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# Diagnostic Accuracy of Lymph Node Metastasis Depends on Metabolic Activity of the Primary Lesion in Thoracic Squamous Esophageal Cancer

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The metabolic activity of the primary tumor is an important variable in $^{18}$F-FDG PET interpretation for presurgical staging, because this activity is likely to affect the possibility of detection of malignant involvement in lymph nodes (LNs). The purpose of this study was to reevaluate the diagnostic accuracy of $^{18}$F-FDG PET/CT for the presurgical staging of esophageal squamous cell carcinoma (SCC) in correlation with the $^{18}$F-FDG avidity of the primary lesions. **Methods:** One hundred fifty-six patients (mean age ± SD, 61.4 ± 8.0 y) underwent $^{18}$F-FDG PET/CT before surgical esophagectomy and LN dissection. LN metastasis was identified using the fusion of PET and CT images with increased $^{18}$F-FDG uptake greater than the background activity of the adjacent structures. The results of the patients' $^{18}$F-FDG PET/CT examinations for LN involvement were compared with the histopathologic results to investigate the diagnostic accuracy of $^{18}$F-FDG PET/CT for tumor staging. In addition, we examined the correlation between the diagnostic accuracy of $^{18}$F-FDG PET/CT for LN involvement and the $^{18}$F-FDG avidity of the primary lesions, to investigate the effect of tumor aggressiveness on the diagnosis of LN metastasis. **Results:** The diagnostic accuracy of $^{18}$F-FDG PET/CT for LN metastasis showed a low sensitivity, ranging from 29.3% to 53.3%, whereas the specificity was higher than 89.8% in regional thoracic nodes and in remote areas of the cervical and abdominal regions. The $^{18}$F-FDG uptake of the primary lesions positively correlated with that of the metastatic LNs in the thoracic field ($R = 0.52$, a $P < 0.05$). As a result, our receiver-operating-characteristic analyses demonstrated an area under the curve value of 0.73, with the optimal cutoff value at a maximum standardized uptake value of 3.3 in patients with mid to high $^{18}$F-FDG avidity in the primary lesions (maximum standardized uptake value ≥ 5). **Conclusion:** This study showed that the avidity of the primary esophageal SCCs affected the detectability of lymph nodal metastases. If primary lesions of esophageal SCC present with a low $^{18}$F-FDG uptake, PET/CT may have a limited role for initial staging because of low sensitivity to detect lymph node metastases.

**Key Words:** esophageal cancer; squamous cell carcinoma; FDG PET; pathology

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Esophageal cancer is the third most common malignancy of the digestive tract and a leading cause of cancer mortality worldwide, with an estimated 5-y survival of 15% (*1*). Even after potentially curative surgery, long-term survival rates rarely exceed 35% (*2*). The available therapeutic options for esophageal cancer vary depending on the tumor stage, and therefore accurate pretherapeutic staging is crucial to the selection of the appropriate type of therapy (*3*).

There have been multiple investigations of the clinical utility of $^{18}$F-FDG PET for the presurgical staging of esophageal cancer, and the investigators generally concluded that $^{18}$F-FDG PET has a limited role in the identification of early regional lymph node (LN) metastasis but is highly useful for detecting remote lymph nodal involvement and metastasis to remote organs (*4,5*). A nonspecific inflammatory process probably explains the poor detection of regional LN metastasis. However, the aggressiveness of the primary tumor may also influence the metabolic activity of the LNs, which may affect the ability of $^{18}$F-FDG PET/CT to accurately demonstrate LN metastasis. In non–small cell lung cancer (NSCLC), $^{18}$F-FDG uptake within the primary lesion correlates with aggressiveness on PET studies, indicating intratumoral lymphatic vessel invasion and LN involvement (*6,7*). The metabolic activity of the primary tumor and tumor size are important variables in $^{18}$F-FDG PET interpretation for NSCLC, because they affect the likelihood of malignant involvement in nodes (*8*).

For esophageal cancer with squamous cell carcinoma (SCC), there have been no established findings regarding

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the $^{18}$F-FDG uptake of the primary lesions and LN metastasis. The diagnostic accuracy of $^{18}$F-FDG PET/CT for the presurgical staging of esophageal cancer should be reevaluated on the basis of the $^{18}$F-FDG avidity of the primary lesions. The purpose of the present study was to evaluate the clinical utility of $^{18}$F-FDG PET/CT for the presurgical staging of thoracic esophageal cancer with SCC pathology. We investigated the diagnostic ability of $^{18}$F-FDG PET/CT to accurately detect metastasized LNs, and we examined this diagnostic accuracy in relation to the metabolic activity of the primary lesions. We attempted to evaluate the accuracy of this imaging modality for identifying lymph nodal metastasis in regional (thoracic) versus remote (cervical and abdominal) fields separately, to clarify the possible regional differences in the diagnostic value of $^{18}$F-FDG PET/CT. We also investigated the possibility of distinguishing true- versus false-positive LN metastasis, using a semiquantitative value of the maximum standardized uptake value (SUVmax). This was a retrospective study, conducted in a clinical center that specializes in the surgical treatment of esophageal cancer.

## MATERIALS AND METHODS

### Study Design

Patients with known esophageal cancer underwent $^{18}$F-FDG PET/CT before esophagectomy. Their PET/CT images were used for the diagnosis of esophageal cancer and for presurgical clinical staging based on the TNM classification of the American Joint Committee on Cancer, seventh edition (*9*). LN involvement was visually and quantitatively inspected in the cervical, thoracic, and abdominal regions. The results of each patient's $^{18}$F-FDG PET/CT examination for LN involvement were compared with their histopathology results to investigate the diagnostic accuracy of $^{18}$F-FDG PET/CT for tumor stating. In particular, the diagnostic accuracy of LN involvement was correlated with the $^{18}$F-FDG avidity of the primary lesion to investigate the effect of tumor aggressiveness on the diagnosis of LN metastasis. This is a retrospective study on a population that underwent a standard treatment procedure at the institution. All patients gave written informed consent before PET/CT for the possible future use of their anonymized clinical data for scientific or clinical research purpose. The institutional review board at Keiyukai Sapporo Hospital, Sapporo, Japan, approved the retrospective analyses and the publication of the study results.

**TABLE 1**
Sensitivity of Primary Lesions

| pT stage | $^{18}$F-FDG positive | Total | Sensitivity (%) |
|---|---|---|---|
| T1a | 10 | 16 | 62.5 |
| T1b | 42 | 57 | 73.7 |
| T2 | 12 | 12 | 100 |
| T3 | 69 | 69 | 100 |
| T4 | 2 | 2 | 100 |
| Total | 135 | 156 | 86.5 |

### Subjects

The study population retrospectively included patients with esophageal cancer who underwent $^{18}$F-FDG PET/CT before esophagectomy from April 2006 to June 2008. The inclusion criteria were a primary lesion located in the thoracic esophagus, histologically proven SCC, and PET/CT performed before surgical esophagectomy and LN dissection. Patients who met the following criteria were excluded from the study: coexisting cancer that was located outside the thoracic esophagus or the primary lesion had been treated with chemotherapy or radiotherapy before PET/CT acquisition. The final study population comprised 156 patients (125 men and 31 women), ranging in age from 40 to 84 y (mean age ± SD, 61.4 ± 8.0 y). Serum glucose level was 100.4 ± 13.1 mg/dL (range, 67–171 mg/dL) before $^{18}$F-FDG administration.

### Pathologic Assessment

All patients underwent surgical LN dissection at the same time as the esophagectomy. Specimens from the primary tumors were histopathologically classified based on T factors. T1 stage tumors were classified as T1a when the tumor invaded into but not through the muscularis mucosa and as T1b when there was submucosal invasion. For the LN involvement, 3-field (cervical, thoracic, and abdominal) LN dissections were performed in 147 patients, and 2-field (thoracic and abdominal) dissections were performed in the remaining 9 patients. All of the LNs in the 3 surgical fields were dissected, and their locations were identified according to the TNM classification system of the American Joint Committee on Cancer. A board-certified pathologist performed the standard histopathologic examination with hematoxylin and eosin staining for both primary lesions and dissected LNs. The LN involvement was summarized in regional (thoracic) and remote (cervical and abdominal) categories to determine the postsurgical therapeutic strategy as proposed in the previous literature (*10*).

### PET/CT Imaging

All patients underwent PET/CT scanning with a GEMINI GXL (Philips Healthcare). The matrix size was 144 × 144, and the full width at half maximum was 5.6 mm (*11*), with multidetector CT. The imaging protocol required that the patient fast for at least 4 h before the injection of $^{18}$F-FDG. A mean dose of 241.3 ± 70.0 MBq of $^{18}$F-FDG was administered intravenously, which was 4.23 ± 0.98 MBq per kg of body weight. After the injection, the patient rested comfortably on a sofa for 60 min. Image acquisition was initiated with a CT scan for attenuation correction and anatomic localization (30–80 mA, 120 keV), followed by 3-dimensional PET acquisition with 2 min per bed position, covering from the vertex to the upper thighs. Acquired datasets were corrected for attenuation, dead-time, and scatter, and the images were reconstructed using the line-of-response row-action maximum-likelihood algorithm method (*12*).

### Image Analyses

Two nuclear medicine physicians visually interpreted the reconstructed images to identify the primary lesions and LN metastases, using a 3-dimensional computer display workstation in consensus. The locations of the primary lesions were sought using the endoscopic examination report as a reference, because early-stage esophageal cancers often infiltrate the mucosal surface of the esophagus, thus limiting the visualization on a CT image. LN metastasis was identified using the fusion of PET and CT images with increased $^{18}$F-FDG uptake greater than the background activity of the blood pool. The symmetric hilum accumulations were



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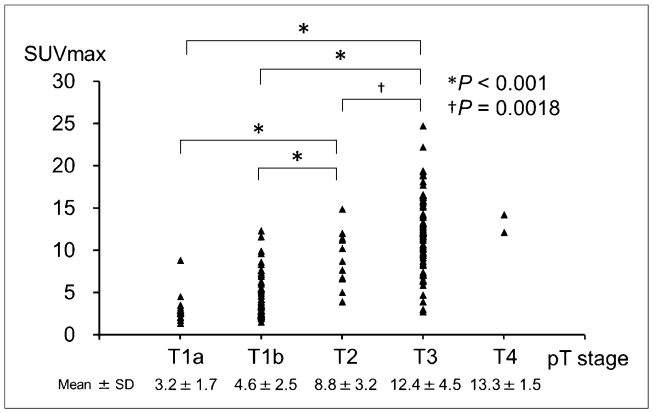


**FIGURE 1.** SUVmax of primary lesions among different pT stages.

excluded from the analysis, because esophageal cancer rarely metastasizes to the hilum (*13*), and the symmetric hilar uptake generally represents a chronic inflammatory process. For the quantitative analysis, regions of interest were manually placed on primary lesions and nodal metastases, to obtain SUVmax.

### Statistical Analysis

Data are expressed as mean ± SD. The correlation between the SUVmax of the primary lesions and T stage was analyzed using a Spearman rank correlation because T stage was discrete. The correlations of SUVmax between primary esophageal cancer and LN metastases were analyzed using Pearson correlation coefficients. For both analyses, $P$ values less than 0.05 were considered significant. The diagnostic accuracy of $^{18}$F-FDG PET/CT for LN metastases was investigated using receiver-operating-characteristics (ROC) analyses.

## RESULTS

### Primary Tumors

[**Table 1**] Table 1 summarizes the sensitivity of the primary lesions. Visual inspection of the $^{18}$F-FDG PET/CT images failed to identify the primary lesion for 21 of the 73 patients with T1 tumors (6/16 in T1a and 15/57 in T1b), but it succeeded in detecting all of the primary tumors more advanced than T1 stage. The mean SUVmax was positively correlated with the T stage of the tumors ($P < 0.0001$), although there were [**Fig. 1**] significant overlaps among the different T stages (Fig. 1). The distribution of SUVmax of the primary lesions was determined for all 156 patients: 58 presented with low $^{18}$F-FDG avidity (SUVmax < 5), 41 with medium $^{18}$F-FDG avidity (5 ≤ SUVmax < 10), and 57 with high $^{18}$F-FDG avidity (SUVmax ≥ 10).

**TABLE 2**
$^{18}$F-FDG PET/CT and Pathologic Findings of LN Metastasis

| N stage | PET | Pathology |
|---|---|---|
| N0 | 100 | 67 |
| N1 | 50 | 46 |
| N2 | 6 | 23 |
| N3 | 0 | 20 |

### LN Metastases

Compared with the histopathologic analyses, $^{18}$F-FDG PET/CT tended to underestimate N staging. For the N staging, PET/CT agreed with the histopathologic findings in 85 of 156 (54.5%) patients, underestimated stage in 64 of 156 (41.0%), and overestimated stage in 7 of 156 (4.5%). Among the 156 patients investigated, $^{18}$F-FDG PET/CT showed visually abnormal $^{18}$F-FDG uptake in 56 (35.9%) patients in 1 of the regional LNs (≥N1), indicating possible metastasis, whereas the histopathologic analysis demonstrated regional micrometastasis in 89 (57.1%) patients (Table 2). [**Table 2**]

### $^{18}$F-FDG Avidity of Primary Lesion and LN Metastasis

$^{18}$F-FDG avidity of the primary lesion was positively associated with the prevalence of pathologically confirmed LN micrometastasis (Table 3). As a result, positive predictive values (PPVs) of visual inspection of $^{18}$F-FDG PET/CT were lower in patients with low $^{18}$F-FDG avidity in the primary lesions (SUVmax < 5) than in patients with medium and high $^{18}$F-FDG avidity (SUVmax ≥ 5) in the primary lesions (Table 4). [**Table 3**] [**Table 4**]

### Association of $^{18}$F-FDG Avidity Between Primary and LN Metastases

The $^{18}$F-FDG avidity of the primary lesion also affected metabolic activity of metastatic LNs. Higher $^{18}$F-FDG uptake in the primary lesion generally associated with pathologic LN metastasis, which was also positive with visual inspection of PET/CT (Fig. 2). In particular, $^{18}$F-FDG uptake [**Fig. 2**]

**TABLE 3**
Pathologic N Stages Among Each Avidity Group of Main Lesion

| | Avidity | | |
|---|---|---|---|
| N stage | Low (SUVmax < 5) | Mid (5 ≤ SUVmax < 10) | High (10 < SUVmax) |
| N0 | 35 (60.3) | 15 (36.6) | 17 (29.8) |
| N1 | 15 (25.9) | 10 (24.4) | 21 (36.8) |
| N2 | 6 (10.3) | 9 (22.0) | 8 (14.0) |
| N3 | 2 (3.4) | 7 (17.1) | 11 (19.3) |
| Total | 58 | 41 | 57 |

Data in parentheses are percentages.



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**TABLE 4**
Diagnostic Value of Nodal Involvements by Activity of Main Lesion

| Parameter | All nodes | | Regional nodes | | Remote nodes | |
|---|---|---|---|---|---|---|
| | Low | Mid to high | Low | Mid to high | Low | Mid to high |
| Sensitivity (%) | 15.2 | 41.5 | 15.4 | 33.7 | 15.0 | 46.9 |
| Specificity (%) | 95.7 | 92.3 | 91.1 | 89.6 | 97.9 | 93.5 |
| Positive predictive value (%) | 45.5 | 76.3 | 33.3 | 74.0 | 60.0 | 78.3 |
| Negative predictive value (%) | 82.8 | 71.3 | 78.8 | 61.6 | 84.7 | 76.4 |

Low = SUVmax < 5; mid to high = SUVmax ≥ 5.

of pathologically confirmed LN metastases positively correlated with that of the primary lesions ($R = 0.52$, $P <$ 0.05; Fig. 3) in the thoracic region, although the association did not reach the level of significance in the remote regions. The metabolic activity of the primary lesion affected the sensitivity of visual inspection of $^{18}$F-FDG PET/CT for LN metastasis (Fig. 4).

[Fig. 3]
[Fig. 4]

### Best-Cutoff Criteria for LN Metastasis

In accordance with the visual inspection, $^{18}$F-FDG avidity of the primary lesion affected the semiquantitative approach of diagnosing LN metastases (Figs. 5A–5C). Discrimination between metastatic versus reactive LNs was difficult using SUVmax in patients with low $^{18}$F-FDG avidity in the primary lesions (SUVmax < 5), with an area under the curve of 0.56 (Fig. 5B). In contrast, this semiquantitative approach was fairly successful at diagnosing LN metastases in patients with medium to high $^{18}$F-FDG avidity in the primary lesions (SUVmax ≥ 5), with an area under the curve of 0.73. The ROC analysis revealed the best discrimination of true- versus false-positives (highest sensitivity – (1 – specificity)) at the SUVmax of 3.3 (Fig. 5C). The application of this cutoff value (SUVmax, 3.3) resulted in the sensitivity and specificity of 66.1% and 85.7%, respectively, to identify metastatic LNs with visually positive $^{18}$F-FDG uptake. Use of the same cutoff value on the patients with mid to high $^{18}$F-FDG uptake in the primary lesion improved the PPV from 74.0% (visual) to 87.5% (semiquantitative) in regional (thoracic) LNs. The same cutoff value resulted in 100% PPV for remote-region metastasis (Table 5).

[Fig. 5]
[Table 5]

## DISCUSSION

The visual inspection of $^{18}$F-FDG PET/CT images had limited sensitivity to detect LN metastasis, ranging from 29.3% to 53.3% in regional thoracic nodes and in remote areas of the cervical and abdominal regions. However, $^{18}$F-FDG PET/CT of aggressive esophageal cancers had a better diagnostic accuracy, because the $^{18}$F-FDG uptake of the primary lesions was positively correlated with that of the metastatic LNs in the thoracic field. Semiquantitative investigation using an SUVmax cutoff of 3.3 further improved the diagnostic accuracy, with higher specificity and PPVs.

The presurgical staging of primary esophageal cancer defines the therapeutic options. In particular, it is important to distinguish between patients with locoregional and systemic disease, to avoid unnecessary curative therapeutic options (*3*). There are multiple investigations regarding the clinical utility of $^{18}$F-FDG PET for such presurgical staging. In general, the investigators concluded that $^{18}$F-FDG PET/CT had a limited role in the identification of early regional LN metastasis but was highly useful to detect remote LN involvement and metastases to the remote organs (*4,5*). The results of the present study confirmed the low sensitivity of the visual inspection of $^{18}$F-FDG PET/CT images for both regional and remote LN metastases.

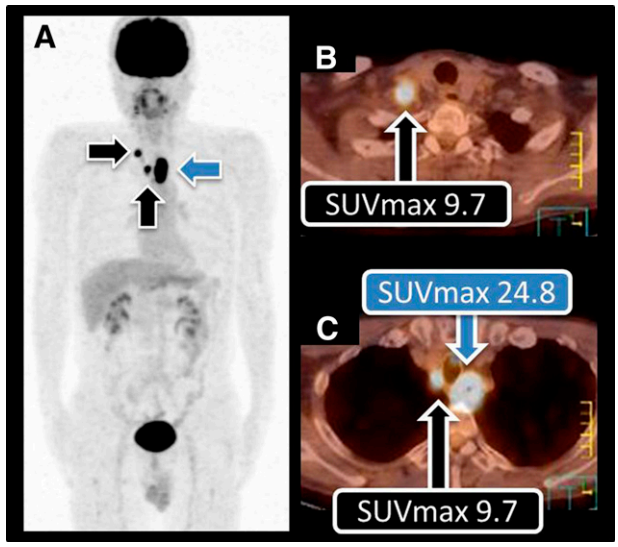


**FIGURE 2.** Representative $^{18}$F-FDG PET images of 52-y-old man with SCC of upper thoracic esophagus showing high $^{18}$F-FDG avidity in primary lesion. (A) Whole-body maximum-intensity-projection image demonstrating high $^{18}$F-FDG avidity in primary lesion (blue arrow; SUVmax, 24.8) and LN uptake in the cervical and thoracic regions (black arrows). (B) Axial image of cervical region showing abnormal $^{18}$F-FDG uptake in metastatic LN (SUVmax, 9.7). (C) Axial image of upper thoracic region showing abnormal $^{18}$F-FDG uptake in metastatic LN (SUVmax, 9.7). Pathologic analyses disclosed T3, LN metastasis of cervical and thoracic regions, which were concordant with $^{18}$F-FDG PET/CT findings.

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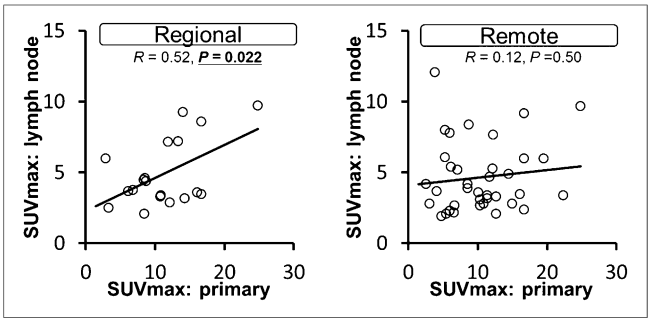


**FIGURE 3.** Representative SUVmax of regional and remote LN metastases was plotted against SUVmax of primary lesions. Representative value of LN SUVmax was defined as highest SUVmax of metastatic LNs in each region (cervical, thoracic, and abdominal).

The low sensitivity of PET for locoregional nodal involvement at initial staging may be related to the presence of microscopic spread, high $^{18}$F-FDG uptake in the adjacent primary tumor, or hypermetabolic activity associated with a chronic inflammatory process—all of which often coexist with the microscopic metastasis. Hybrid PET/CT imaging can overcome some of these limitations by improving the characterization of $^{18}$F-FDG activity in the vicinity of highly tracer-avid primary tumors (*14*), but it still provides only low signals due to microscopic spread of the metastatic malignant cells. In particular, esophageal cancer with low glucose transporter 1 (Glut-1) expression accumulates less $^{18}$F-FDG, resulting in a low signal-to-background ratio for detecting metastatic legions. As suggested by pathologic analyses, Glut-1 expression of the metastatic LNs positively correlated with that of the primary lesions, possibly affecting the sensitivity of the PET/CT scan to detect LN metastases (*15*). In the present study, we reexamined the diagnostic accuracy of PET/CT to identify LN metastases in primary esophageal cancer with the correlation of the $^{18}$F-FDG avidity of the primary lesions. To our knowledge, this is the first clinical investigation regarding the association of $^{18}$F-FDG avidities between primary esophageal SCC and its LN metastases.

Here, the visual inspection of $^{18}$F-FDG PET/CT images failed to identify the primary lesion for 21 of 73 patients with T1 tumors, but it succeeded in detecting all of the primary tumors more advanced than T1 stage. $^{18}$F-FDG avidity of the primary lesion was associated with tumor length, depth of invasion, macroscopic type, nodal metastasis, vascular invasion, and Glut-1 expression (*16–18*). Overlaps of $^{18}$F-FDG avidity among T1, T2, T3, and T4 tumors probably indicated a range of Glut-1 expression (*15*), which in turn indicated variation in the aggressiveness of the primary lesion (*19*).

The detection of LN metastases is another factor affecting the clinical staging of esophageal cancer. We found that $^{18}$F-FDG PET/CT, compared with the diagnosis based on histopathologic analyses, tended to underestimate lymph nodal involvement. The underestimation was particularly clear in patients with low $^{18}$F-FDG avidity in the primary lesions (SUVmax $<$ 5). However, the $^{18}$F-FDG PET/CT images of primary lesions with higher $^{18}$F-FDG avidity (SUVmax $\geq$ 5) showed relatively better diagnostic accuracy, with a higher sensitivity for LN metastases. Previously, Mamede et al. reported a similar trend in a mixed population mostly consisting of esophageal adenocarcinoma. They reported that a pretherapeutic SUVmax greater than 12.7 complemented the visual analysis by raising the sensitivity to predict nodal metastases from 30.8% to 69.2% (*20*). The results of the present study were consistent with the previous investigation, although our study population included only patients with esophageal SCC. One of the explanations for the better diagnostic accuracy of LN metastasis in the tumors with higher $^{18}$F-FDG avidity was their higher metabolic potential to metastasize, which affects prevalence of LN involvement (Table 3) (*21*). In addition, metabolically active primary lesions probably resulted in an improved sensitivity of visual inspection as an outcome of increased $^{18}$F-FDG avidity in the metastatic LNs. Theoretically, metabolic activity of the primary lesion parallels with that of the metastatic LNs, because the nodes are filled with the same type of cells as the primary. In the present study, we found no significant difference in diagnostic accuracy between medium and high $^{18}$F-FDG avidity in the primary lesion, possibly suggesting a nonlinear relationship between primary metabolic activity and the diagnostic accuracy of visual inspection of PET/CT.

Positive correlations of $^{18}$F-FDG avidity between primary and regional metastatic lesions were reported in NSCLC (*7,22,23*) and in advanced gastric cancer (*24*). In NSCLC, $^{18}$F-FDG uptake within the primary lesion indicated aggressiveness of the tumor, representing intratumoral lymphatic

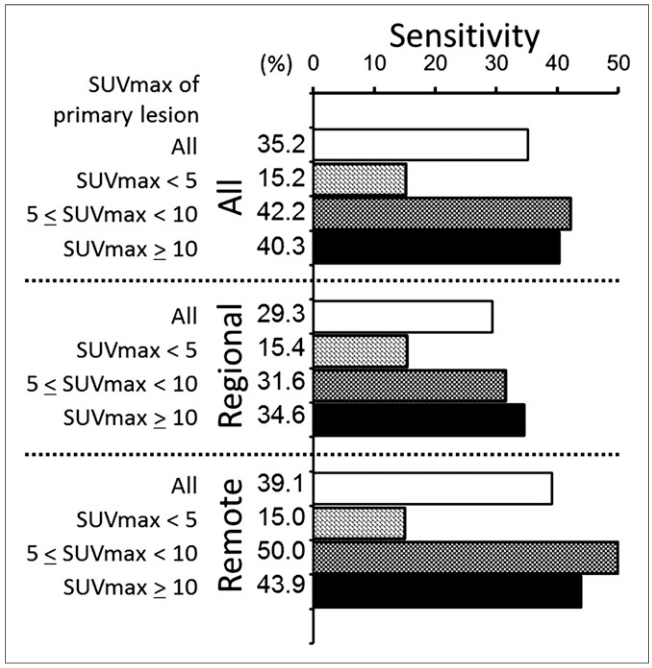


**FIGURE 4.** Comparison of sensitivities with visual analysis among different $^{18}$F-FDG avidity in primary lesions.



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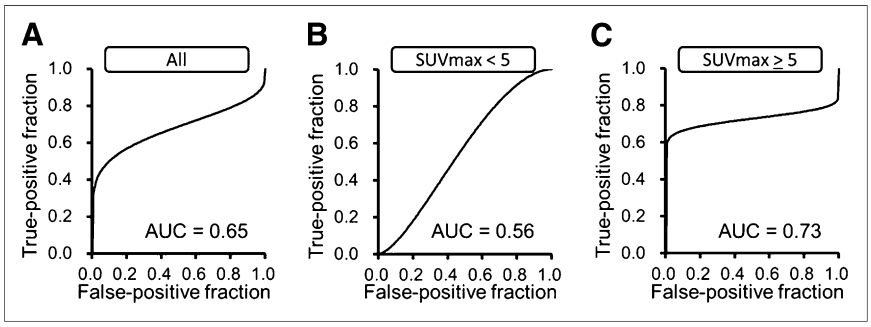


**FIGURE 5.** Results of ROC analyses: all patients (A), patients with low $^{18}$F-FDG avidity in primary lesions (SUVmax $<$ 5) (B), and patients with mid to high $^{18}$F-FDG avidity in primary lesions (SUVmax $\geq$ 5) (C).

vessel invasion and LN involvement (*6,7*). The metabolic activity of the primary tumor and tumor size are important variables in $^{18}$F-FDG PET interpretation for NSCLC, because they affect the likelihood of malignant involvement in nodes (*8*). A similar relationship was reported in advanced gastric cancer, suggesting the possibility of false-negative results with $^{18}$F-FDG PET in primary advanced gastric cancers exhibiting low uptake of $^{18}$F-FDG (*24*). The results of the present study are in line with these previous investigations, and they suggest the importance of assessing the $^{18}$F-FDG avidity of the primary lesions when using PET/CT for the presurgical staging of thoracic esophageal cancer. The present results did not clarify the reason for the lack of correlation between the SUVmax of the primary lesions and that of remote LNs, but the lack of correlation may suggest a difference in aggressiveness from primary lesions.

The results of our ROC analysis demonstrated that the best-cutoff value for malignant regional metastasis is the SUVmax of 3.3. This value is higher than the previously reported mean SUVmax of metastatic LNs of esophageal SCC (*25*). We suspected that the higher prevalence of reactive inflammatory LNs in the thoracic field elevated the optimal cutoff criterion to separate the malignant versus inflammatory pathologies. In the present study, we observed a significant overlap of SUVmax between the inflammatory and metastatic LNs, making it technically difficult to distinguish using a single cutoff value. Separating the 2 processes using a single cutoff criterion is not feasible in cases with low $^{18}$F-FDG uptake of the primary cancer, because metastatic nodes probably show low $^{18}$F-FDG uptake. In contrast, if a primary lesion is highly $^{18}$F-FDG–avid, using the cutoff criterion may reasonably identify the regional metastasis.

To determine the therapeutic options, it is important to distinguish between patients with locoregional and systemic disease, because of the limited availability of curative therapeutic options for patients with distant LN metastasis or organ metastasis (*3*). Although there are multiple investigations debating the role of $^{18}$F-FDG PET/CT for presurgical treatment planning (*26*), our study draws attention to the finding that primary lesions with low $^{18}$F-FDG uptake have high false-negative rates for regional lymph nodal metastases, limiting the clinical utility of this technique for presurgical staging. Specifically, regional nodes could not be adequately assessed with the $^{18}$F-FDG PET/CT scan if the primary tumor SUVmax was less than 5.0, because the diagnostic accuracy for identifying metastatic regional nodes is suboptimal. However, the noninvasive nature of this technique supports its clinical utility for presurgical staging, particularly with esophageal cancer with medium to high $^{18}$F-FDG avidity in the primary lesions.

The present study had methodologic limitations. The pathologic analyses did not measure the size of the metastatic LNs or the diameter of the cancerous area in the LNs. Because volume information is known to improve diagnostic accuracy in LN staging (*27*), further investigations should examine the relation between the size of LNs and the $^{18}$F-FDG uptake of the primary lesions.

## CONCLUSION

This study showed that the avidity of the primary esophageal SCCs affected the detectability of lymph nodal metastases. If primary lesions of esophageal SCC present with a low $^{18}$F-FDG uptake, PET/CT may have a limited role for initial staging because of a low sensitivity to detecting LN metastases.

## DISCLOSURE

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**TABLE 5**
Diagnostic Value of LN Metastasis Using Best-Cutoff Criteria in Mid to High Avidity in Primary Lesions

| Parameter | All ($n$ = 73) | Regional ($n$ = 26) | Remote ($n$ = 47) |
|---|---|---|---|
| Sensitivity (%) | 66.1 | 70.0 | 64.1 |
| Specificity (%) | 85.7 | 66.7 | 100.0 |
| Positive predictive value (%) | 95.1 | 87.5 | 100.0 |
| Negative predictive value (%) | 37.5 | 40.0 | 36.4 |

Best-cutoff criteria (SUVmax, 3.3) was determined from all nodes and then applied to both regional and remote groups.



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