PET and PET/CT in the Diagnosis and Staging of Esophageal and Gastric Cancers

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KEYWORDS

• Esophageal cancer • Gastric cancer • FDG • PET-CT

The incidence of cancers of the distal esophagus and the gastric cardia is increasing in developed countries, and esophageal and gastric cancers are among the leading causes of cancer-related deaths worldwide.[1] Radical surgical resection is the primary curative treatment for early esophageal and gastric cancers; however, there are numerous treatment options. Multimodality treatment that employs preoperative chemotherapy with or without radiation followed by surgical resection in suitable candidates is increasingly being used in patients who have locally advanced cancer.[2–5] This evolving treatment strategy, together with the substantial morbidity and mortality associated with surgical resection, makes appropriate patient selection important for optimal management. In fact, management is determined to a large extent by patient performance status, location of the primary cancer, and stage of disease at presentation. Accordingly, accurate determination of the anatomic extent of the primary tumor and nodal and distant metastases is important.

Patients who have esophageal and gastric cancers are usually staged before therapy according to the recommendations of the American Joint Commission on Cancer (AJCC)/Union Internationale Contre le Cancer (UICC) system for pathologic and clinical staging, which follows a standardized evaluation of the primary tumor (T), regional lymph nodes (N), and distant metastatic disease (M). The clinical staging of esophageal and gastric cancers is usually performed using endoscopy or endoscopic ultrasound (EUS) and CT.[6–15] PET with fludeoxyglucose F 18 (FDG) is being increasingly used in the initial staging of patients who have esophageal and gastric cancers and may have a role in the assessment of therapeutic response. Because of the poor spatial resolution of PET compared with CT, however, the accurate assessment of the primary tumor and localization of nodal metastases and the detection of small pulmonary metastases are often difficult. Integrated PET-CT imaging with coregistration of anatomic and functional imaging data can improve the localization of regions of increased FDG uptake and the accuracy of staging in patients who have esophageal cancer.[16,17] MR imaging is infrequently used in the imaging algorithm of esophageal and gastric cancers; however, advances in MR imaging, including the use of high-resolution T2-weighted techniques and the recent development of endoluminal imaging, may result in MR imaging becoming useful in the staging of the primary esophageal cancer.[18–20] This

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article reviews the appropriate role of FDG-PET and FDG-PET-CT imaging in the diagnosis, initial staging, and detection of recurrent disease in patients who have esophageal and gastric cancers.

ESOPHAGEAL CANCER

The findings of two recent meta-analyses reviewing the staging investigations for esophageal cancer provide an indication of the overall roles that EUS, CT, and FDG-PET have in the evaluation of patients who have esophageal cancer.[8,13] EUS with fine-needle aspiration biopsy is the optimal modality for the detection and evaluation of the primary tumor and the detection of regional lymph node metastases (sensitivities for EUS, CT, and FDG-PET are 80%, 50%, and 57%, respectively; specificities are 70%, 83%, and 85%, respectively). FDG-PET and CT are useful in the detection of distant metastases (sensitivities are 71% and 52%, respectively; specificities are 93% and 91%, respectively). The following sections expand and clarify aspects of the findings of these meta-analyses as they pertain to the imaging performed in the clinical staging of patients who have esophageal cancer.

Diagnosis

Primary tumor detection by FDG-PET imaging has historically been considered high (greater than 90%) in patients who have esophageal carcinoma; however, the limitations in the spatial resolution of PET imaging and the stage and size of the primary tumor at presentation affect the accuracy of detection.[21–23] In a recent study by Kato and colleagues[22] comparing FDG-PET imaging with CT for staging patients who have esophageal cancer, the uptake of FDG was related to the stage of the primary esophageal tumor. Overall, FDG uptake in the primary tumor was visualized in 119 of 149 patients (80%) at initial evaluation. In the 81 patients who were treated with curative resection, FDG uptake was detected in 17 of 40 (43%) T1 tumors, 83% of T2 tumors, 97% of T3 tumors, and 100% of T4 tumors (**Figs. 1** and **2**). Himeno and colleagues[21] reported that FGD-PET imaging could reliably detect the primary esophageal tumor when the stage was T1b (invasion of the submucosa) or higher but could not detect tumors with less locoregional invasion (ie, Tis [in situ] and T1a tumors [invasion of the muscularis mucosae]).

The limitations of esophageal tumor detection by PET imaging are greater in the assessment of superficial esophageal cancers because these tumors are typically small. In this regard, in a recent study, Little and colleagues[23] reported that FDG-PET imaging had a poor detection rate for superficial esophageal cancers. In 58 patients who had superficial tumors, only 31 (53%) had increased FDG uptake in the primary esophageal tumor (median standardized uptake value 3.5, range 2.1–16.6). Similarly, Miyata and colleagues[24] reported that only 21 of 41 patients

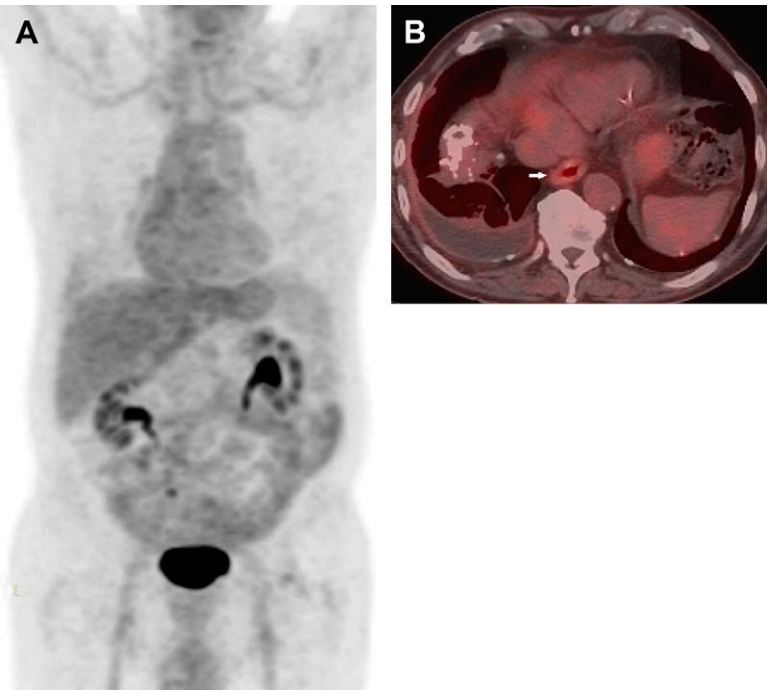

Fig. 1. Early-stage esophageal cancer (T1a—invasion of the muscularis mucosae) in an 83-year-old man in which the primary esophageal tumor is not visualized on PET-CT imaging. (*A*) Whole-body maximum-intensity projection image shows FDG uptake in the esophagus and absence of nodal and distant metastases. (*B*) Axial integrated PET-CT shows a normal-appearing esophagus with background uptake of FDG in the region of the primary esophageal cancer (*arrow*). Note that right pleural effusion and pleural calcification are a manifestation of asbestos exposure.

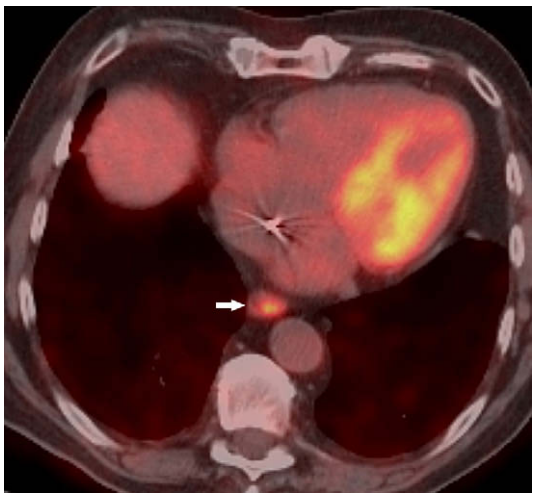

Fig. 2. Early-stage esophageal cancer (T1b—invasion of the submucosa) in an 81-year-old man in which the primary esophageal tumor has increased uptake of FDG on PET imaging. Axial integrated PET-CT shows focal increased uptake of FDG (maximum standardized uptake value 5.8) by the primary esophageal cancer. Note that FDG-PET imaging has a poor detection rate for T1 esophageal tumors.

(51.2%) who had superficial esophageal cancers had increased FDG uptake in the primary esophageal tumor.

Initial Staging

Patients who have esophageal cancer are typically staged before therapy according to the recommendations of the AJCC and UICC 2002 guidelines for pathologic and clinical staging (**Box 1**).[25] Because of the limitations of CT and PET imaging in the assessment of the primary tumor (T), it is the comprehensive understanding of the descriptors used for lymph node involvement (N) and metastatic disease (M) that is important in the appropriate use and interpretation of PET and PET-CT imaging. In this regard, the N1 descriptor for regional nodes includes paraesophageal and abdominal nodes cephalad to the celiac axis, with the important understanding that these nodal metastases do not preclude surgical resection. M1 disease is subdivided into nonregional lymph nodes (M1a) and distant metastases (M1b). An exception to subdividing M1 disease is when the primary cancer is located in the midesophagus, because nodal metastases in this subset of patients have a similar prognosis as hematogenous metastases to other distant sites (see **Box 1**). It is important to note that the designation of distant metastatic disease (M1b) from nonregional nodal disease (M1a) also depends on the location of the primary esophageal tumor (**Fig. 3**; see **Box 1**).

Box 1
American Joint Committee on Cancer TNM staging system for esophageal cancer

T—Primary tumor
- *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

N—Regional lymph nodes
- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

M—Distant metastasis
- 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[a]
    - M1b Nonregional lymph nodes and other distant metastasis
  - Tumors of the upper thoracic esophagus:
    - M1a Metastasis in cervical nodes
    - M1b Other distant metastasis

[a] For tumors of midthoracic esophagus, only M1b is used because these tumors with metastasis in nonregional lymph nodes have an equally poor prognosis as those with metastasis in other distant sites.
Adapted from American Joint Committee on Cancer: AJCC Cancer Staging Manual. 6th ed. New York, NY: Springer, 2002, pp 91–98; with permission.

Small studies have reported a 3% to 22% change in management due to the addition of FDG-PET imaging to the preoperative assessment of patients who have esophageal cancer.[26–32] FDG-PET imaging followed by EUS has been proposed as the most cost-effective strategy in the preoperative staging and management of patients who have esophageal cancer.[12,33] The precise role of FDG-PET and PET-CT in the staging

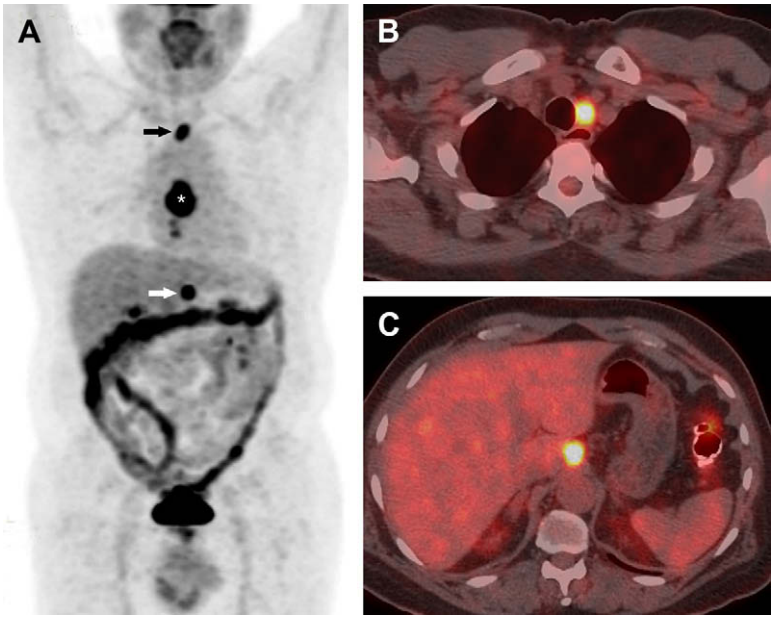

Fig. 3. Distant metastases in a 67-year-old man who had a midesophageal cancer. (*A*) Whole-body maximum-intensity projection image shows increased FDG uptake in the primary esophageal cancer (*asterisk*) and nonregional lymph nodes (*arrows*). (*B*, *C*) Axial integrated PET-CT shows increased uptake of FDG in metastases in a superior mediastinal node and a left gastric node. Note that metastases in nonregional lymph nodes are considered distant metastases (M1b) when the tumor is located in the midesophagus.

algorithm of patients who have potentially resectable esophageal cancer is not clearly defined, however. In the authors' experience, the optimal imaging/staging strategy is a combination of EUS, contrast-enhanced CT of the chest and abdomen, and integrated PET-CT imaging. The following sections review the use of PET and PET-CT imaging in the clinical staging of patients who have esophageal cancer.

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 (see **Box 1**). The assessment of local tumor invasion is one of the most significant factors in determining appropriate treatment. PET and PET-CT offer little information regarding the depth of invasion, due to the spatial resolution limits of the scan. Furthermore, there is no consistent relationship between the intensity of FDG uptake and the depth of tumor invasion (T staging). Although FDG uptake and T staging are positively related, this association is poor.[21–23,28,34,35] This poor association is largely due to the fact that the intensity of FDG uptake is determined by the metabolic activity of the tumor and the volume of the tumor mass, whereas T staging is a based on a unidimensional measurement of the depth of invasion of the tumor. The inability to differentiate between T1, T2, and T3 parameters and the poor ability to identify invasion of adjacent structures that would preclude resection (T4 disease) are major limitations in the use of PET and PET-CT in evaluation of the primary tumor. In this regard, Lowe and colleagues[14] reported that local tumor staging (T) was done correctly by CT and PET in only 42% of patients who had esophageal cancer (compared with 71% who underwent EUS). Furthermore, in a study by Little and colleagues[23] that evaluated 58 patients who had superficial esophageal cancers to determine whether FDG-PET-CT imaging could accurately classify the primary tumor (T), including distinguishing high-grade dysplasia (Tis) from invasive cancer (T1), PET could not differentiate Tis from T1. Of interest, increased FDG uptake was detected more frequently with increasing depth of tumor invasion (5/11 [45%] for Tis compared with 11/16 [69%] for T1), and the standardized uptake value also increased (median 0 for Tis compared with 2.7 for T1) (see **Figs. 1** and **2**). The results of this study led the investigators to conclude that not only should PET not be used in the T staging of patients who have superficial esophageal tumors but FDG-PET imaging is also not indicated in the overall T, N, and M staging of superficial esophageal tumors because of the poor sensitivity in detecting nodal metastases and the low prevalence of distant metastases in these patients.

In the evaluation of the primary esophageal tumor, FDG-PET may also have a potential role in the determination of the length of the tumor.[36] The accurate delineation of the superior and inferior extent of viable esophageal tumor is important in radiotherapy planning, and tumor length is also a strong independent predictor of prognosis in patients who have esophageal cancer.[37–40]

Griffiths and colleagues[38] reported that a tumor length greater than 3.5 cm is associated with a worse stage of disease at presentation and with poor overall survival. Currently, tumor length is measured by EUS; however, accurate clinical delineation of tumor length can be difficult. Mamede and colleagues[36] recently evaluated a three-dimensional tumor segmentation method using FDG-PET to estimate metabolic esophageal tumor length and its correlation with the length observed in surgical specimens. Their preliminary report in 17 patients who underwent primary esophageal resection showed that FDG-PET–derived tumor metabolic lengths correlated well with tumor length assessed by EUS and surgical pathology results.

Regional Lymph Nodes

Nodal metastases in a paraesophageal location adjacent to the primary tumor are considered regional nodal metastases (N1). Abdominal nodes cephalad to the celiac axis are also designated N1 when the primary esophageal cancer is located in the distal esophagus, and these nodes do not preclude surgical resection (see **Box 1**). EUS with or without transesophageal endoscopic biopsy of nodes is routinely performed to determine the presence of locoregional nodal metastases.[8,11–15] CT has poor sensitivity and specificity in the detection of N1 disease, and the addition of FDG-PET to the imaging algorithm of patients who have esophageal cancer has not significantly improved N1 nodal staging.[14,15,41] The sensitivity of PET in the detection of nodal metastatic disease is overall poor (**Fig. 4**).[14,22,28,42,43] In a recent meta-analysis of 12 studies concerning the value of FDG-PET in the preoperative staging of patients who have esophageal cancer, the pooled sensitivity and specificity values for the detection of locoregional nodal disease were 51% and 84%, respectively.[26] In addition, in a recent prospective study to assess preoperative staging in patients who had esophageal cancer, Flamen and colleagues[28] compared the accuracy FDG-PET with conventional noninvasive modalities. In 39 of 74 patients who underwent a two- or three-field lymphadenectomy in conjunction with primary curative esophagectomy, FDG-PET sensitivity, specificity, and accuracy in the detection of regional nodal metastasis were 33%, 89%, and 59%, respectively. It is important to note that FDG-PET did not lead to an increase in accuracy of regional nodal staging compared with the current standard of combined CT and EUS.

Metastatic Disease

Distant metastases are common in patients with esophageal cancer who are being considered for surgical resection. Accurate determination of the M stage is important because these patients do not benefit from surgical resection. EUS and CT imaging of the chest and abdomen are typically performed to detect these metastases.[12,14,26,44–46] FDG-PET imaging may be more accurate than conventional imaging with CT and EUS in the detection of distant metastatic disease at presentation in patients who have esophageal cancer. Flamen and colleagues[28] reported that FDG-PET had a superior accuracy (82%) for the diagnosis of distant lymph node involvement or organ metastasis compared with the combined use of CT and EUS (64%). In a study by Lowe and colleagues,[14] the sensitivity and specificity for distant metastases were reported to be 81% and 82% for CT, 73% and 86% for EUS, and 81% and 91% for PET. Recent studies suggest that the addition of PET imaging to the staging algorithm improves the accuracy of preoperative staging and prevents inappropriate esophageal resection (**Figs. 5** and **6**).[15,27,28,33,47–51] In this regard, PET imaging has been reported to detect distant nodal and organ metastases in up to 20% of patients who are initially considered to have resectable disease based on conventional staging.[27]

A prospective multi-institutional trial study by the American College of Surgeons Oncology Group, however, has reported little additional value of including FDG-PET imaging in the staging

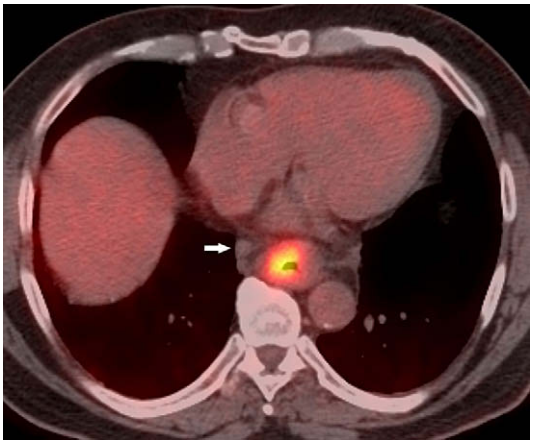

Fig. 4. False-negative PET-CT in regional nodal metastasis in a 55-year-old man who had distal esophageal cancer. Axial integrated PET-CT shows increased uptake of FDG in the primary esophageal cancer. Note the 1-cm regional lymph nodes with background FDG activity (*arrow*). EUS-guided biopsy revealed nodal metastatic disease. Note that the sensitivity of PET in the detection of nodal metastatic disease is not optimal and does not improve the accuracy of regional nodal staging compared with the combined use of CT and EUS.

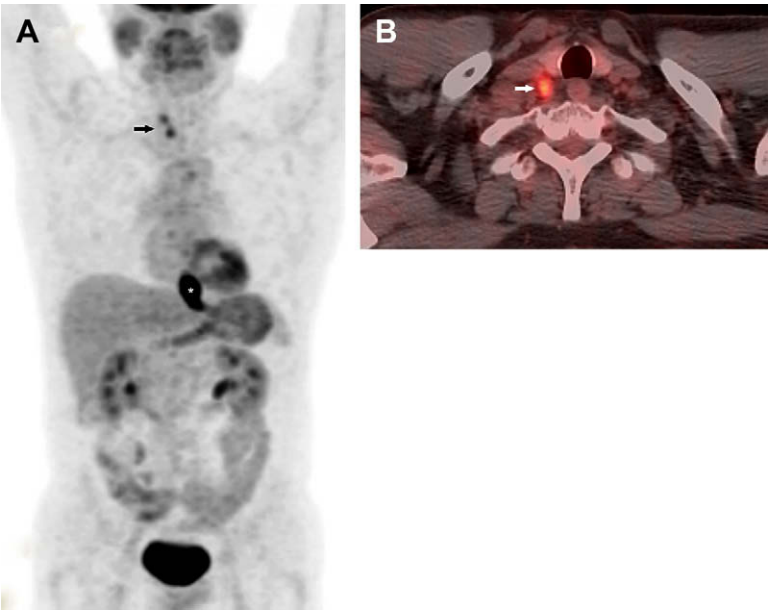

Fig. 5. Nonregional nodal metastases in a 57-year-old man who had distal esophageal cancer. (*A*) Whole-body maximum-intensity projection image shows increased FDG uptake in the primary esophageal cancer (*asterisk*) and nonregional lymph nodes (*arrow*). (*B*) Axial integrated PET-CT shows increased uptake of FDG in metastases in a right supraclavicular node (*arrow*) and a superior mediastinal node (not shown). Note that metastases in nonregional lymph nodes are considered distant metastases (M1a).

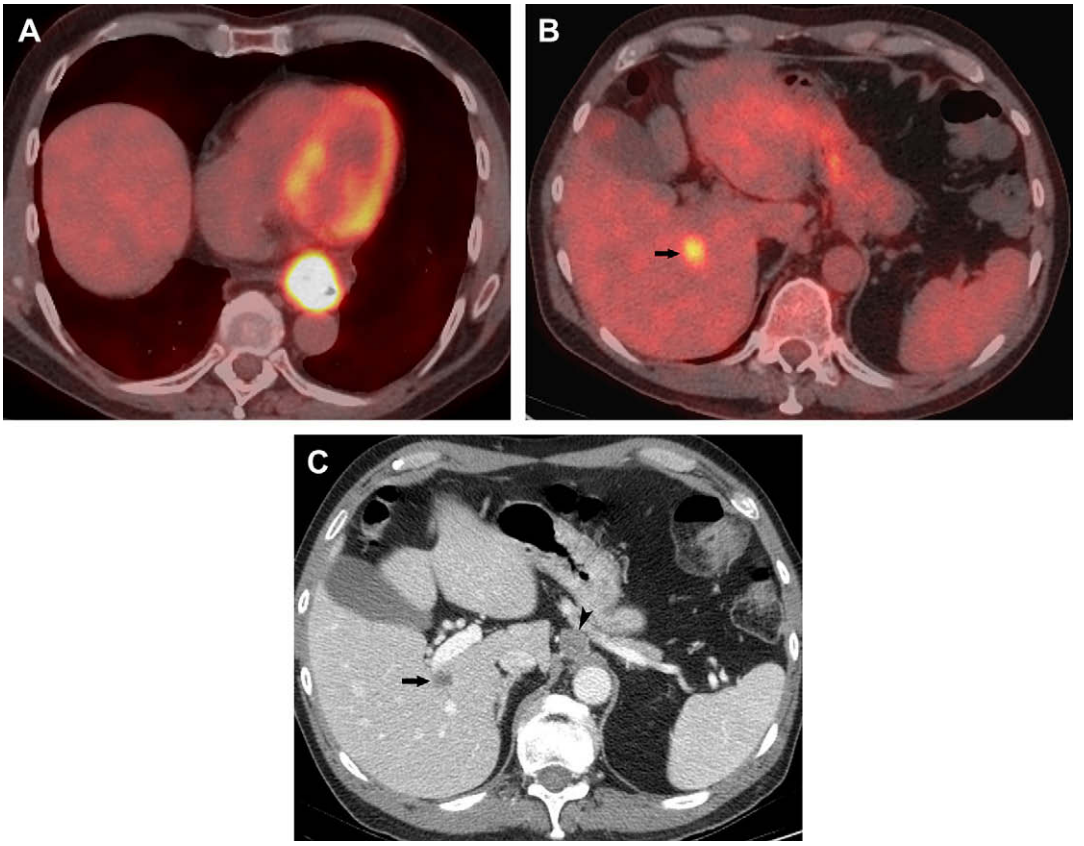

Fig. 6. Hepatic metastasis in a 63-year-old man being evaluated for curative resection who had distal esophageal cancer. (*A*, *B*) Axial integrated PET-CT shows increased uptake of FDG in the distal esophageal cancer and focal increased FDG-uptake in a hepatic metastasis (M1b) (*arrow*). (*C*) Contrast-enhanced CT of the abdomen shows a small, low-attenuation lesion in the liver (*arrow*) that is suspicious, but not diagnostic, for a metastasis. Note the enlarged left gastric node due to N1 metastatic disease (*arrowhead*). Integrated PET-CT improves the accuracy of staging because of the ability to detect distant metastases.

of patients who have resectable esophageal cancer after completion of routine staging procedures.[48] PET imaging identified biopsy-proven unsuspected distant metastatic disease in only 4.8% of the patients after complete conventional staging was performed. An additional 3.7% of the patients, however, had unconfirmed PET-detected distant metastases (M1b disease) and were treated nonsurgically. Overall, there were 9.5% of patients who had apparent PET-detected metastases in which histologic confirmation was not obtained. Accordingly, the overall rate of detected metastases could be as high as 14.3%; however, it is unlikely that all the patients who had unconfirmed metastatic disease had metastases, because many of these patients subsequently underwent successful surgical resection. At least 3.7% of patients who had findings of distant metastases on PET imaging were falsely positive, and accordingly, PET findings suspicious for metastases should be confirmed before excluding a patient from surgical consideration. It is of interest that the impact of PET on surgical resection in this study extended further than the detection of M1 disease: several patients did not undergo resection after PET revealed multistation nodal metastases (N1).

In a more recent prospective study by van Westreenen and colleagues,[52] FDG-PET imaging performed after a preoperative staging protocol that included multidetector CT, EUS, and sonography of the neck revealed distant metastases in only 8 of 199 (4%) of the patients who had esophageal cancer and prevented unnecessary resection in only 3% because all these patients had advanced disease. There was also a high rate of false-positive PET findings (7.5%) that resulted in unnecessary additional investigations. Accordingly, the investigators concluded that although FDG-PET improves the selection of patients who have esophageal cancer for curative resection, the diagnostic benefit is limited after comprehensive conventional staging.

Diagnosis of Recurrent Esophageal Cancer

Recurrence of esophageal cancer is common after curative surgical resection and typically occurs within 2 years after resection.[53] Although locoregional recurrence of malignancy is not uncommon, most patients present with distant metastases.[28,54,55] Because the survival of patients who have recurrent esophageal cancer is poor and the treatment options are limited, routine surveillance imaging for recurrent malignancy is not usually performed in asymptomatic patients; however, early detection of recurrent disease may be beneficial because treatment may prolong tumor-free survival.[56]

Flamen and colleagues[28] reported preliminary work indicating that FDG-PET imaging has a high sensitivity for detecting recurrent malignancy after curative resection of cancer of the esophagus or gastroesophageal junction. In their study, perianastomotic, regional, and distant recurrent esophageal cancer was found in 33 of 41 patients who had clinical or radiologic findings suspicious for recurrent disease. FDG-PET has an overall sensitivity of 95% for the detection of locoregional and distant metastases; however, PET did not improve the diagnostic accuracy for locoregional recurrences compared with conventional imaging. FDG-PET imaging was inaccurate for the diagnosis of perianastomotic recurrence due to frequent false-positive FDG uptake as a result of inflammation (sensitivity 100%, specificity 57%, and accuracy 74% compared with 100%, 93%, and 96%, respectively, for conventional diagnostic work-up) (**Fig. 7**). For the diagnosis of regional and distant recurrences, the sensitivity, specificity, and accuracy of PET were 94%, 82%, and 87%, respectively, compared with 81%, 82%, and 81%, respectively, for conventional diagnostic work-up. Overall, PET provided additional information in 11 of 41 (27%) patients and had a major impact on diagnosis in 5 patients by confirming malignancy that was equivocal or negative on diagnostic work-up (**Fig. 8**).

PET-CT imaging can also detect distant metastases after neoadjuvant therapy and before planned esophagectomy. A few small studies have reported that detection of metastases occurs in up to 17% of these patients.[57–59] In a more recent study, Bruzzi and colleagues[60,61] reported that PET-CT imaging detected metastatic disease in 7 of 88 patients (8%) who had potentially resectable esophageal carcinoma after neoadjuvant therapy. Of clinical relevance, in 2 of 7 patients, the use of PET imaging allowed detection of metastases that were not detected on conventional staging. In addition, similar to a previous report by these investigators, metastatic disease also occurred in an unusual site (skeletal muscle). The investigators concluded that because the metastases can be clinically occult and in unusual and uncommon locations after induction therapy, whole-body PET-CT is the best imaging method for their detection.

GASTRIC CANCER

Although gastric cancer is among the most common malignant diseases worldwide, it is much less frequent in the United States and Europe.[1]

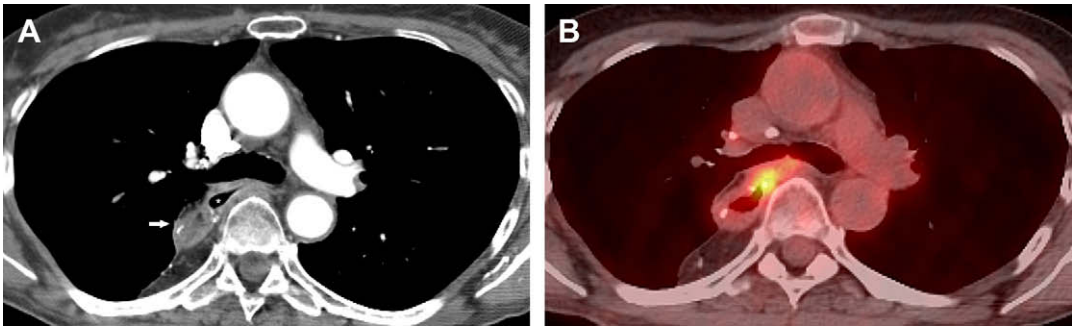

Fig. 7. False-positive FDG uptake in perianastomotic inflammation in a 74-year-old woman after resection of esophageal cancer. (*A*) Contrast-enhanced CT shows normal appearance of the anastomosis of the residual native esophagus (*asterisk*) and gastric conduit (*arrow*) 11 months after esophagectomy. (*B*) Axial integrated PET-CT shows focal increased uptake of FDG uptake in the region of the anastomosis that is suspicious for local recurrence of malignancy. Endoscopic biopsy revealed acute and chronic inflammation and no malignancy. Note that FDG-PET imaging is inaccurate for the diagnosis of perianastomotic recurrence due to frequent false-positive FDG-uptake as a result of inflammation.

Gastric cancer is often diagnosed at an advanced stage, with most resected gastric carcinomas having already spread to the regional lymph nodes. For staging purposes, the classification system used in the Western world is the AJCC/UICC system, which relies on the local invasion (T), number of lymph node metastases (N), and presence of distant metastases (M).

FDG-PET performs poorly for diagnosing gastric cancer, with a sensitivity ranging from 60% to 91%.[62,63] The intensity of uptake is variable and tends to be lower in mucinous carcinomas and signet ring cell carcinomas than in other pathologic types.[62] Compared with other techniques such as endoscopy, EUS, and CT, PET has no role for evaluating the T stage of the disease. Few data are available regarding PET for nodal staging, but the sensitivity appears to be extremely low.[64,65] On the other hand, PET is more specific than CT, especially for assessing the proximal lymph node status, and it may change the clinical management by detecting additional distal lesions in patients initially selected for surgery.[66,67] The added value of PET-CT over PET has not yet

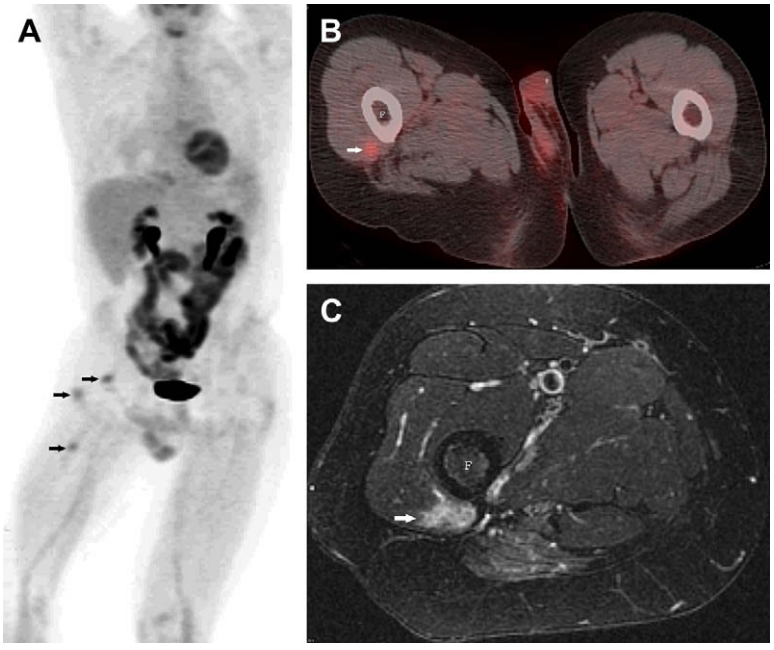

Fig. 8. Intramuscular metastases in a 61-year-old man who had esophageal cancer 10 months after preoperative chemoradiotherapy and surgical resection. (*A*) Whole-body maximum-intensity projection image shows focal increased FDG uptake in the soft tissues of the thigh (*arrows*). (*B*) Axial integrated PET-CT of the thighs shows a show focus of low-grade increased uptake (standardized uptake value 2.9) of FDG within the vastus lateralis muscle with no corresponding abnormality on CT (*arrow*). F, femur. (*C*) Axial T2-weighted MR image of the right thigh shows increased signal in the vastus lateralis muscle (*arrow*). The patient was asymptomatic, and resection revealed an intramuscular esophageal metastasis. F, femur.

been appropriately studied, and although the technique is often suggested as a potentially useful adjunct to the conventional work-up, it is not considered standard procedure. FDG-PET[68] and PET-CT[69] have been proposed for detecting and staging recurrent disease. Taking advantage of their high positive predictive value, they appear to be particularly useful in patients who have a high suspicion of recurrence based on other findings. Conversely, the negative predictive value is low, which requires an appropriate selection of patients being tested. Obviously, PET and PET-CT cannot be proposed as a screening tool in the postoperative follow-up.

SUMMARY

In summary, PET and integrated PET-CT are useful in the initial staging of patients who have esophageal and, to a lesser extent, gastric cancers being considered for curative surgical resection. Although PET has a limited role in the evaluation of the primary tumor and in the detection of locoregional nodal metastases, PET imaging is important in the detection of distant metastases. In this regard, PET and PET-CT can decrease inappropriate surgical resection mainly because of the detection of distant metastases not diagnosed by conventional evaluation. In addition, in patients who have suspected recurrent disease, PET and PET-CT can be helpful to detect sites of metastatic disease.

REFERENCES

1. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol 2006;24(14):2137–50.
2. Swisher SG, Ajani JA, Komaki R, et al. Long-term outcome of a phase II trial evaluating chemotherapy, chemoradiotherapy, and surgery for locoregionally advanced esophageal cancer. Int J Radiat Oncol Biol Phys 2003;57(1):120–7.
3. Swisher SG, Hunt KK, Holmes EC, et al. Changes in the surgical management of esophageal cancer from 1970 to 1993. Am J Surg 1995;169(6):609–14.
4. Berger AC, Farma J, Scott WJ, et al. Complete response to neoadjuvant chemoradiotherapy in esophageal carcinoma is associated with significantly improved survival. J Clin Oncol 2005;23(19): 4330–7.
5. Moehler M, Lyros O, Gockel I, et al. Multidisciplinary management of gastric and gastroesophageal cancers. World J Gastroenterol 2008;14(24):3773–80.
6. Xi WD, Zhao C, Ren GS. Endoscopic ultrasonography in preoperative staging of gastric cancer: determination of tumor invasion depth, nodal involvement and surgical resectability. World J Gastroenterol 2003;9(2):254–7.
7. Puli SR, Batapati Krishna Reddy J, Bechtold ML, et al. How good is endoscopic ultrasound for TNM staging of gastric cancers? A meta-analysis and systematic review. World J Gastroenterol 2008; 14(25):4011–9.
8. Puli SR, Reddy JB, Bechtold ML, et al. Staging accuracy of esophageal cancer by endoscopic ultrasound: a meta-analysis and systematic review. World J Gastroenterol 2008;14(10):1479–90.
9. Kwee RM, Kwee TC. Imaging in local staging of gastric cancer: a systematic review. J Clin Oncol 2007; 25(15):2107–16.
10. Chen CY, Hsu JS, Wu DC, et al. Gastric cancer: preoperative local staging with 3D multi-detector row CT–correlation with surgical and histopathologic results. Radiology 2007;242(2):472–82.
11. Wakelin SJ, Deans C, Crofts TJ, et al. A comparison of computerised tomography, laparoscopic ultrasound and endoscopic ultrasound in the preoperative staging of oesophago-gastric carcinoma. Eur J Radiol 2002;41(2):161–7.
12. Wallace MB, Nietert PJ, Earle C, et al. An analysis of multiple staging management strategies for carcinoma of the esophagus: computed tomography, endoscopic ultrasound, positron emission tomography, and thoracoscopy/laparoscopy. Ann Thorac Surg 2002;74(4):1026–32.
13. van Vliet EP, Heijenbrok-Kal MH, Hunink MG, et al. Staging investigations for oesophageal cancer: a meta-analysis. Br J Cancer 2008;98(3):547–57.
14. Lowe VJ, Booya F, Fletcher JG, et al. Comparison of positron emission tomography, computed tomography, and endoscopic ultrasound in the initial staging of patients with esophageal cancer. Mol Imaging Biol 2005;7(6):422–30.
15. Pfau PR, Perlman SB, Stanko P, et al. The role and clinical value of EUS in a multimodality esophageal carcinoma staging program with CT and positron emission tomography. Gastrointest Endosc 2007; 65(3):377–84.
16. Bar-Shalom R, Guralnik L, Tsalic M, et al. The additional value of PET/CT over PET in FDG imaging of oesophageal cancer. Eur J Nucl Med Mol Imaging 2005;32(8):918–24.
17. Schreurs LM, Pultrum BB, Koopmans KP, et al. Better assessment of nodal metastases by PET/CT fusion compared to side-by-side PET/CT in oesophageal cancer. Anticancer Res 2008;28(3B):1867–73.
18. Heye T, Kuntz C, Duxc M, et al. CT and endoscopic ultrasound in comparison to endoluminal MRI—preliminary results in staging gastric carcinoma. Eur J Radiol 2008 Mar 10. [Epub ahead of print].

19. Ozawa S, Imai Y, Suwa T, et al. 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.
20. Riddell AM, Davies DC, Allum WH, et al. High-resolution MRI in evaluation of the surgical anatomy of the esophagus and posterior mediastinum. AJR Am J Roentgenol 2007;188(1):W37–43.
21. Himeno S, Yasuda S, Shimada H, et al. Evaluation of esophageal cancer by positron emission tomography. Jpn J Clin Oncol 2002;32(9):340–6.
22. Kato H, Miyazaki T, Nakajima M, et al. The incremental effect of positron emission tomography on diagnostic accuracy in the initial staging of esophageal carcinoma. Cancer 2005;103(1):148–56.
23. Little SG, Rice TW, Bybel B, et al. Is FDG-PET indicated for superficial esophageal cancer? Eur J Cardiothorac Surg 2007;31(5):791–6.
24. Miyata H, Doki Y, Yasuda T, et al. Evaluation of clinical significance of 18F-fluorodeoxyglucose positron emission tomography in superficial squamous cell carcinomas of the thoracic esophagus. Dis Esophagus 2008;21(2):144–50.
25. American Joint Commission on Cancer. Esophagus. In: Greene FL PD, Fleming ID, Fritz AG, editors. American Joint Commission on Cancer, cancer staging manual. 6th edition. New York: Springer-Verlag; 2002. p. 301–46.
26. van Westreenen HL, Westerterp M, Bossuyt PM, et al. Systematic review of the staging performance of 18F-fluorodeoxyglucose positron emission tomography in esophageal cancer. J Clin Oncol 2004; 22(18):3805–12.
27. Block MI, Patterson GA, Sundaresan RS, et al. Improvement in staging of esophageal cancer with the addition of positron emission tomography. Ann Thorac Surg 1997;64(3):770–6 [discussion: 6–7].
28. Flamen P, Lerut A, Van Cutsem E, et al. Utility of positron emission tomography for the staging of patients with potentially operable esophageal carcinoma. J Clin Oncol 2000;18(18):3202–10.
29. Wren SM, Stijns P, Srinivas S. Positron emission tomography in the initial staging of esophageal cancer. Arch Surg 2002;137(9):1001–6 [discussion: 6–7].
30. Kluetz PG, Meltzer CC, Villemagne VL, et al. Combined PET/CT imaging in oncology. Impact on patient management. Clin Positron Imaging 2000;3(6): 223–30.
31. Kole AC, Plukker JT, Nieweg OE, et al. Positron emission tomography for staging of oesophageal and gastroesophageal malignancy. Br J Cancer 1998;78(4):521–7.
32. Downey RJ, Akhurst T, Ilson D, 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.
33. Westerterp M, van Westreenen HL, Reitsma JB, et al. Esophageal cancer: CT, endoscopic US, and FDG PET for assessment of response to neoadjuvant therapy—systematic review. Radiology 2005; 236(3):841–51.
34. Cerfolio RJ, Bryant AS. Maximum standardized uptake values on positron emission tomography of esophageal cancer predicts stage, tumor biology, and survival. Ann Thorac Surg 2006;82(2):391–4 [discussion: 4–5].
35. Rizk N, Downey RJ, Akhurst T, et al. Preoperative 18[F]-fluorodeoxyglucose positron emission tomography standardized uptake values predict survival after esophageal adenocarcinoma resection. Ann Thorac Surg 2006;81(3):1076–81.
36. Mamede M, Abreu ELP, Oliva MR, et al. FDG-PET/CT tumor segmentation-derived indices of metabolic activity to assess response to neoadjuvant therapy and progression-free survival in esophageal cancer: correlation with histopathology results. Am J Clin Oncol 2007;30(4):377–88.
37. Eloubeidi MA, Desmond R, Arguedas MR, et al. Prognostic factors for the survival of patients with esophageal carcinoma in the U.S.: the importance of tumor length and lymph node status. Cancer 2002;95(7):1434–43.
38. Griffiths EA, Brummell Z, Gorthi G, et al. Tumor length as a prognostic factor in esophageal malignancy: univariate and multivariate survival analyses. J Surg Oncol 2006;93(4):258–67.
39. Konski A, Doss M, Milestone B, et al. The integration of 18-fluoro-deoxy-glucose positron emission tomography and endoscopic ultrasound in the treatment-planning process for esophageal carcinoma. Int J Radiat Oncol Biol Phys 2005;61(4):1123–8.
40. Moureau-Zabotto L, Touboul E, Lerouge D, et al. Impact of CT and 18F-deoxyglucose positron emission tomography image fusion for conformal radiotherapy in esophageal carcinoma. Int J Radiat Oncol Biol Phys 2005;63(2):340–5.
41. Rice TW. Clinical staging of esophageal carcinoma. CT, EUS, and PET. Chest Surg Clin N Am 2000; 10(3):471–85.
42. Kneist W, Schreckenberger M, Bartenstein P, et al. Positron emission tomography for staging esophageal cancer: does it lead to a different therapeutic approach? World J Surg 2003;27(10):1105–12.
43. Heeren PA, Jager PL, Bongaerts F, et al. Detection of distant metastases in esophageal cancer with (18)F-FDG PET. J Nucl Med 2004;45(6):980–7.
44. Romagnuolo J, Scott J, Hawes RH, 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.

45. Parmar KS, Zwischenberger JB, Reeves AL, et al. 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 [discussion: 20–1].
46. Eloubeidi MA, Wallace MB, Hoffman BJ, et al. Predictors of survival for esophageal cancer patients with and without celiac axis lymphadenopathy: impact of staging endosonography. Ann Thorac Surg 2001;72(1):212–9 [discussion: 9–0].
47. Katsoulis IE, Wong WL, Mattheou AK, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography in the preoperative staging of thoracic oesophageal and gastro-oesophageal junction cancer: a prospective study. Int J Surg 2007;5(6):399–403.
48. Meyers BF, Downey RJ, Decker PA, et al. The utility of positron emission tomography in staging of potentially operable carcinoma of the thoracic esophagus: results of the American College of Surgeons Oncology Group Z0060 trial. J Thorac Cardiovasc Surg 2007;133(3):738–45.
49. Flanagan FL, Dehdashti F, Siegel BA, et al. Staging of esophageal cancer with 18F-fluorodeoxyglucose positron emission tomography. AJR Am J Roentgenol 1997;168(2):417–24.
50. Luketich JD, Friedman DM, Weigel TL, et al. Evaluation of distant metastases in esophageal cancer: 100 consecutive positron emission tomography scans. Ann Thorac Surg 1999;68(4):1133–6 [discussion: 6–7].
51. Liberale G, Van Laethem JL, Gay F, et al. The role of PET scan in the preoperative management of oesophageal cancer. Eur J Surg Oncol 2004;30(9):942–7.
52. van Westreenen HL, Westerterp M, Sloof GW, et al. Limited additional value of positron emission tomography in staging oesophageal cancer. Br J Surg 2007;94(12):1515–20.
53. Law SY, Fok M, Wong J. Pattern of recurrence after oesophageal resection for cancer: clinical implications. Br J Surg 1996;83(1):107–11.
54. van Lanschot JJ, Tilanus HW, Voormolen MH, et al. Recurrence pattern of oesophageal carcinoma after limited resection does not support wide local excision with extensive lymph node dissection. Br J Surg 1994;81(9):1320–3.
55. Hsieh C, Chow K, Fahn H, et al. Prognostic significance of HER-2/neu overexpression in stage I adenocarcinoma of lung. Ann Thorac Surg 1998;66:1159–64.
56. Raoul JL, Le Prise E, Meunier B, et al. Combined radiochemotherapy for postoperative recurrence of oesophageal cancer. Gut 1995;37(2):174–6.
57. Flamen P, Van Cutsem E, Lerut A, et al. Positron emission tomography for assessment of the response to induction radiochemotherapy in locally advanced oesophageal cancer. Ann Oncol 2002;13(3):361–8.
58. Weber WA, Ott K, Becker K, et al. Prediction of response to preoperative chemotherapy in adenocarcinomas of the esophagogastric junction by metabolic imaging. J Clin Oncol 2001;19(12):3058–65.
59. Cerfolio RJ, Bryant AS, Ohja B, et al. The accuracy of endoscopic ultrasonography with fine-needle aspiration, integrated positron emission tomography with computed tomography, and computed tomography in restaging patients with esophageal cancer after neoadjuvant chemoradiotherapy. J Thorac Cardiovasc Surg 2005;129(6):1232–41.
60. Bruzzi JF, Swisher SG, Truong MT, et al. Detection of interval distant metastases: clinical utility of integrated CT-PET imaging in patients with esophageal carcinoma after neoadjuvant therapy. Cancer 2007;109(1):125–34.
61. Bruzzi JF, Truong MT, Macapinlac H, et al. Integrated CT-PET imaging of esophageal cancer: unexpected and unusual distribution of distant organ metastases. Curr Probl Diagn Radiol 2007;36(1):21–9.
62. Stahl A, Ott K, Weber WA, et al. FDG PET imaging of locally advanced gastric carcinomas: correlation with endoscopic and histopathological findings. Eur J Nucl Med Mol Imaging 2003;30(2):288–95.
63. Yoshioka T, Yamaguchi K, Kubota K, et al. Evaluation of 18F-FDG PET in patients with a, metastatic, or recurrent gastric cancer. J Nucl Med 2003;44(5):690–9.
64. McAteer D, Wallis F, Couper G, et al. Evaluation of 18F-FDG positron emission tomography in gastric and oesophageal carcinoma. Br J Radiol 1999;72(858):525–9.
65. Yun M, Lim JS, Noh SH, et al. Lymph node staging of gastric cancer using (18)F-FDG PET: a comparison study with CT. J Nucl Med 2005;46(10):1582–8.
66. Tian J, Chen L, Wei B, et al. The value of vesicant 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET) in gastric malignancies. Nucl Med Commun 2004;25(8):825–31.
67. Chen J, Cheong JH, Yun MJ, et al. Improvement in preoperative staging of gastric adenocarcinoma with positron emission tomography. Cancer 2005;103(11):2383–90.
68. De Potter T, Flamen P, Van Cutsem E, et al. Whole-body PET with FDG for the diagnosis of recurrent gastric cancer. Eur J Nucl Med Mol Imaging 2002;29(4):525–9.
69. Park MJ, Lee WJ, Lim HK, et al. Detecting recurrence of gastric cancer: the value of FDG PET/CT. Abdom Imaging 2008.