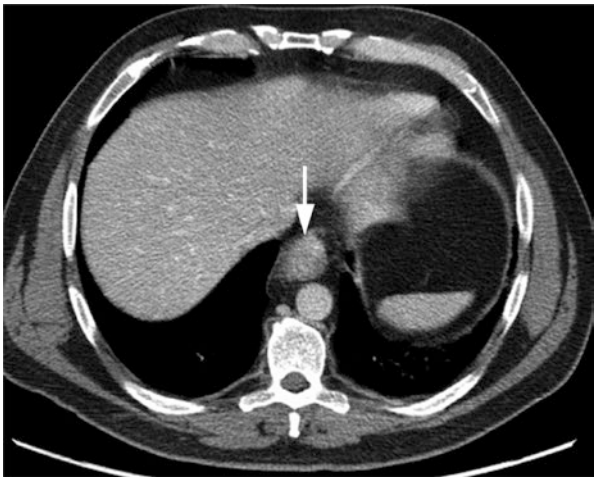

Fig. 7.3 Axial contrast-enhanced CT of the upper abdomen shows marked circumferential thickening of the distal esophagus (arrow), consistent with known esophageal cancer. Unfortunately, CT was not able to properly determine T staging as the assessment of esophageal wall layers was limited with this imaging technique

In addition, local invasion is suggested by a contact angle of more than 90° between the cancer and the aorta or thickening and displacement or indentation of the posterior membrane of the trachea or left mainstem bronchus, yet neither of these findings is definitive [1, 4, 6]. Finally, tumor extension in the airway or a fistula between the esophagus and airway may be visualized; still bronchoscopic confirmation is necessary. Pleural effusion and pleural wall thickening are suspicious findings on CT for tumoral invasion. Direct extension of tumor to the heart or loss of pericardial fat plane can also be detected by CT.

With recent advances in CT technology, it is possible to provide higher quality images with isotropic voxels as well as CT esophagography or virtual endoscopy [4].

Multi-planar reformatted images (MPRs) are useful to estimate tumor length and assessment of the exact location of esophageal cancer is more accurate compared to that achieved with axial images only [1, 4]. MPRs are also useful in evaluating esophageal cancers at the esophagogastric junction (EGJ) [1]. Pneumo-CT is a technique developed to image stenotic lesions, optimizing tumor visualization at the esophageal wall [17]. Administration of effervescent granules, air insufflations, or ingestion of large amounts of water is another method to better visualize the esophageal wall by CT [4].

Magnetic resonance imaging (MRI) has a limited role in imaging of esophageal cancer due to technical shortcomings. Early studies with MRI demonstrated poor quality especially due to motion artifacts and cardiac/respiratory-related artifacts. Recent developments in cardiac respiratory gating, availability of high field magnets (1.5 and 3 T) for imaging, and the development of new and faster imaging sequences have resulted in better-quality images. The addition of sequences such as diffusion-weighted imaging and dynamic contrast enhancement has improved esophageal cancer imaging. Preliminary studies with high-resolution MR imaging report high accuracies for T staging, close to that of EUS [18–20].

FDG PET

The first report in the literature of the use of FDG PET in a patient with esophageal cancer was described in 1995, by Yasuda [10, 21]. Given that FDG PET provides mostly metabolic information about the tumor, determination of T stage is not one of its strengths. Though 92–100% of esophageal cancers are FDG avid, lack of visualization of esophageal wall layers, even with combined FDG PET/CT limits accurate assessment of T stage. Some authors, such as Kato, report that T1 tumors lack FDG uptake, likely due to their size below the resolution for PET (0.7–1 cm) [22]. In the study by Kato, it was found that T2, T3, and T4 tumors have similar levels of FDG uptake [23]. Advanced T staging could be seen with combined PET/CT, when the metabolic activity extends to adjacent soft tissues in the mediastinum, and the fat planes are lost suggesting invasion [1].

Increasing data exist to support the use of quantitative measures or metabolic parameters of the primary tumor as prognostic predictors. These include standardized uptake value (SUV), metabolic tumor volume (MTV) and total tumor glycolysis (TLG), among others [23–25]. A meta-analysis of ten studies with 542 patients by Pan reports that high SUVs are associated with a significantly poorer overall survival and disease free survival. Foley studied these independent predictors of survival, and the most significant was TLG (defined by the product of metabolic volume of primary tumor times SUVmean). In Foley's study, another significant predictive factor was the "Metastatic Length of Disease" defined as the total length of disease including nonregional lymph node metastases and distant metastases measured in mm. The total count of involved local lymph node metastases on PET/CT was also a significant predictor of survival [24].

Finally, FDG uptake secondary to inflammation from esophagitis may confound accurate T staging, although the pattern of FDG uptake is usually linear and diffuse compared to focal for malignancies [26].

N Stage

Lymphatic involvement can occur at very early stages of esophageal cancer due to the unique bidirectional lymphatic drainage system of the esophagus. The intramural (mucosal) drainage system is located in the lamina propria. Unlike other parts of the gastrointestinal system, this location can result in early dissemination of tumor cells. The second, longitudinal system is localized in the submucosa, within the muscular layer [4].

EUS

EUS and EUS FNA are primary tools to identify regional nodal involvement. EUS has an accuracy of 72–80% [2]. CT has an accuracy ranging between 46 and 58% [1]. Although EUS is superior to CT in detecting lymph node metastasis, the sensitivity and specificity vary depending on location; for example, detection of celiac axis lymph nodes is better than that of mediastinal lymph nodes with EUS [1].

Combined use of EUS with FNA improves accuracy [1, 2, 4]. However, EUS FNA can only be performed in lymph nodes that are approachable [4]. Metastatic lymph nodes can appear as well-defined (clear border), round, homogeneous, and low-echoic lesions measuring more than 10 mm in diameter [4]. According to Rice et al. [7], the accuracy of detecting nodal metastasis in lymph nodes with all five of these features is 100% [7]. However, very few metastatic lymph nodes present with all of these findings, especially in a peri-esophageal location.

Recent study by Goense et al. showed that cervical ultrasonography has no additional value over PET/CT in assessment of cervical lymph node metastases. PET/CT provides a better diagnostic confidence compared to cervical ultrasonography. However, FNA can be still needed for cervical lesions that are identified on PET/CT [27].

CT and MRI

CT provides information about nonregional lymph nodes, mainly supraclavicular, abdominal, retrocrural lymph nodes. A short axis of more than 1 cm of a lymph node on CT is the most widely used criterion for suspicious lymph node involvement (Fig. 7.4). The cut offs for retrocrural and supraclavicular nodes are 0.6 cm and 0.5 cm, respectively. However, normal-sized lymph nodes may contain tumor deposits, resulting in false negative examination. Also an enlarged lymph node may not be malignant but could be inflammatory, resulting in false positive results with CT [2, 4]. Therefore, sensitivity and specificity of detection of nodal metastasis with CT are low, with reported accuracy of 46–58% [2, 4].

MRI in its current state has moderate-to-poor diagnostic value for N staging. There are studies showing markedly improved diagnostic accuracy of MRI for N staging by using fast sequences and SPIO contrast agent [28, 29].

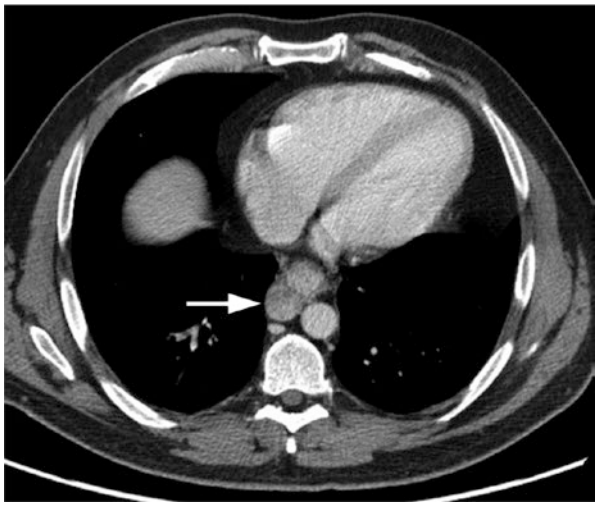

Fig. 7.4 Axial contrast-enhanced CT of the lower thoracic/upper abdomen region shows periesophageal lymphadenopathy, most consistent with malignant lymphadenopathy (arrow) as well as abnormal thickening of adjacent esophageal wall consistent with known esophageal cancer

FDG PET

FDG PET/CT combines the anatomic delineation of CT with PET, which can also identify tumoral deposits by the presence of FDG activity. FDG PET is limited in the detection of locoregional lymph nodes in close proximity to the primary tumor in which intense FDG activity may obscure FDG uptake in small adjacent lymph nodes [1, 4, 19]. The reported sensitivity and specificity for detection of locoregional lymph nodes by PET/CT is 59% and 81%, respectively, from a meta-analysis of 12 publications [5]. The sensitivity of EUS compared with PET/CT is superior for the detection of lymph nodes, although specificity is lower [9, 30]. The presence of locoregional lymph nodes does not preclude surgery; yet, if lymph nodes are seen beyond these boundaries, such as in the retroperitoneum or upper/mid-neck, the patient would be considered to have distant metastatic disease where surgery is contraindicated [31].

Compared to the detection of lymph node metastasis from lung cancer and other cancers, FDG PET/CT is less accurate in esophageal cancer [5]. The addition of FDG PET to EUS FNA does not change N classification significantly [5]. The sensitivity of PET/CT for the detection of distant nodal metastasis is 90% [2]. The combined use of PET and CT improves the detection rate of nodal disease (Fig. 7.5). Still, false-positive findings due to chronic inflammation may be a limitation [1].

Metabolic parameters have also been used in the evaluation of N staging. A study by Moon evaluated patients with clinically N0 disease, and reported that combined use of T classification and SUVmax were strong predictors of occult metastatic disease [32]. Other metabolic parameters such as TLG and MTV have been also studied by different groups. Hsu found a significant correlation between extratumoral maximum SUV and N classification [33].

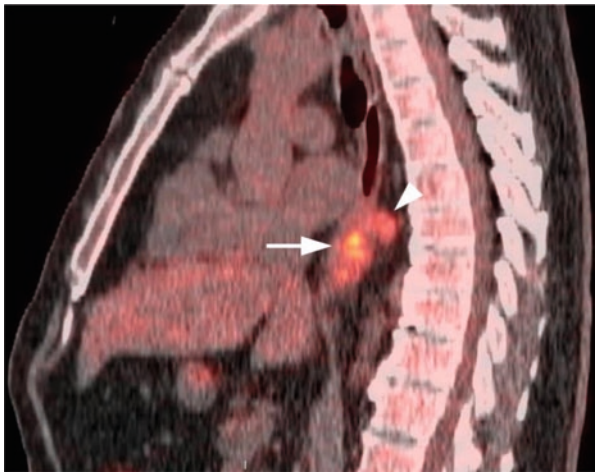

Fig. 7.5 Sagittal fused PET/CT image of the thoracic level shows the hypermetabolic esophageal cancer (arrow) and more cranially located hypermetabolic periesophageal lymph node (arrowhead)

M Stage

In patients with recent diagnosis of esophageal cancer, 20–30% will have distant metastasis at the time of diagnosis [1, 2]. Metastases are mostly found in the liver, lung, adrenals, and bones [1, 2, 4, 7]. Except for the brain, contrast-enhanced CT of the chest, abdomen, and pelvis will cover most of the areas that may have metastatic deposits. The most updated National Comprehensive Cancer Network (NCCN) guidelines propose the use of PET/CT in initial staging when upper gastrointestinal endoscopy, biopsy, and CT scan with and without contrast of the chest and abdomen fail to reveal M1 disease [34].

EUS

EUS has limited value in the assessment of distant metastasis. EUS can only detect distant metastasis if there is direct contact between the involved organ and the EUS probe, as in the retroperitoneum, left lateral segment of the liver, or celiac axis lymph nodes [1, 4, 7].

CT and MRI

Although CT is only 63–74% sensitive, it remains the mainstay for imaging of distant metastasis [4]. Hepatic metastases are visualized as low-density ill-defined lesions. Contrast-enhanced CT imaging during portal venous phase is mostly used for hepatic metastasis [1]. Lesions less than 1 cm are difficult to detect with CT, which may result in false-negative results [5]. Adrenal metastases usually appear as focal adrenal enlargement or an adrenal nodule. Optimized CT, MR imaging, percutaneous FNA, or laparoscopy may be required to confirm the etiology of these lesions [7, 35].

Solitary pulmonary metastases are rare at initial presentation. Solitary pulmonary nodules are more likely to be either benign or synchronous lung malignancies [5]. Therefore, tissue confirmation of solitary pulmonary nodules detected during staging should be considered [4]. Multiple pulmonary metastatic nodules are uncommon at initial presentation, though are seen more at late stages. CT is very sensitive at detecting pulmonary metastasis. Most pulmonary metastases are round, well defined, and noncalcified [1].

Brain metastases are reported in 2–4% of patients presenting with esophageal cancer. They tend to occur in patients with large EGJ adenocarcinomas, which have local invasion or lymph node metastasis [5, 36], and are best detected with optimized CT or brain MRI.

FDG PET

The most common sites for distant metastasis from esophageal cancer are liver, lung, bones, and adrenal glands. Less commonly seen are metastases to the brain, subcutaneous tissues, thyroid gland, skeletal muscles, and pancreas [37]. The pivotal role of FDG PET in esophageal cancer is the detection of distant metastases (Figs. 7.6 and 7.7). As M stage is a major determinant of treatment planning, PET/CT performed at initial workup is becoming the standard of care [1].

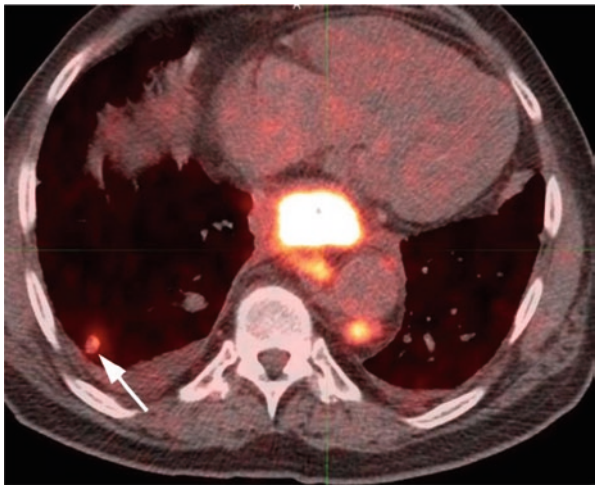

Fig. 7.6 Axial fused PET/CT images of the lower thoracic region show the large markedly hypermetabolic esophageal mass, two metastatic pulmonary nodules (one is hypermetabolic marked with arrow), and periesophageal metastatic adenopathy

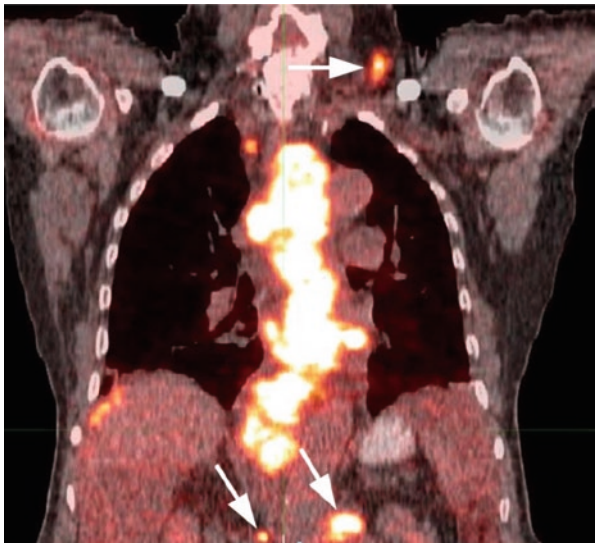

Fig. 7.7 Coronal fused PET/CT image shows hypermetabolic esophageal cancer with multiple periesophageal metastatic adenopathy. There is also left supraclavicular and celiac axis hypermetabolic metastatic lymph nodes (arrows). There is also curvilinear hypermetabolic activity at the right perihepatic region, consistent with subdiaphragmatic metastatic implants

In comparison with other modalities, PET alone is superior to CT in detecting metastatic cancer [1, 2, 5], yet combined PET/CT has lower sensitivity for lesions less than 1 cm. PET/CT detects radiologically occult distant metastases in 10–20% of cases [1, 7, 22]. FDG PET can be cost effective in preventing noncurative surgery by the detection of metastasis that are not identified with conventional imaging [1]. A meta-analysis reported that PET has 71% sensitivity and 93% specificity in the detection of distant metastases in comparison to 52% and 91% for CT, respectively [7, 38]. Disease management strategies may change in up to 38% of cases, by using PET/CT [39, 40].

Co-registered PET/CT has greater sensitivity, specificity, and overall accuracy than PET alone [1]. The combination of PET with CT has diagnostic accuracy of 80–92%. A relative limitation of PET/CT is lower sensitivity for liver metastases, secondary to the use of noncontrast CT by most centers [1]. Magnetic resonance is now considered the most sensitive noninvasive imaging modality for the detection of liver metastasis from gastrointestinal tract malignancies, followed closely by PET/CT in comparison with ultrasonography and CT [41]. Distant lymph node metastases without involvement of locoregional lymph nodes have been reported to occur in 25% of cases [37, 42, 43] (Fig. 7.7).

Therapeutic Response

The same staging modalities used for clinical staging can be used during assessment of therapeutic response.

EUS

EUS is inaccurate in determining T stage after therapy as it cannot distinguish inflammation/fibrosis from cancer; hence overstaging is the most common error [1]. Understaging can also occur secondary to difficulty in detection of residual microscopic disease [1]. Accuracy of EUS for detection of pathologic lymph nodes is also reduced by alterations in the appearance of pathological lymph nodes after therapy and possibly smaller metastatic deposits within the lymph nodes that are difficult to detect by ultrasound [7]. Use of EUS is also limited in some post-therapy conditions, including luminal stenosis and post-radiation esophagitis [1].

CT

Although CT is widely used during staging of esophageal cancer, it has very limited value in the assessment of therapy response as both viable tumor and post-therapy inflammatory changes have similar appearance on CT [1].

FDG PET

The prediction of tumor response early, during the neoadjuvant regimen, is of crucial importance. FDG PET is very useful in this regard. Decrease in FDG uptake early in the process, compared with initial metabolic activity in the primary tumor has been validated as a potential prognostic predictor in several studies [44] (Fig. 7.8).

It is important to remember that patients who have had radiation therapy may demonstrate higher levels of FDG uptake compared to patients receiving only chemotherapy [44]. Metabolic parameters may aid in assessing response to neoadjuvant therapy. Hatt studied SUV and TLG and found that the latter had better sensitivity and specificity for tumor response [45]. A prospective, multicenter study by Palie found that tumor volume, TLG, and maximum SUV are good predictors of poor response to neoadjuvant therapy. Other studies have found that a decrease in

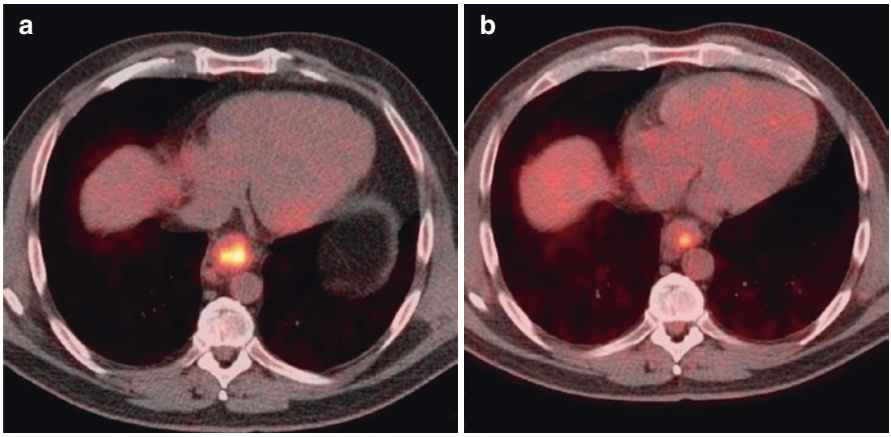

Fig. 7.8 Axial fused PET/CT images before (**a**) and after (**b**) therapy show the marked improvement of FDG activity of the tumor, most consistent with good therapy response

SUVmax of 35–60% between initial staging and after therapy PET/CT correlates with pathologic response [37, 46–49]. PET/CT has been found useful and superior to other modalities in the detection of new interval metastasis after neoadjuvant chemotherapy in 8–17% of cases [37]. Further studies are still needed to define the role of FDG PET in measuring response to therapy.

The NCCN guidelines recommend the use of PET/CT for the assessment of disease response at 5–8 weeks after preoperative or definite chemoradiation before surgery or initiation of postoperative treatment. PET alone is no longer offered in clinical practice. Also, these guidelines emphasize that ulceration caused by radiation therapy is a common false positive finding on PET/CT, therefore its combination with endoscopy may be useful to identify patients with high risk of residual tumor after preoperative chemoradiation [34].

Surveillance and Restaging

CT

The presence of new regional adenopathy or new soft tissue thickening is a CT finding concerning for recurrence [31].

FDG PET

FDG PET has a very good detection rate of recurrence or metastatic disease. It has been shown that FDG PET can provide additional information in up to 27% of cases [31]. One of the shortcomings of FDG PET is the presence of FDG activity with infection or inflammation. Hence, tissue sampling is required when an FDG avid focus is noted that is concerning for recurrence [31].

Treatment Complications

Patients undergoing multimodality therapy are at risk for more acute toxicities. Nonhematologic toxicities including esophagitis, infection, aspiration**,** and gastrointestinal or cardiac events can be diagnosed with the combination of clinical/laboratory and imaging information (Fig. 7.9) [31].

Anastomotic leakage is the most common surgical complication, with cervical anastomosis having higher risk than distal anastomosis [31]. Fluoroscopic esophagography with water-soluble contrast agents is the study of choice [31]. CT evaluation by an initial noncontrast study followed with oral administration of a low-osmolar IV contrast material is also used [31]. A recent study by Lantos concluded that esophagography had slightly lower sensitivity and substantially higher specificity compared to CT. Combined use of both modalities had 100% sensitivity. Hence, both studies can confidently exclude postoperative leaks [50]. Shoji et al. suggested a positive air bubble sign on CT as an objective and a noninvasive screening method for esophageal leaks [51].

A major surgical challenge is to have an adequate resection without compromising the blood supply for the esophageal conduit. Esophageal conduit necrosis is a rare but a life-threatening complication. A recent study by Lainas et al. suggested that esophageal conduit necrosis after esophagectomy may be due to preexisting celiac axis stenosis, either extrinsic stenosis by the median arcuate artery or intrinsic stenosis by atherosclerosis. Both of these findings can be evaluated by preoperative CT [52].

Late complications include esophageal stricture and perforation, which may be assessed with esophagography. Pulmonary toxicities such as pneumonitis may also be diagnosed with cross-sectional imaging, including CT or PET/CT [31].

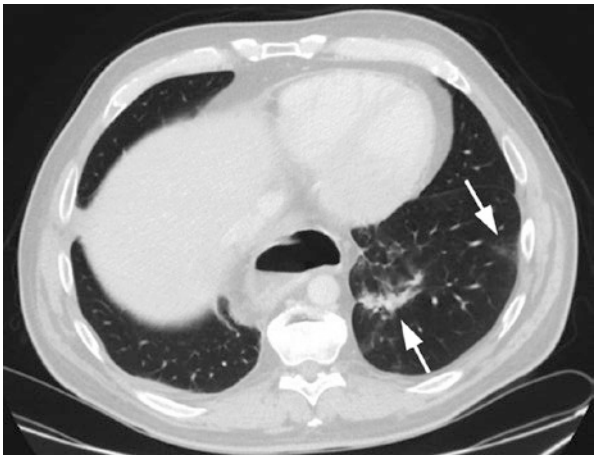

Fig. 7.9 Axial CT at lower thoracic level of a patient after esophageal cancer resection and gastric pull through. There are foci of ground glass opacities (arrow), and focal areas of pulmonary nodules (arrow) secondary to aspiration

Novel Imaging Modalities for Esophageal Cancer

A recently available hybrid modality (PET/MR) imaging allows the combination of both anatomic and functional information [35]. Lee investigated the role of PET/MR imaging in preoperative staging of esophageal cancer patients and compared MRI with FDG PET, EUS, and CT. In this study, PET/MR showed T staging accuracy comparable to EUS, and higher accuracy than EUS and PET in the prediction of N staging. PET/MR may have substantial potential in the imaging of esophageal cancer [35].

There is ongoing research in nuclear oncology with the development of novel radiotracers. 18F-fluorothymidine (FLT), a nucleoside analogue which is a marker of cell proliferation, has been evaluated as a potential relevant radiotracer in esophageal cancer. Early studies testing the capabilities of 18F-FLT PET for initial T and N staging were not encouraging, as 18F-FLT PET/CT scans showed less uptake in the tumors and more false negative findings [53, 54]. However, several more recent studies have evaluated 18F-FLT for the prediction of tumor response after chemotherapy, suggesting that this radiotracer could perform superiorly to F18-FDG, although more studies are needed to further validate its use [55–57].

Other novel PET radiotracers include 18F-FAMT, which accumulates in tumor cells via the L-type amino-acid transporter 1 (LAT1), which has been found to be associated with cell proliferation and angiogenesis. Suzuki correlated PET parameters with the development of lymph node metastasis in clinically N0 esophageal SCC cancer patients and it was found that elevated uptake correlated with advanced stage and lymph node metastasis. Although more studies are needed to determine the clinical use of F18-FAMT, it represents a potential target for guided therapeutic interventions [58].

CT texture analysis assessing components of the tumor and intratumoral heterogeneity has been studied in preoperative evaluation of esophageal cancer. A recent texture analysis study by Liu et al. showed that texture analysis has great potential in differentiating different T and N stages of esophageal cancer [59].

Machine learning methods have gained use to predict complex biological problems. One of the machine learning models is support vector models (SVMs). A recent study showed that assessment of CT images by using SVMs performed better than CT size criteria in diagnosing lymph node metastases in esophageal cancer before chemotherapy [60].

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