Diagnostic Imaging: PET/CT(PET)

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Abstract

PET (Positron-Emission Tomography) has a unique feature that is visualized "metabolic activities" of cell, or tissue. Malignant tumors including esophageal cancers usually show hypermetabolism of glucose to be depicted clearly by using FDG-PET.

The role of FDG-PET for esophageal cancer includes staging (detecting lymph node, distant metastases), response assessment for chemo (radiation) therapy, and early detection of recurrence (surveillance). FDG-PET/CT is a very useful imaging modalities not for all, but for selected esophageal cancer patients.

Keywords

FDG · PET · Esophageal cancer · Staging · Response assessment

4.1 PET/CT(PET)

PET (Positron-Emission Tomography) is a unique imaging modality that has different features from CT and MRI. Generally speaking, CT and MRI are called "morphological imaging" as these modalities composed images based on anatomical information. On the other hand, PET makes images based on metabolic information such as glucose and amino acid in cells or tissues.

^{18}F-FDG (2-[^{18F}]-fluoro-2-deoxy-D-glucose) is the most widely used radiopharmaceuticals in oncological PET in the world, and most common probe for diagnosing esophageal cancer same as other kinds of malignancy. ^{18}F-FDG is a glucose analog

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labeled with ^{18}F, and has the disposition of strongly accumulating in cells or tissues that shows hypermetabolism of glucose. The principle of PET is to capture the weak gamma rays emitted from accumulated ^{18}F using a special camera (PET camera), and image the lesion and tissue distribution with increased glucose metabolism.

Though it is sure that many kinds of malignancy including esophageal cancer shows hyper glycolysis to have strong accumulations in FDG-PET, FDG deposit is not specific. For example, inflammatory tissue also reveals strong FDG uptake as active inflammatory cells such as macrophage, neutrophil shows hypermetabolism of glucose. On the other hand, FDG accumulation is sometimes weak in low glade malignancy or slow-growing tumors for it reflects low glucose metabolism. Size of the tumor is another important factor that affects tumor detectability. Though recent advancement of PET camera improves the performance of tumor detection, the smaller the tumor, and the lower the detection rate. PET/CT has great advantage as we can evaluate not only FDG uptake but also tumor size by CT part simultaneously.

The degree of accumulation in FDG is expressed by a numerical value "SUV" (Standardized Uptake Value), which is calculated by the following equation:

$$\begin{aligned}\mathrm{SUV} = {} & \text{tissue radioactivity}\left(\mathrm{cpm}*/\mathrm{g}\right) / \text{administrative radiation dose}\left(\mathrm{cpm}*\right) \\ & \cdot \text{body weight}\left(\mathrm{g}\right) * \mathrm{cpm};\mathrm{count}/\mathrm{minute}\end{aligned}$$

SUV is often used as an index of semiquantitative analysis in FDG deposit, but it is a relative value and it varies due to many kinds of factors such as imaging time, equipment, algorism for reconstruction, blood sugar level, etc. Therefore, in case of using SUV for evaluating the therapeutic effect, it is necessary to establish the acquisition parameters identical with previous study as much as possible. In clinical practice, measurement of SUV is not indispensable because the visual assessment is identical diagnostic performance to that of based on SUV.

FDG accumulation is affected by the level of blood sugar. Though the efficacy of FDG-PET worsens in DM patients due to insufficient tumor contrast, FDG-PET is not contraindicated with high-BS patients. FDG-PET may be performed according to clinical requirements.

The detection rate of esophageal cancer is 0% in pT1a where the tumor confined in the mucosal layer, and 20% in pT1b up to the submucosal layer, and 100% when depth reached pT2 or more [1].

According to NCCN (National Comprehensive Cancer Network) guidelines Ver.1. 2019. [2]· FDG-PET/CT is recommended as one of the workup if no evidence of M1 disease. The guideline described that clinical staging should be performed to assess resectability by CT scan of the chest and abdomen, wholebody FDG-PET and endoscopic ultrasound.

4.2 N Staging by Imaging

Though the frequency of lymph node metastasis in esophageal cancer is high, accurate diagnosis remains still challenging. Evaluation based on size criteria using CT, MRI, or US is proved to be insufficient diagnostic performance in many literatures.

FDG-PET shows additional value, especially it improves specificity over morphological image to assess locoregional lymph node metastases [3, 4].

Lymph nodes with higher accumulation than background are basically diagnosed as metastasis regardless of its size. Although high specificity for the diagnosis of lymph node metastases, microscopic metastasis sometimes causes false negative. On the other hand, mediastinum lymphadenopathy due to inflammatory diseases such as COPD, interstitial pneumonia, and sarcoidosis may cause false positives. In such cases, a comprehensive diagnosis combining with contrast-enhanced CT or MRI findings are important. The distribution, shape, size of lymph nodes are sometimes crucial to discriminate metastatic lymph nodes with inflammatory lymphadenopathy.

4.3 M Staging by Imaging

As PET can cover a wide area of the body for screening, it is possible to detect metastasis that appears in unexpected sites. Moreover, high contrast of PET enables to clearly delineate a lesion that is missed or overlooked only by CT and MRI (Fig. 4.1). Therefore, it is particularly useful in advanced cancer which has a possibility of distant metastasis. Though dedicated PET shows low special

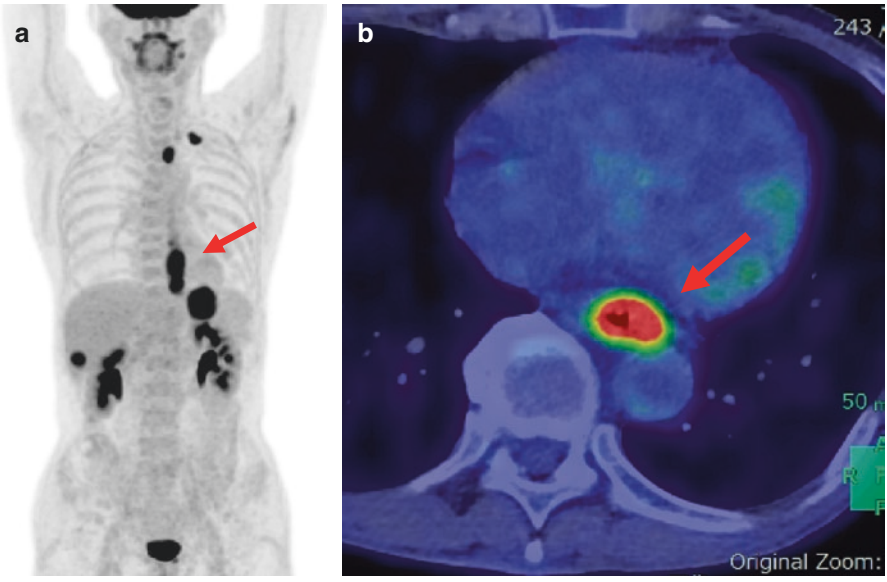

Fig. 4.1 Detection of multiple metastases (**a**) MIP (maximum intensity projection) image of FDG-PET. Primary esophageal cancer was clearly revealed (arrow). (**b**) Image of esophageal cancer on axial section of PET/CT. (**c**) Detection of supraclavicular lymph node (arrow) is difficult by contrast-enhanced CT(CECT). (**d**) PET/CT apparently demonstrated the metastatic lymph node (arrow). (**e**) Liver metastases (arrow) is sometimes misdiagnosed for cyst only by CECT. (**f**) PET/CT showed a strong accumulation in liver metastases (arrow)

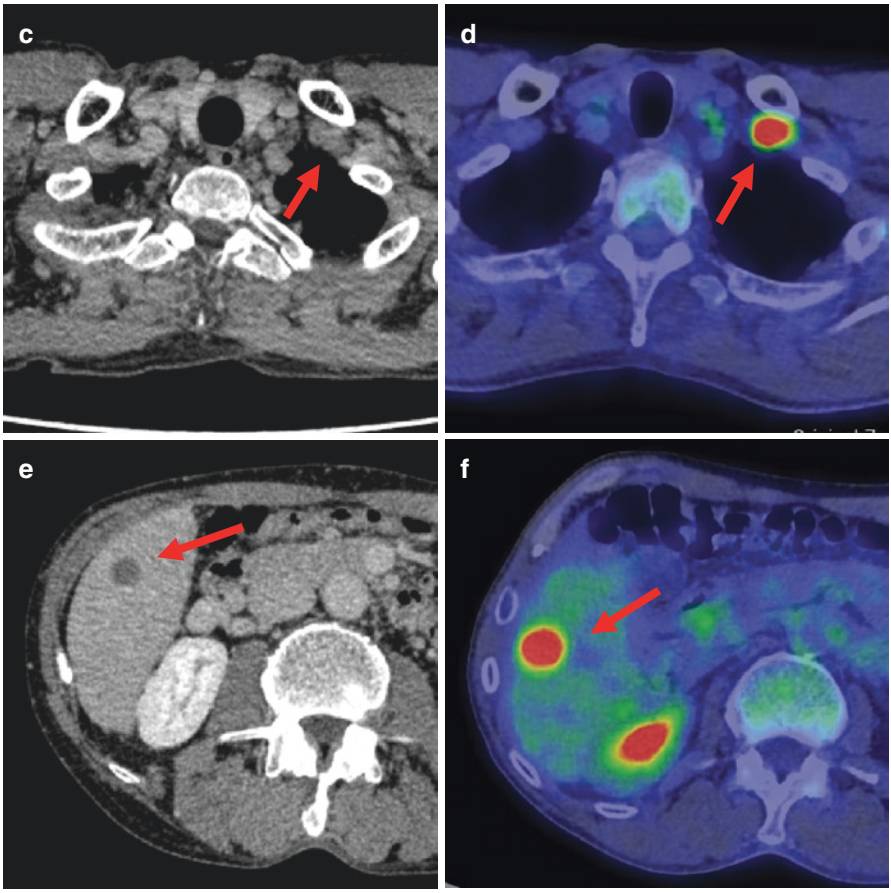

Fig. 4.1 (continued)

resolution, PET/CT can compensate the demerit and it can detect small lung metastases by using CT part.

PET/CT sometimes can play a role of "one-stop shopping" for screening distant metastases, however, MRI is indispensable for screening brain metastasis.

Esophageal cancer is known to have a high incidence of double cancer. PET sometimes can detect unexpected lesions that are difficult to find conventional preoperative imaging [5]. The possibility of multiple (synchronous) cancers should be considered rather than metastases if FDG accumulation is found at unreasonable sites.

4.4 Follow-up

4.4.1 Response Assessment

According to NCCN guidelines [2], FDG-PET(PET/CT) are recommended as response assessment for preoperative chemoradiation and definitive chemoradiation, that is, the same role of CT and endoscopy. The guideline also defined that the assessment by FDG-PET should be performed from 5 to 8 weeks after completion of preoperative therapy. The implementation time of PET is very important because if it is performed too early, the treatment effect will not be reflected properly. Especially when radiation therapy is added, longer intervals are required because radiation-induced inflammation affects the degree of accumulation of FDG.

In case responders and non-responders were separated by a threshold of 35% or more decreased in SUVmax, PET after induction chemotherapy highly predicts outcomes in esophageal cancer patients who receive chemoradiation (Fig. 4.2). On the

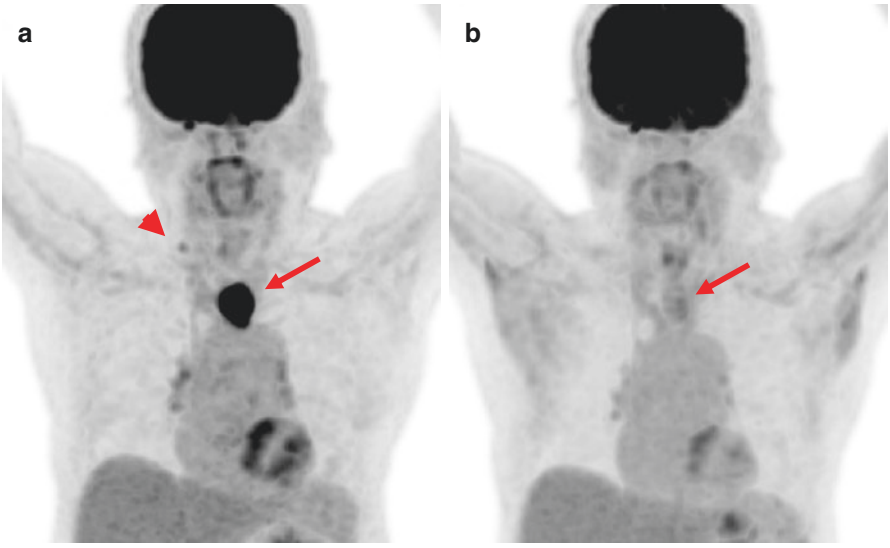

Fig. 4.2 Evaluation of therapeutic effect after neoadjuvant chemotherapy (NAC), a case of the responder. (**a**) PET image before NAC. Primary tumor showed strong FDG uptake (SUVmax;20.7, arrow) with right supraclavicular lymph node metastases (arrowhead). (**b**) PET after NAC revealed a remarkable decrease of FDG accumulation (SUVmax;3.1, arrow) in the primary tumor with almost disappearance of lymph node

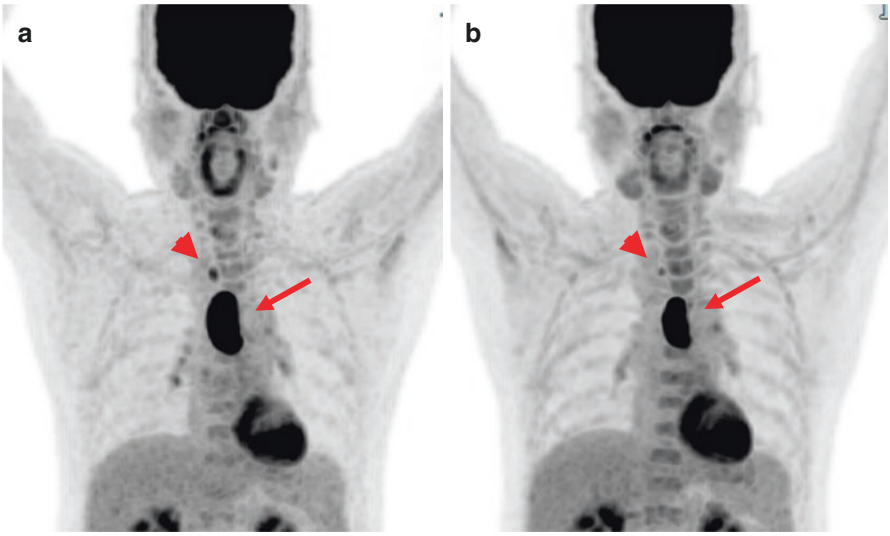

Fig. 4.3 Evaluation of therapeutic effect after neoadjuvant chemotherapy (NAC), a case of non-responder. (**a**) PET image before NAC. Primary tumor showed strong FDG uptake (SUVmax;31.3, arrow) with right mediastinal lymph node metastases (arrowhead). (**b**) PET after NAC still showed strong FDG accumulation in the primary tumor (SUVmax;27.0, arrow), which represented insufficient therapeutic effect. A mediastinal lymph node also remained FDG uptake though slightly decreasing metabolic activity (arrowhead)

other hand, non-responders do not benefit from changing chemotherapy during radiation (Fig. 4.3) [6]. Another report described that TLG (total lesion glycolysis) based on 40% SUV threshold are the best criteria to discriminate histopathologic responders on AUC (area under the receiver operating characteristic curve) analysis [7].

4.4.2 Surveillance

Although there is no evidence of PET examination as postoperative follow-up of esophageal cancer, implementation may be considered (image diagnostic guideline by JRS [8] recommends as grade C1).

Regarding NCCN guidelines [2], recommended surveillance varies according to the depth of invasion and treatment modality. In the case of "T1b, any N after the treatment of chemoradiation," CT (chest/abdomen with contrast unless contraindicated or FDG-PET/CT) should be considered every 6–9 months for the first 2 years, then annually up to 5 years (Fig. 4.4).

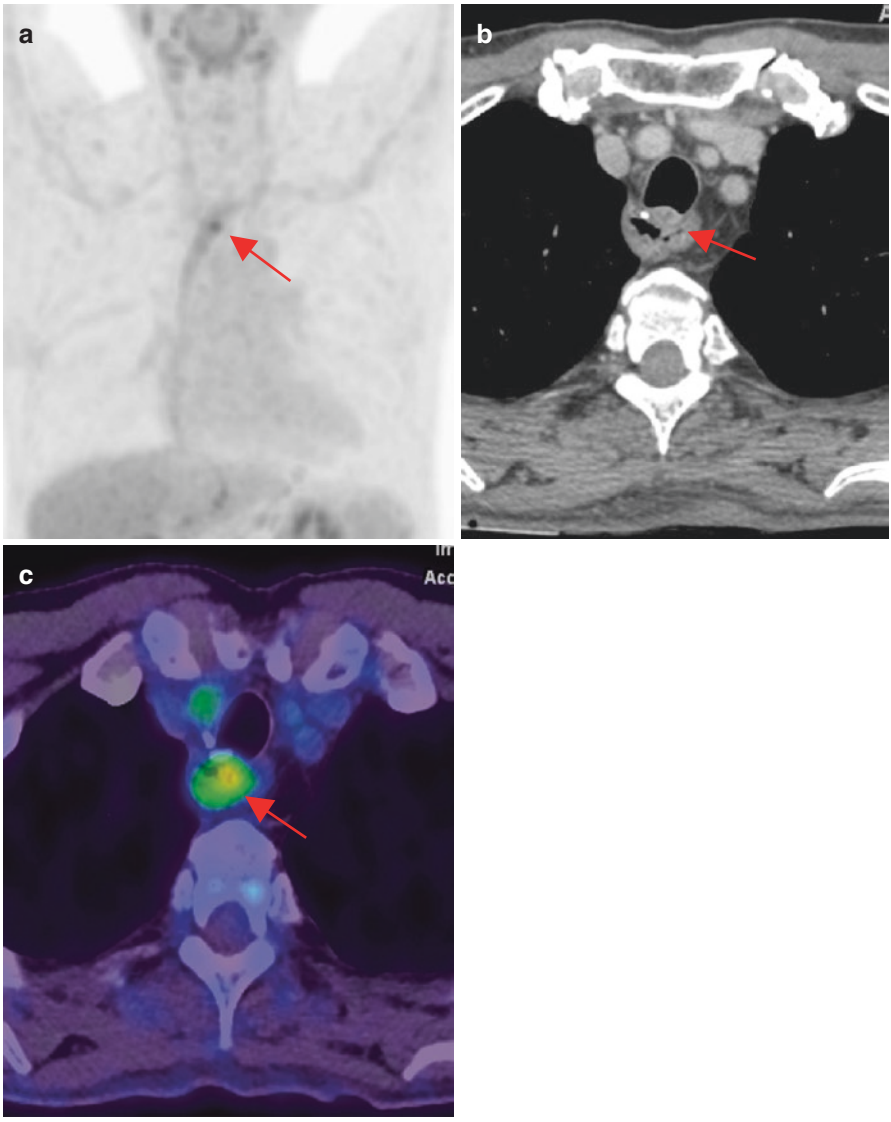

Fig. 4.4 Early detection of local recurrence. (**a**) A faint FDG accumulation was noted at reconstructed esophagus (arrow). (**b**) A small nodule was disclosed adjacent to surgical clip though detection may be difficult only by CT. (**c**) PET/CT fusion image clarified the FDG spot was consistent with the nodule, which was proved to recurrent focus later by biopsy

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