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ORIGINAL ARTICLE

# Integrated FDG-PET/CT compared with intravenous contrast-enhanced CT for evaluation of metastatic regional lymph nodes in patients with resectable early stage esophageal cancer

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**Abstract**
*Objective* To assess whether integrated fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) can improve the diagnostic accuracy of metastatic regional lymph nodes (LNs) in esophageal cancer compared with contrast enhanced CT (CECT).
*Methods* We examined 180 consecutive patients with esophageal cancer by integrated PET/CT between April 2006 and March 2007. Eighteen patients (M:F 14:4) underwent radical esophagectomy after evaluations by PET/CT and CECT of 5–7-mm-thick slices 70–80 s after injection. Regional LNs of esophageal cancer were retrospectively reviewed on CECT images by two blinded evaluators on the basis of the following cutoff sizes: 7 mm for all regional LNs (Protocol A), 10 mm for paratracheal LNs (Protocol B), and 7 mm for others. In addition, the maximum standardized uptake value ($SUV_{max}$) on PET/CT was evaluated for positive uptake by LNs.
*Results* Of 210 LNs excised at surgery, 25 were positive and 185 were negative for metastasis at pathology. The PET/CT images identified 15 true-positive and 184 true-negative LNs, whereas CECT identified 15 true positives and 176 true negatives in Protocol A, and 14 true positives and 180 true negative in Protocol B. The sensitivity, specificity, accuracy, positive, and negative predictive values of PET/CT were respectively 60.0%, 99.5%, 94.8%, 93.8%, and 94.8%, whereas those of CECT were 60.0%, 95.1%, 91.0%, 62.5%, and 94.6% (Protocol A) and 56.0%, 97.3%, 92.4%, 73.7%, and 94.2% (Protocol B). A comparison of the two CECT protocols revealed fewer false-positive LNs in Protocol B, but slightly lower sensitivity in Protocol B than in Protocol A. Substantial numbers of false-positive LNs were determined by CECT in the paratracheal regions (6 of 9, 66.7%) and CECT revealed central necrosis in 4 of 15 (26.7%) true-positive LNs > 1.8 cm. The mean $SUV_{max}$ on PET/CT was 2.9 (range 1.7–5.5) in true-positive LNs. The smallest LN metastasis detectable by PET/CT was 6 mm.
*Conclusions* Integrated PET/CT improves the PPV of regional LNs when compared with CECT.

**Keywords** Contrast-enhanced CT · FDG-PET/CT · Esophageal cancer · Metastatic lymph nodes

## Introduction

Esophageal cancer is a very high-grade malignancy with a poor prognosis. The 5-year survival rate between 1996 and 2002 was 16%, with death rates of 7.74 and 1.74 per 100 000 for men and women, respectively [1]. Esophagectomy is a substantially curative treatment for patients with early stage resectable esophageal cancer; however, the prognosis of advanced esophageal cancer remains poor. Accurate surgical staging of all regional lymph nodes (LNs) affects the cure rates among patients with

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esophageal cancer [2]. Because LN metastases frequently arise from T1 tumors [3, 4], the major aim of imaging in esophageal cancer is to distinguish between regional LNs and benign inflammatory nodes [5]. The accuracy of detecting regional and distal metastases by thoracoscopy and laparoscopy is high [6]; however these methods are invasive. The detection of malignant lymphadenopathy in computed tomography (CT) was historically based on size criteria; LNs > 1 cm are generally judged as malignant. However, some nodes can reach this size as a result of a reaction to benign inflammation, whereas those <1 cm can often be malignant [7].

Although fluorodeoxyglucose-positron emission tomography (FDG-PET) can detect disease in LNs that are not enlarged according to CT criteria, spatial resolution confers limitations upon PET that prevents detection of small LN metastases. Ott et al. [8] reported that the specificity of FDG-PET for evaluating regional LN metastasis is high at low sensitivity. Furthermore, FDG-PET is more sensitive than CT for revealing regional and distant metastases [9, 10] and when FDG-PET is used for the primary staging of esophageal cancer, clinical management can be changed and prognostic stratification can be improved [11].

Integrated PET/CT is a new and useful imaging modality. Bar-Shalom et al. [12] reported that PET/CT had an incremental value over PET for the interpretation of 25 (22%) of 115 sites, and confidence was increased and lesion localization was improved in 15% of these sites. The detection of esophageal cancer sites by PET/CT in that study was also more specific and accurate than PET alone.

At present, PET/CT has become a routine imaging modality in Japan that provides anatomical-metabolic information for most cancer patients. This approach has also several advantages, such as faster attenuation correction and lower locational mismatches when compared with PET. The combination of PET and CT is useful for cancer staging and evaluation following treatment; however, consensus regarding its utility for esophageal cancer has not been established. Metabolic FDG-PET images are not only complementary to the images obtained with more traditional modalities, but may also be more sensitive because alterations in tissue metabolism generally precede anatomical changes. Intravenous contrast-enhanced CT (CECT) is frequently applied to the clinical setting, especially for detecting regional LNs in esophageal cancer. Yet, the abilities of PET/CT and CECT to detect LN metastasis in esophageal cancer have not apparently been compared. Thus, this study was undertaken to assess whether PET/CT can improve the accuracy of CECT in identifying metastatic regional LNs of esophageal cancer.

## Materials and methods

### Patients

We enrolled 180 consecutive patients with esophageal cancer for an integrated PET/CT study between April 2006 and March 2007, and all provided written, informed consent to participate. Because 162 of the 180 patients had previously started therapy or reference CECT imaging data were insufficient, we analyzed data from only 18 (14 men and 4 women; age 59–79 years; mean age 68 years), who had not undergone therapy prior to radical surgery (Table 1). All patients fasted for at least 4 h before this evaluation, and none had diabetes mellitus.

### Surgery and pathology

The diagnosis of esophageal cancer in all patients was histologically confirmed as squamous cell carcinoma ($n$ = 17) and adenocarcinoma ($n$ = 1) (Table 1). Surgically resected areas comprised two regions (defined as routes of access via the chest and abdomen) in 13 patients and three regions (defined as routes via the neck, chest, and abdomen) in 5 patients. Following surgery, surgeons separated LNs and adjacent tissues from the resected esophagus, and then assigned numbers and localizations according to the guidelines of the Japanese Society for Esophageal Diseases [13]. The pathological and PET/CT findings were compared and the LN localizations were classified as cervical, upper thoracic, mid-thoracic, lower thoracic and abdominal, and the paratracheal LN was localized to the upper thoracic and mid-thoracic regions.

### FDG-PET/CT and CECT imaging

We obtained FDG-PET/CT scans using an integrated PET/CT scanner (Biograph; Siemens Japan, Tokyo, Japan) 1 h after FDG injection. The Biograph scanner combines a dual-detector spiral CT scanner (Somatom Emotion Duo; Siemens) and a high-resolution PET scanner with 4.5-mm spatial resolution and three-dimensional image acquisition. The CT component was operated with an X-ray tube voltage peak of 130 keV and a flexible X-ray tube current of 30–240 mA. The fields of view were 50 × 50 cm, or 70 × 70 cm, and the beam width was 2.5 mm × 2 (pitch: 2). Whole-body PET/CT images were acquired at 1 h after an intravenous injection of 3 MBq of FDG per kg of body weight and emission scans were obtained from the orbita to the thigh for 100 s/bed per field of view, each covering 16.2 cm, at an axial sampling thickness of 8 mm/slice.

**Table 1** Patients evaluated by positron emission tomography/computed tomography (PET/CT) and contrast-enhanced computed tomography (CECT)

| Patient no. | Age | Primary site | Pathology | T factor | Primary $SUV_{max}$ | LN-patho | LN-site |
|---|---|---|---|---|---|---|---|
| 1 | 70 | Lt | SCC is | Tis | (–) | 0 | (–) |
| 2 | 61 | Ut | Well SCC | T1 | 6.0 | 0 | (–) |
| 3 | 60 | Mt | Poor SCC | T1 | 3.4 | 0 | (–) |
| 4 | 79 | Mt | Mod SCC | T1 | 3.2 | 1 | U |
| 5 | 59 | Mt | Mod SCC | T1 | 4.3 | 2 | U, A |
| 6 | 68 | Mt | Mod SCC | T2 | 11.3 | 0 | (–) |
| 7 | 64 | Ut | Well SCC | T2 | 11.4 | 1 | A |
| 8 | 61 | Mt | Well SCC | T2 | 5.0 | 1 | U |
| 9 | 71 | Mt | Mod SCC | T2 | 5.0 | 1 | A |
| 10 | 70 | Ae | Adeno ca | T2 | 3.6 | 1 | A |
| 11 | 62 | Mt | Poor SCC | T2 | 6.0 | 3 | U, A |
| 12 | 76 | Lt | Poor SCC | T2 | 15.2 | 7 | C, U, M, L, A |
| 13 | 62 | Mt | Well SCC | T3 | 10.2 | 0 | (–) |
| 14 | 69 | Lt | Mod SCC | T3 | 10.1 | 1 | A |
| 15 | 71 | Mt | Well SCC | T3 | 13.9 | 1 | U |
| 16 | 74 | Mt | Poor SCC | T3 | 18.0 | 1 | A |
| 17 | 73 | Lt | Well SCC | T3 | 14.0 | 5 | A |
| 18 | 70 | Mt | Well SCC | T4 | 14.1 | 1 | A |

*Ut* upper thoracic esophagus, *Mt* middle thoracic esophagus, *Lt* lower thoracic esophagus, *Ae* abdominal esophagus, *C* cervical site of lymph node, *U* upper site of lymph node, *M* middle site of lymph node, *L* lower site of lymph node, *A* abdominal site of lymph node, *LN-patho* pathology of lymph node, *LN-site* site of lymph node, *Mod SCC* moderately differentiated squamous cell carcinoma, *Well SCC* well-differentiated squamous cell carcinoma, *Poor SCC* poorly differentiated squamous cell carcinoma, *SCC is* squamous cell carcinoma in situ, *Adeno ca* adenocarcinoma, *Tis* carcinoma in situ, $SUV_{max}$ maximum standardized uptake value

Transaxial, coronal, and sagittal planes of CT, PET, and fusion PET/CT were reconstructed on a computer platform (Syngo; Siemens), and then imaging data were sent to a viewer (SYNAPSE; FujiFilm Medical, Tokyo, Japan) for review and manipulation.

After a 70–80 s post-injection delay, CECT was performed using a four-channel multi-detector-row CT scanner (Aquillion; Toshiba Medical Systems, Tokyo, Japan) or 64-channel multi-detector-row CT (LightSpeed VCT; GE Healthcare, Milwaukee, WI, USA). Nonionic contrast agent (Iopamiron 370; 100 ml containing 370 mgI/ml; Bayer Healthcare, Osaka, Japan) was intravenously injected at a rate of 2 ml/s, and then CECT images were obtained from the neck to the base of the kidneys. The CT parameters were as follows: tube voltage 120 kV, tube current auto mA exposure setting, reconstruction section and interval thickness 5 or 7 mm.

The interval between surgery and image acquisition was 5–34 days (mean 18 days).

## Image analysis: criteria for detection of LN metastasis

We applied the following criteria on CECT for the cutoff size between LN metastasis and other nodes. Positive was defined as >7 mm for all regional LNs (Protocol A), or >10 mm for paratracheal LNs and 7 mm for others (Protocol B), and negative was defined as less than these sizes.

Positive and negative PET/CT findings were defined as FDG uptake above or equal to the background, respectively.

## Visual analysis PET/CT and CT

The FDG-PET/CT and CECT images were visually assessed by the consensus of two radiologists (M.K. and S.K., with 12 and 16 years of experience, respectively) who were blinded to the results of the PET/CT and CECT. One diagnostic radiologist (M.O.) was the coordinator of this study. Integrated PET/CT data were first used to detect LN metastasis in esophageal cancer and then the CECT data were interpreted. The order of PET/CT and CECT assessment was switched at the next review. Each PET/CT and CECT image was separately interpreted by the two radiologists who were unaware of the LN pathology.

## Semiquantitative analysis

The uptake of FDG by metastatic LNs was calculated for each patient. Regions of interest were placed on regional metastatic LNs. Maximal radioactivity uptake (maximum standardized uptake value $SUV_{max}$) by LNs was calculated using a workstation (esoft; Siemens). We defined SUV as [decay-corrected activity (kBq) per ml of tissue volume]/[injected FDG activity (kBq)/body mass (g)]. We also evaluated the $SUV_{max}$ of primary esopha-

geal cancer. All semiquantitative analyses were performed by one diagnostic radiologist (M.O.).

### Statistical analysis

The sensitivity, specificity, accuracy, and positive predictive value (PPV) and negative predictive value (NPV) associated with PET/CT and CECT were calculated using standard definitions [14]. We applied McNemar's statistic between PET/CT and CECT to analyze *P* values. And Spearman's correlation coefficient by rank test was used for analysis between the depth of invasion (*T* factor) and the $SUV_{max}$ of primary esophageal cancer. The Statistical Package for Social Science programming (version 11.0; SPSS, Chicago, IL, USA) was used for analysis and *P* value less than 0.05 was considered to indicate a statistically significant difference.

## Results

### Primary esophageal cancer

Both FDG-PET/CT and CECT clearly revealed primary esophageal cancer (Figs. 1 and 2) and that in 17 of 18 patients (94%) was evident on FDG-PET/CT. Only one esophageal carcinoma in situ was not detected as FDG uptake higher than the surrounding mediastinum. The uptake of FDG in esophageal cancer was $SUV_{max}$ 3.2–18.0 (mean 8.8). The uptake by primary esophageal cancers was as follows: SUV > 7 in 8 patients and <7 in 10 patients. The depth of invasion, such as T1–T4, was substantially associated with FDG uptake ($SUV_{max}$, Table 1). T factor and $SUV_{max}$ of primary esophageal cancer were correlated using Spearman's correlation coefficient by rank test (statistically significant difference $P = 0.0065$).

### Lymph nodes

Table 2 summarizes the pathological and imaging findings of LN metastasis in esophageal cancer. Of 210 LN regions evaluated at pathology, 25 were positive for metastasis and 185 LNs were negative. The CECT images revealed nine false-positive LNs in the paratracheal (six of nine; 67%) and other (three of nine; 33%) regions. Metastatic LNs were visualized as higher uptake than surrounding regions on PET/CT and appeared as enlarged LNs on CECT images (Figs. 1 and 2). Despite the high specificity of CECT, PPV was significantly lower (62.5% and 73.7% for Protocols A and B, respectively) than that of PET/CT (93.8%) according to McNemar's test (Table 2). None of sensitivity, specificity, accuracy and NPV significantly differed between PET/CT and either CECT protocol. A comparison of the results of Protocols A and B showed that 1 of 15 true-

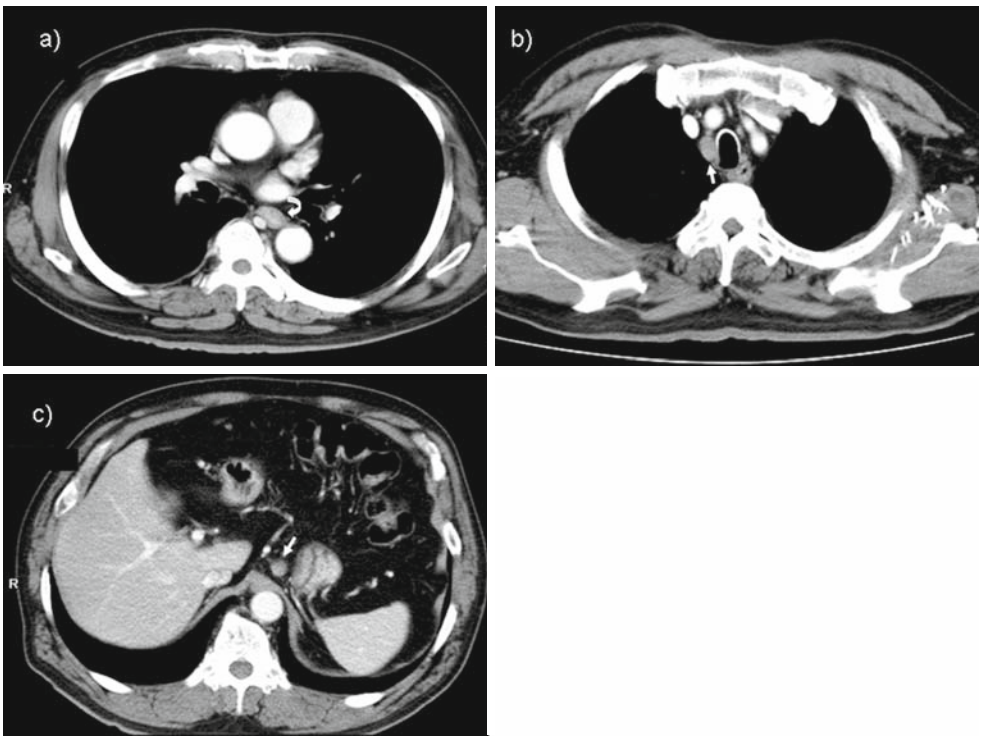


**Fig. 1** Contrast-enhanced computed tomography (CECT) of patient no. 5. **a** *Curved arrow* shows primary esophageal cancer. **b** *Arrow* shows swollen thoracic paratracheal lymph node (LN) of 1.2 cm, indicating metastatic LN of esophageal cancer. **c** *Arrow* shows swollen right cardiac LN of 1.0 cm, indicating metastatic LN of esophageal cancer

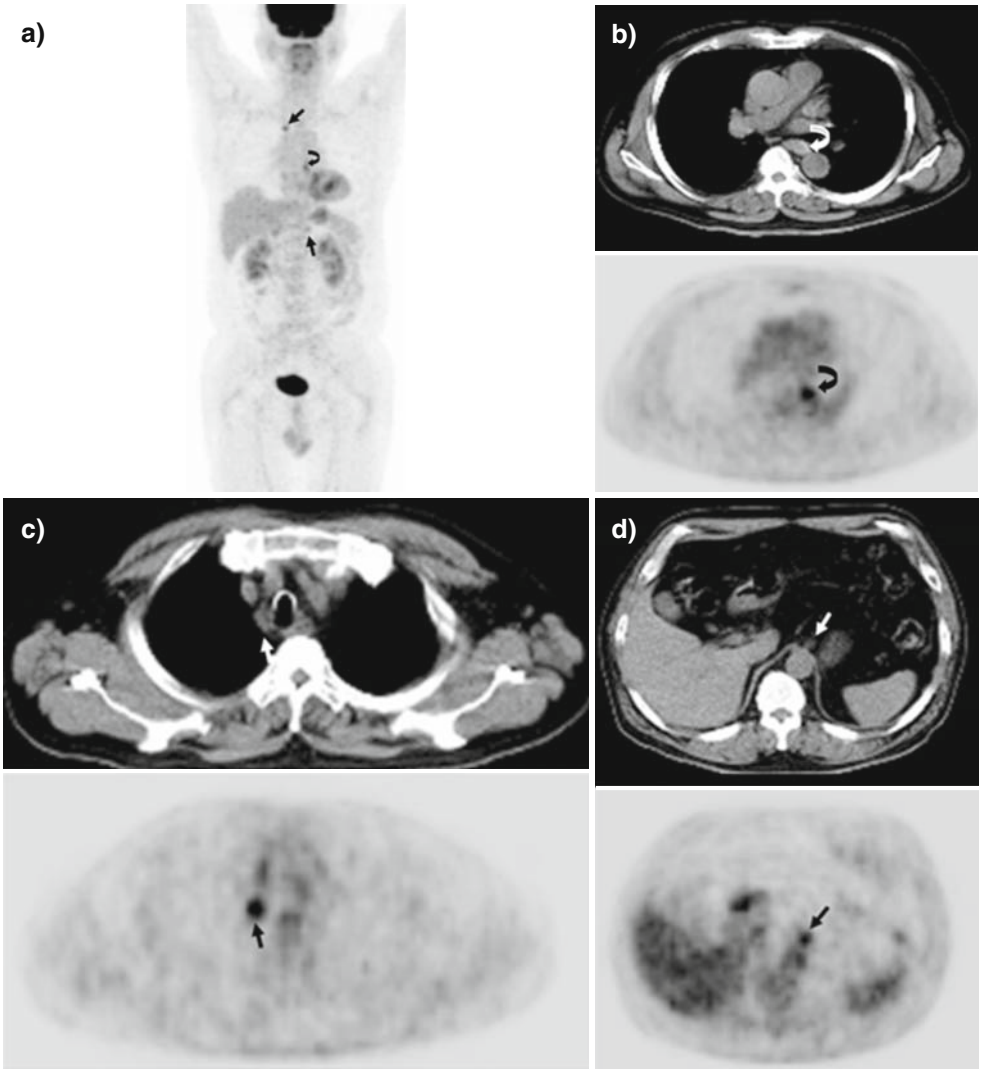


**Fig. 2** F-18-fluorodeoxyglucose positron emission tomography (FDG-PET) of patient no. 5. **a** *Curved arrow* shows primary esophageal cancer. *Arrows* indicate paratracheal (*upper*) and right cardiac (*lower*) LN metastasis in maximum intensity projection. **b** Integrated FDG-PET/CT image (PET and CT represented separately). *Curved arrows* show primary esophageal cancer with higher uptake (maximum standardized uptake value, $SUV_{max}$ 4.3) than surrounding mediastinum. **c** Integrated FDG-PET/CT image (PET and CT represented separately). *Arrows* show thoracic paratracheal LN with higher uptake ($SUV_{max}$ 4.3) than surrounding mediastinum. **d** Integrated FDG-PET/CT image (PET and CT represented separately). *Arrows* show right cardiac LN swelling with higher uptake ($SUV_{max}$ 2.3) than abdominal aorta and surrounding fatty tissue

**Table 2** Comparison of PET/CT and CECT for LN metastasis detection

| | PET/CT (%) | CECT A (%) | CECT B (%) |
|---|---|---|---|
| Sensitivity | 60.0 | 60.0 | 56.0 |
| Specificity | 99.5 | 95.1 | 97.3 |
| Accuracy | 94.8 | 91.0 | 92.4 |
| Positive predictive value* | 93.8 | 62.5 | 73.7 |
| Negative predictive value | 94.8 | 94.6 | 94.2 |

Cutoff CECT Protocol A > 7 mm for all regional LNs; cutoff CECT Protocol B > 10 mm for paratracheal LNs and 7 mm for others
*Positive predictive value $P < 0.05$ by McNemar's statistic between PET/CT and both CECT protocols

positive LNs in Protocol A was a false negative in Protocol B, and 4 of 9 false-positive LNs in Protocol A were true negatives in Protocol B. Thus, the cutoff size of paratracheal LNs of >10 mm compared with >7 mm reduced the incidence of false-positive results in the evaluation of LN metastasis by CECT, and the PPV was higher in Protocol B than in Protocol A (Table 2). Furthermore, the specificity and PPV of PET/CT were high (Table 2).

Central necrosis of larger LN (>1.8 cm) was detected by CECT as regions of low density within LN metastases. The rate of central necrosis in true-positive LNs was 4 of 15 (27%).

The mean $SUV_{max}$ determined by PET/CT was 2.9 (1.7–5.5) in pathologically confirmed metastatic LNs, and the smallest LN metastasis detected by PET/CT was 6 mm.

Distant organ metastasis

We found no distant metastasis in our patients, and equivocal uptake ($SUV_{max}$ 3.2) in the left adrenal gland of one patient on PET/CT images proved to be hypertrophy following surgery.

## Discussion

The role of PET in the detection of metastasis of esophageal cancer is important. This study found that the rates of evaluation of LN metastasis, sensitivity, accuracy, and NPV of PET/CT were similar, whereas the specificity and PPV of PET/CT were higher than those of CECT. Several investigators have demonstrated that the sensitivity, specificity, and accuracy rates of PET in detecting LN metastasis are better than those of CT [15–17], and others have shown that FDG-PET has high specificity at low sensitivity for evaluating regional LN metastasis [8]. However, FDG-PET is more sensitive than CT for revealing regional and distant metastases [9, 10, 18], and Kato et al. [19] stated that the sensitivity, specificity, and accuracy of LN staging are higher with PET than with CECT. We examined 5- or 7-mm-thick slices by CECT whereas they analyzed 10-mm slices. Therefore, CECT evaluations of 5- or 7-mm-thick slices might be able to detect LNs smaller than 10 mm. Moreover, recent advances in multislice CT might allow the detection of LN metastasis in esophageal cancer because the spatial resolution is higher. We found that PET/CT improved the PPV for regional LNs when compared with that of CECT. The >10-mm instead of 7-mm cutoff for paratracheal LNs reduced the incidence of false-positive results for metastasis on CECT. However, Yoon et al. [18] stated that the specificity of PET for detecting metastatic LN is lower than that of CT because of false-positive hilar LNs. Nonspecific inflammation in the mediastinum can confuse false-positive uptake on PET/CT or false-positive lymphadenopathy on CECT with LN metastasis. This study showed that a stricter cutoff (>10 mm for the paratracheal region) allowed a little superior in accuracy when evaluating regional LN metastasis of esophageal cancer, although the sensitivity might be slightly diminished (Table 2).

According to Luketich et al. [20], PET is more accurate than CT for detecting distant metastases because PET detected 51 metastases in 27 of 39 patients (69% sensitivity, 93.4% specificity, and 84% accuracy) when compared with CT, which detected 26 metastases in 18 of 39 patients (46.1% sensitivity, 73.8% specificity, and 63% accuracy). The key task for PET is the accurate identification of esophageal cancer among patients with previously undetected distal metastasis. Other reports have indicated that the management of over 20% of esophageal cancer patients can be changed as a result of the PET findings [15, 21].

Fukunaga et al. [22] evaluated primary esophageal cancer by PET and noted that an SUV of esophageal cancer >7 is associated with a significantly lower survival rate, and that FDG-PET might be useful in distinguishing malignant from benign lesions in preoperative evaluations of prognostic factors. We found uptake of SUV > 7 in primary esophageal cancers in nine patients, seven of whom (77.8%) had regional LN metastases at pathology (Table 1). Thus, these results might be useful for the preoperative evaluation of prognostic factors.

In our results, only one esophageal carcinoma in situ was not detected as FDG uptake higher than the surrounding mediastinum. And a previous study detected the primary site in the esophagus in 14 of 23 patients (61%) by PET [23], indicating a ceiling to the early detection of esophageal cancer. Therefore, PET probably cannot play a significant role in primary screening, whereas the combination of CT and endoscopic ultrasonography (EUS) has possibilities for better detection of metastatic LNs [21].

Luketich et al. [15] stated that small regional LN metastases of a mean greatest dimension (range 2–10 mm) could not be detected by FDG-PET, and Kato et al. [19] detected a minimum size of 6–8 mm LN metastases and noted that detecting LN metastasis near the cardiac-gastric region is difficult. Although some limitations were evident, such as detecTable node size or misdiagnosis of inflammatory LNs, PET/CT nonetheless detected metastasis in normal sized LNs in our clinical study because of integrated functional and anatomical imagings. In addition, PET/CT with anatomical guidance helps to distinguish disease from physiological bowel, cardiac, and gastric uptake. In contrast, judgment of LN metastasis in CECT is based on anatomical evaluation of LN size, although central necrosis of larger swollen LNs was also detected by CECT as low density areas within LN metastases owing to squamous cell carcinoma. We believe that the combination of functional and anatomical imaging can help to diagnose precisely LN metastasis in esophageal cancer because PET/CT allows higher specificity and a higher PPV. However, the sensitivity of PET/CT or CECT for LN metastasis was not satisfactory when compared with that of EUS, because it is well known recently that EUS is the preferred diagnostic method for the detection of LN metastasis.

Our study has some limitations. First, PET/CT can detect local nodal disease, but uptake in nodes adjacent to primary tumors can occasionally be difficult to resolve.

Second, imaging at 1 h after FDG injection has become the standard FDG-PET/CT cancer imaging modality in Japan, although several studies [24–26] have shown advantages in delayed FDG imaging. Nakamoto et al. [25] reported that FDG-PET scanning at 2 h after injection might help to differentiate malignant from benign pancreatic lesions. Boerner et al. [26] found a significantly higher tumor to nontumor ratio at 3 h when compared with 1.5-h images of breast cancer. Moreover, Lowe et al. [24] reported that FDG uptake of lung cancer peaks at 2 h or even later, but the acquisition of emission data should begin approximately 50 min after FDG administration when evaluating pulmonary malignancy [24]. A time course study has shown that FDG uptake in the inflammatory tissue increases gradually until 1 h and decreases thereafter [27]. On the other hand, most malignant lesions show more FDG uptake at 2 h than at 1 h [28]. Therefore, image acquisition at both 1 h and 2 h might help to differentiate metastasis from inflammation when judging mediastinal lymphadenopathies. To the best of our knowledge, it has not been proved that an additional delayed 2 h image will improve the ability of FDG-PET to detect regional esophageal LN metastasis. Thus, a prospective study is recommended to determine the relevance of adding delayed 2-h data acquisition to differentiating LN metastasis from benign inflammatory LNs in esophageal cancer patients. Third, all of our patients were surgical candidates, which caused selection bias. The exclusion of patients with advanced stage might have decreased the prevalence of metastases and increased the false-positive rate, because PPV is substantially affected by the prevalence of regional LN metastasis. Selecting patients without prior chemotherapy or radiation included selection bias, which affects both prevalence and PPV.

In summary, the higher detection specificity of LN metastasis in esophageal cancer is acceptable, and the higher PPV is a characteristic of PET/CT. Because of the limited number of patients and selection bias, further investigation of the value of this modality is required by conducting a randomized study.

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## References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics. CA Cancer J Clin 2007;57:43–66.
2. Buenaventura P, Luketich JD. Surgical staging of esophageal cancer. Chest Surg Clin N Am 2000;10:487–97.
3. Sugimachi K, Ikebe M, Kitamura K, Toh Y, Matsuda H, Kuwano H. Long-term results of esophagectomy for early esophageal carcinoma. Hepatogastroenterology 1993;40:203–6.
4. Rice TW, Zuccaro G Jr, Adelstein DJ, Rybicki LA, Blackstone EH, Goldblum JR. Esophageal carcinoma: depth of tumor invasion is predictive of regional lymph node status. Ann Thorac Surg 1998;65:787–92.
5. Dhar DK, Hattori S, Tonomoto Y, Shimoda T, Kato H, Tachibana M, et al. Appraisal of a revised lymph node classification system for esophageal squamous cell cancer. Ann Thorac Surg 2007;83:1265–72.
6. Luketich JD, Meehan M, Nguyen NT, Christie N, Weigel T, Yousem S, et al. Minimally invasive surgical staging for esophageal cancer. Surg Endosc 2000;14:700–2.
7. Gore RM. Upper gastrointestinal tract tumours: diagnosis and staging strategies. Cancer Imaging 2005;5:95–8.
8. Ott K, Weber W, Siewert JR. The importance of PET in the diagnosis and response evaluation of esophageal cancer. Dis Esophagus 2006;19:433–42.
9. Flanagan FL, Dehdashti F, Siegel BA, Trask DD, Sundaresan SR, Patterson GA, et al. Staging of esophageal cancer with 18F-fluorodeoxyglucose positron emission tomography. AJR Am J Roentgenol 1997;168:417–24.
10. Yeung HW, Macapinlac HA, Mazumdar M, Bains M, Finn RD, Larson SM. FDG-PET in esophageal cancer: incremental value over computed tomography. Clin Positron Imaging 1999;2:255–60.
11. Duong CP, Demitriou H, Weih L, Thompson A, Williams D, Thomas RJ, et al. Significant clinical impact and prognostic stratification provided by FDG-PET in the staging of oesophageal cancer. Eur J Nucl Med Mol Imaging 2006;33:759–69.
12. Bar-Shalom R, Guralnik L, Tsalic M, Leiderman M, Frenkel A, Gaitini D, et al. The additional value of PET/CT over PET in FDG imaging of oesophageal cancer. Eur J Nucl Med Mol Imaging 2005;32:918–24.
13. Japanese Society for Esophageal Diseases. Guidelines for the clinical and pathologic studies on carcinoma of the esophagus [in Japanese], 10th ed. Tokyo: Kanehara Shuppan; 2007.
14. Beck JR. Likelihood ratios: another enhancement of sensitivity and specificity. Arch Pathol Lab Med 1986;110:685–6.
15. Luketich JD, Schauer PR, Meltzer CC, Landreneau RJ, Urso GK, Townsend DW, et al. Role of positron emission tomography in staging esophageal cancer. Ann Thorac Surg 1997;64:765–9.
16. Rankin SC, Taylor H, Cook GJ, Mason R. Computed tomography and positron emission tomography in the pre-operative staging of oesophageal carcinoma. Clin Radiol 1998;53:659–65.
17. Choi JY, Lee KH, Shim YM, Lee KS, Kim JJ, Kim SE, et al. Improved detection of individual nodal involvement in squamous cell carcinoma of the esophagus by FDG PET. J Nucl Med 2000;41:808–15.
18. Yoon YC, Lee KS, Shim YM, Kim BT, Kim K, Kim TS. Metastasis to regional lymph nodes in patients with esophageal squamous cell carcinoma: CT versus FDG PET for presurgical detection prospective study. Radiology 2003;227:764–70.
19. 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;94:921–8.
20. 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;68:1133–6; discussion 1136–7.
21. 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 gastro-esophageal junction: a prospective study based on primary surgery with extensive lymphadenectomy. Ann Surg 2000;232: 743–52.
22. Fukunaga T, Okazumi S, Koide Y, Isono K, Imazeki K. Evaluation of esophageal cancers using fluorine-18-fluorodeoxyglucose PET. J Nucl Med 1998;39:1002–7.
23. Kato H, Miyazaki T, Nakajima M, Takita J, Kimura H, Faried A, et al. The incremental effect of positron emission tomography on diagnostic accuracy in the initial staging of esophageal carcinoma. Cancer 2005;103:148–56.
24. Lowe VJ, DeLong DM, Hoffman JM, Coleman RE. Optimum scanning protocol for FDG-PET evaluation of pulmonary malignancy. J Nucl Med 1995;36:883–7.
25. Nakamoto Y, Higashi T, Sakahara H, Tamaki N, Kogire M, Doi R, et al. Delayed (18)F-fluoro-2-deoxy-D-glucose positron emission tomography scan for differentiation between malignant and benign lesions in the pancreas. Cancer 2000;89: 2547–54.
26. Boerner AR, Weckesser M, Herzog H, Schmitz T, Audretsch W, Nitz U, et al. Optimal scan time for fluorine-18 fluorodeoxyglucose positron emission tomography in breast cancer. Eur J Nucl Med 1999;26:226–30.
27. Yamada S, Kubota K, Kubota R, Ido T, Tamahashi N. High accumulation of fluorine-18-fluorodeoxyglucose in turpentine-induced inflammatory tissue. J Nucl Med 1995;36: 1301–6.
28. Kubota K, Itoh M, Ozaki K, Ono S, Tashiro M, Yamaguchi K, et al. Advantage of delayed whole-body FDG-PET imaging for tumour detection. Eur J Nucl Med 2001;28:696–703.