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Prediction of Occult Lymph Node Metastasis by Metabolic Parameters in Patients with Clinically N0 Esophageal Squamous Cell Carcinoma

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The aim of this study was to investigate the value of ^{18}F-FDG parameters of the primary tumor in predicting occult lymph node metastasis in patients with clinically N0 esophageal squamous cell carcinoma. **Methods:** The study comprised 143 consecutive patients (mean age ± SD, 63.9 ± 8.6 y; range, 31.8–81.2 y) from May 2003 to January 2010 who had clinically N0 esophageal squamous cell carcinoma based on preoperative imaging studies including chest CT, ^{18}F-FDG PET/CT, and endoscopic ultrasound. We measured maximum standardized uptake value (SUV_{max}), mean SUV (SUV_{mean}), total lesion glycolysis (TLG), and metabolic tumor volume (MTV) of the primary tumor and analyzed the relationship between clinicopathologic variables including PET parameters and occult lymph node metastasis using a logistic regression model. **Results:** Univariate analysis indicated that clinical T classification, SUV_{max}, SUV_{mean}, MTV, TLG, and longitudinal diameter of tumor were significant risk factors associated with occult lymph node metastasis. Optimal thresholds were cT2–4, $SUV_{max} \geq 4.8$, $SUV_{mean} \geq 3.2$, MTV ≥ 5.5 cm^3, TLG ≥ 220, and diameter ≥ 3.8 cm. After multivariate analysis, the logistic regression model revealed that clinical T classification (hazard ratio [HR], 4.6; 95% confidence interval [CI], 1.7–12.4; $P = 0.003$) and SUV_{max} (HR, 3.5; 95% CI, 1.3–9.2; $P = 0.012$) were independent risk factors. The combination of SUV_{max} and clinical T classification (HR, 13.2; 95% CI, 5.4–31.9; $P < 0.001$) was a significantly better powerful risk factor for occult lymph node metastasis than SUV_{max} or clinical T classification alone. Sensitivity, specificity, positive predictive value, and negative predictive value of the combination of clinical T classification and SUV_{max} were 73.0%, 81.5%, 60.0%, and 89.7%, respectively. **Conclusion:** SUV_{max}, combined with clinical T classification, may be useful for predicting occult lymph node metastasis in patients with clinically N0 squamous cell carcinoma of the esophagus.

Key Words: esophageal cancer; ^{18}F-FDG; PET/CT; lymph node; occult metastasis; SUV_{max}

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The accurate detection of regional lymph node metastasis in esophageal cancer is important for the selection of the proper treatment strategy. The presence of regional lymph node metastasis is particularly critical when making decisions about treatment, especially when tumor invasion is limited to submucosa of the esophagus. Current evaluation methods for preoperative tumor classification include multiimaging modalities such as CT, endoscopic ultrasonography (EUS), and ^{18}F-FDG PET/CT (*1*). However, current imaging modalities have limited capabilities, and diagnostic performance for the detection of regional lymph node metastases is incomplete (*2*). Despite comprehensive assessment using multiimaging modalities, a considerable percentage of patients with clinically N0 esophageal cancer are found to have regional lymph node metastasis after esophagectomy. The prevalence rate of occult lymph node metastasis ranges from 11% to 56% (*3*).

^{18}F-FDG PET/CT has an advantage over conventional imaging modalities in that it provides quantitative information on metabolic activity of the tumor (*4*). Quantified metabolic activity measured by ^{18}F-FDG PET can reflect tumor burden and disease activity; therefore, it is useful for both predicting prognosis and assessing treatment response in the field of clinical oncology (*5–7*). Recently, it was reported that metabolic PET parameters were independent risk factors associated with occult lymph node metastasis in patients with non–small cell lung cancer who were diagnosed as N0–1 by preoperative staging work-up and in patients with clinically node-negative squamous cell carcinoma of the tongue (*8,9*). This finding suggests a potential benefit of ^{18}F-FDG PET/CT in preoperative assessments of lymph node metastasis in cancer patients who have been diagnosed as clinically node-negative.

The purpose of this study was to investigate whether ^{18}F-FDG PET parameters of the primary tumor have the potential to predict occult lymph node metastasis in patients with clinically N0 esophageal cancer.

MATERIALS AND METHODS

Patients

We retrieved data on all consecutive patients with esophageal cancer who underwent ^{18}F-FDG PET/CT for initial staging from May 2003 to January 2010 by searching the institutional medical database. Patients were included if they had a pathologically proven esophageal squamous cell carcinoma with clinically N0 classification, based on preoperative studies including chest CT, ^{18}F-FDG PET/CT, and EUS. To be included, patients also had to have undergone esophagectomy with lymph

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node dissection without neoadjuvant treatment. Patients with concurrent cancer at the time of diagnosis or uncontrolled diabetes or high blood glucose level (>150 mg/dL) during the PET/CT scan were excluded.

Study patients were selected from a total of 892 patients with squamous cell carcinoma who underwent PET/CT for initial staging work-up. After exclusion of 365 (40.9%) patients who did not undergo EUS or who did not cooperate during the EUS, 270 (30.3%) patients with cN1–3 disease, 78 (8.7%) patients who had endoscopic mucosal resection or preoperative therapy, 12 (1.3%) patients who had concurrent cancer, 23 (2.6%) patients who had uncontrolled diabetes or high blood glucose level, and 1 (0.1%) patient with PET/CT data loss, 143 (16.0%) patients were finally included for analysis.

The institutional review board our institution approved this retrospective study, and the requirement to obtain informed consent was waived.

PET/CT Imaging

Patients were instructed to fast for at least 6 h before the PET/CT scan. Blood glucose levels were measured before injection of ^{18}F-FDG in all patients. PET/CT imaging was performed using 1 of 2 dedicated PET/CT scanners (Discovery LS for 89 subjects or Discovery STe for 96 subjects; GE Healthcare) without intravenous or oral contrast material.

When the Discovery LS scanner was used, whole-body CT was performed with a continuous spiral technique with an 8-slice helical CT (140 keV; 40–120 mA; section width, 5 mm) at 60 min after injection of ^{18}F-FDG (5.5 MBq/kg). After the CT scan, an emission scan was obtained from head to toe for 4 min per frame in 2-dimensional mode. Attenuation-corrected PET images (4.3 × 4.3 × 3.9 mm) were reconstructed from the CT data using an ordered-subset expectation maximization algorithm (28 subsets, 2 iterations). When the Discovery STe scanner was used, whole-body CT was performed with a continuous spiral technique with 16-slice helical CT (140 keV; 30–170 mA; section width, 3.75 mm) at 60 min after injection of ^{18}F-FDG. After the CT scan, an emission scan was obtained from the thigh to head for 2.5 min per frame in 3-dimensional mode. Attenuation-corrected PET images (3.9 × 3.9 × 3.3 mm) were reconstructed from the CT data using a 3-dimensional ordered-subset expectation maximization algorithm (20 subsets, 2 iterations).

Measurements of PET Parameters

Two experienced nuclear medicine physicians reviewed all PET/CT images. Metabolic and volumetric parameters were measured using Volume Viewer software (GE Healthcare). Metabolic tumor volume (MTV) was defined as the total tumor volume segmented by the threshold standardized uptake value (SUV). Mediastinal blood-pool activity was used as a threshold for determining the volume-of-interest (VOI) boundary. To determine the threshold using the mediastinal blood pool, a VOI consisting of 5 × 5 × 1 voxels was manually drawn at the aortic arch. The mean SUV (SUV_{mean}) plus 2 SDs of the VOI in the aortic arch was chosen as the threshold SUV for the selected measurable tumors. VOIs of the tumors were automatically generated using the threshold SUV. The software calculated the maximum SUV (SUV_{max}), SUV_{mean}, and MTV of the entire tumor. Total lesion glycolysis (TLG) was obtained by multiplying the SUV_{mean} by the number of voxels (*10*).

Lymph Node Grouping

All visible and palpable lymph nodes in the surgical field were dissected thoroughly by experienced thoracic surgeons as presented in the previous study conducted at Samsung Medical Center (*11*). We classified the lymph nodes into 5 categories according to lymph node region for the purpose of analysis, according to previous studies (*11,12*). In the present study, cervical nodes included cervical and supraclavicular lymph nodes. Upper mediastinum nodes included upper paraesophageal lymph nodes, recurrent nerve lymph nodes, aortopulmonary nodes, and paratracheal lymph nodes. Middle mediastinum nodes included subcarinal nodes, middle paraesophageal lymph nodes, and hilar lymph nodes. Lower mediastinum nodes included lower paraesophageal and diaphragmatic lymph nodes. Abdominal nodes included cardiac, left gastric, and celiac lymph nodes.

TABLE 1
Clinicopathologic Characteristics of Patients with Clinically N0 Esophageal Squamous Cell Carcinoma (n = 143)

Characteristic	No. of patients
Age (y)	
Range	31–81
Median	64
Sex	
Male	131 (91.6)
Female	12 (8.4)
Tumor location	
Upper	10 (7.0)
Middle	82 (57.3)
Lower	48 (33.6)
Esophagogastric junction	3 (2.1)
Histologic grade	
Well	16 (11.2)
Moderate	111 (77.6)
Poor	16 (11.2)
Operation	
Two-field	140 (97.9)
Three-field	3 (2.1)
cT classification	
Tis-T1	65 (45.4)
T2	48 (33.6)
T3	28 (19.6)
T4	2 (1.4)
pT classification	
Tis-T1a	35 (24.5)
T1b	63 (44.0)
T2	18 (12.6)
T3–4	27 (18.9)
pStage	
0-I	86 (60.1)
IIA	9 (6.3)
IIB	27 (18.9)
III	21 (14.7)
Occult lymph node metastasis	37 (25.9)
No. of dissected lymph nodes (mean ± SD)	35.5 ± 14.8
cLongitudinal diameter of tumor (cm; mean ± SD)	2.9 ± 1.7

c = clinical; p = pathologic.
Data in parentheses are percentages.

Statistical Analysis

Statistical analyses were performed using commercial software (PASW Statistics 18; IBM Inc.). PET parameters and clinicopathologic characteristics were analyzed to identify risk factors for occult lymph node metastasis. Information including tumor location, histology, and histologic grade was obtained from surgical records and pathology reports. Clinical tumor depth (cT classification) and clinical longitudinal diameter of tumor were determined by EUS.

Receiver-operating-characteristic curve analysis was performed to determine the optimal cutoff values for the continuous variables that divided patients into 2 subgroups according to presence of occult lymph node metastasis. Univariate and multivariate analyses using backward

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TABLE 2
Comparison of PET Parameters Between Patients With and Without Occult Lymph Node Metastasis

Parameter	Metastasis (+)	Metastasis (−)	*P*
SUV_{max}			<0.001
Median	10.3	3.5	
Mean ± SD	9.9 ± 6.2	5.5 ± 6.5	
Range	1.0–22.3	1.0–39.8	
SUV_{mean}			0.02
Median	3.4	2.4	
Mean ± SD	3.3 ± 1.3	2.5 ± 2.0	
Range	1.0–6.70	1.0–15.0	
MTV (cm^3)			0.03
Median	10.2	2.9	
Mean ± SD	17.9 ± 23.4	9.9 ± 20.3	
Range	0.0–104.0	0.0–120.0	
TLG			0.14
Median	640.2	125.1	
Mean ± SD	1,427.4 ± 2,664.8	843.6 ± 2,224.6	
Range	0.0–12,243.3	0.0–13,107.0	

stepwise logistic regression modeling were performed to identify the risk factors associated with occult lymph node metastasis. In addition, subgroup analysis was performed in the cT1N0 and cT2N0 patients group separately. The McNemar test was used to compare the accuracy of factors significance on multivariate analysis for predicting occult lymph node metastasis. Continuous variables were expressed as mean ± SD. All tests were 2-sided, and *P* values less than 0.05 were considered statistically significant.

RESULTS

Patient Characteristics

The patients' clinicopathologic characteristics are summarized in Table 1. The mean time interval between ^{18}F-FDG PET/CT and operation was 11 ± 7 d, ranging from 1 to 30 d. The incidence of occult lymph node metastasis was 25.9% (37/143 patients). Lymph nodes (n = 5,079) were dissected, and 98 (1.9%) were histologically confirmed metastatic lymph nodes.

The mean SUV_{max}, SUV_{mean}, MTV, and TLG of the primary tumors of all patients were 6.6 ± 6.7 (range, 1.0–39.8), 2.7 ± 1.9 (range, 1.0–15.0), 12.0 ± 21.3 cm^3 (range, 0.0–120.0 cm^3), and 994.7 ± 2,350.7 (range, 0.0–13,108.8), respectively. Differences in the metabolic parameters between the patients with and without occult lymph node metastasis are presented in Table 2. The values for SUV_{max}, SUV_{mean}, and MTV of the primary tumor in patients with occult lymph node metastasis were significantly higher than those of the primary tumor in patients without occult lymph node metastasis (Fig. 1), whereas TLG of the primary tumor was not significantly different between the 2 groups.

Risk Factors for Occult Lymph Node Metastasis

Univariate analysis indicated that clinical T classification, SUV_{max}, SUV_{mean}, MTV, TLG, and longitudinal diameter of tumors were significant risk factors associated with occult lymph node metastasis. Optimal thresholds were cT2–4, $SUV_{max} \geq 4.8$, $SUV_{mean} \geq 3.2$, MTV ≥ 5.5 cm^3, TLG ≥ 220, and diameter ≥ 3.8 cm (Table 3). In multivariate analysis without a combination of clinical T classification and SUV_{max}, clinical T classification and SUV_{max} were independent risk factors (Table 4). With a combination of clinical T classification and SUV_{max}, cT2–4 and $SUV_{max} \geq 4.8$ was the only independent risk factor for occult lymph node metastasis.

In subgroup analysis, there was no significant risk factor in the cT1N0 group. However, in the cT2N0 group, SUV_{max} (≥4.8) was the only risk factor (hazard ratio, 9.0; 95% confidence interval, 1.7–48.4; P = 0.011).

Predicting performance of the selected risk factors for occult lymph node metastasis is summarized in Table 5. The combination of clinical T classification (cT2–4) and SUV_{max} (≥4.8) was the most reliable parameter.

Patterns of Occult Lymph Node Metastasis According to Primary Tumor Location

The regions of occult lymph node metastasis according to the primary tumor location are summarized in Supplemental Table 1 (available at http://jnm.snmjournals.org).

Of 5 patients with upper thoracic esophageal cancer, 4 showed occult lymph node metastasis in the cervical area or upper mediastinum (80.0%). Only 1 patient had skip metastasis in the upper abdomen (20.0%). Recurrent laryngeal lymph nodes were most commonly involved (71.4%, 5/7 lymph nodes).

Among 18 patients who had a primary tumor on the middle thoracic esophagus, 8 showed occult lymph node metastasis only in the mediastinum (44.4%), whereas another 8 had occult lymph node metastasis in both the mediastinum and the upper abdomen (44.4%) and 2 had metastasis only in the abdominal region (11.1%). The tumors most commonly involved the left gastric lymph node (37.8%, 17/45 lymph nodes) in these patients.

Of 14 patients with a primary tumor on the lower thoracic esophagus or esophagogastric junction, 5 patients showed occult lymph node metastasis only in the upper abdomen (35.7%). Another 4 patients had metastasis in both the mediastinum and the upper abdomen (28.6%), and the others had metastasis only in the mediastinum (35.7%). The left gastric lymph node was most commonly involved (33.3%, 14/42 lymph nodes). Importantly, almost half of the patients in whom the primary tumor was located in the lower thoracic esophagus or esophagogastric junction had occult lymph node metastasis involving the upper mediastinum (42.8%, 6/14 patients).

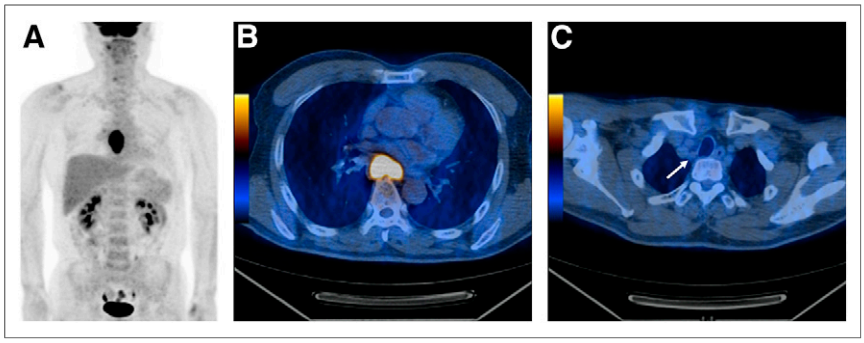


FIGURE 1. Images of a 60-y-old male patient with newly diagnosed esophageal cancer. (A) Maximum-intensity-projection image shows hypermetabolic mass in mid to lower thoracic esophagus area. (B) Transverse image of PET/CT scan obtained at subcarinal level shows hypermetabolic mass with high SUV_{max} of 14.7 in esophagus. No significant hypermetabolic or enlarged lymph nodes suggestive of metastasis were noted in staging work-up. (C) Small-sized right recurrent laryngeal lymph node without significant ^{18}F-FDG uptake is observed (arrow). After esophagectomy with node dissection, lymph node was found to be metastatic.

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TABLE 3
Univariate Analysis of Risk Factors Associated with Occult Lymph Node Metastasis

Variable	Category	Hazard ratio	95% confidence interval	*P*
cT classification	cT2–4	8.4	3.5–20.3	<0.001
SUV_{max}	≥4.8	7.2	3.1–16.9	<0.001
MTV (cm^3)	≥5.5	6.3	2.5–15.6	<0.001
TLG	≥220	5.8	2.3–14.4	<0.001
SUV_{mean}	≥3.2	5.0	2.3–11.1	<0.001
cLongitudinal diameter of tumor (cm)	≥2.5	2.2	1.0–4.9	0.044
Age (y)	≥77	3.2	0.9–11.6	0.084
Sex	Male	4.2	0.5–33.5	0.179
Tumor location	Upper			0.329
	Middle	2.0	0.1–29.8	0.615
	Lower	0.6	0.1–6.7	0.655
	Esophagogastric junction	0.7	0.1–8.9	0.815
Histologic grade	Well	0		0.962
	Moderate	1.2	0.2–6.8	0.827
	Poor	1.2	0.3–4.7	0.782

c = clinical.

DISCUSSION

The present study demonstrates that SUV_{max} of the primary tumor and cT classification are independent risk factors associated with occult lymph node metastasis in patients with clinically N0 esophageal squamous cell carcinoma. Our data further suggest that SUV_{max} might be useful in identifying patients at risk of occult lymph node metastasis who should be managed more carefully.

Occult lymph node metastasis is important because it hinders exact assessment of the tumor status and selection of an appropriate treatment strategy. In addition, occult lymph node metastasis is itself a significant prognostic factor in patients with esophageal cancer (*3*). However, despite comprehensive assessment using multiimaging modalities, preoperative nodal staging work-up with conventional methods has a considerable rate of false-negative results. In this study, the rate of occult lymph node metastasis was 25.9% (37/143), which is consistent with previous studies (11%–56%) (*3*).

The diagnostic sensitivity of imaging modalities for detecting nodal involvement in clinically N0 patients is limited. PET/CT could not improve the detection rate of subclinical lymph node metastasis in the previous study (*13*). EUS with fine-needle aspiration has an excellent sensitivity in detecting the locoregional node metastasis of esophageal cancer (*14*); however, concerns exist regarding the interobserver variation and machine-dependent factors of EUS (*15*). In addition, patient cooperation is essential, therefore safe and successful EUS is not practical in all patients. In these circumstances, knowledge of risk factors related with occult lymph node metastasis could improve our perception of node metastasis.

Various characteristics of esophageal cancer have been reported as important factors for lymph node metastasis (*11,13–15*). Immunohistochemical findings, such as depth of tumor infiltration and grade of lymphocytic infiltration, are important factors in early esophageal cancer (*11,14,15*). However, before endoscopic resection or esophagectomy, accurate immunohistochemical factors related to lymph node metastasis could not be obtained. In practice, histology obtained from endoscopic biopsies, tumor size or depth determined by preoperative evaluation, and other clinical characteristics of patients constitute available information for the prediction of occult lymph node metastasis. To date, however, risk factors for the prediction of occult lymph node metastasis in patients with esophageal cancer have not been fully investigated.

The presence of muscularis propria invasion determined by EUS (cT2) is an independent risk factor associated with occult lymph node metastasis in this study, corresponding with the earlier studies that reported that endoscopically determined clinical tumor depth was a significant independent factor for predicting lymph node metastasis in esophageal cancer (*13,16*). In addition, cT classification with SUV_{max} (≥4.8) is a powerful parameter predicting occult lymph node metastasis (Tables 4 and 5). In patients undergoing esophagectomy, the primary tumor with muscularis propria invasion with high SUV_{max} may justify extensive and careful regional lymph node dissection, especially in the upper mediastinum

TABLE 4
Multivariate Analysis of Risk Factors Associated with Occult Lymph Node Metastasis

Variable	Category	Hazard ratio	95% Confidence interval	*P**
cT classification†	cT2–4	4.6	1.7–12.4	0.003
SUV_{max}†	≥4.8	3.5	1.3–09.2	0.012
cT classification + SUV_{max}	cT2–4 and ≥4.8	13.2	5.4–31.9	<0.001

*Adjusted for age and sex.
†Obtained from multivariate analysis excluding cT classification + SUV_{max}.
c = clinical.

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TABLE 5
Predicting Performance of Selected Parameters for Occult Lymph Node Metastasis

Variable	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
cT classification	78.4%	69.8%	47.5%	90.2%	72.0%
SUV_{max}	75.7%	69.8%	46.7%	89.2%	71.3%
cT classification + SUV_{max}	73.0%	81.5%*	60.0%*	89.7%	80.4%*

*$P < 0.001$, compared to cT classification and SUV_{max}.
c = clinical.

and abdomen, due to the probability of occult metastasis (Supplemental Table 1).

To the best of our knowledge, the predictive value of PET parameters for postoperative nodal status in clinically N0 squamous cell carcinoma of the esophagus has not been established. However, we could reasonably infer that PET parameters may be related to postoperative nodal involvement in clinically N0 patients because the previous studies have shown that PET parameters are positively correlated with N classification in various cancers (*8, 17–19*). SUV_{max} of the primary tumor was significantly associated with postoperative nodal status in patients with clinically N0 non–small cell lung cancer (*17*). $SUV_{max} > 12.7$ and average SUV > 5.9 yielded the best result to predict nodal metastases in a study population consisting of patients with mainly adenocarcinoma of the esophagus (*19*). Results of our study are in close agreement with those of previous studies. Our findings and those of others suggest that physicians should be careful to establish node status when they deal with an esophageal cancer patient who has a high SUV_{max} of the primary tumor even when the size and ^{18}F-FDG uptake of lymph nodes may not be significant enough to suggest metastasis in preoperative staging.

In our institution, cTis–T1N0 esophageal cancer patients underwent esophagectomy or endoscopic mucosal resection without preoperative chemoradiotherapy, and cT1N-positive esophageal cancer patients mainly underwent preoperative chemoradiotherapy according to the recommendations of the guideline (*20*). In the cT1N0 group, there were no significant risk factors related with occult lymph node metastasis, which may be partly explained by a low event rate of occult lymph node metastasis in the cT1N0 group (12.3%; 8/65). This finding suggests that PET parameters do not affect the decision-making process in cT1N0 disease. On the other hand, in other groups including cT2N0, SUV_{max} (cutoff, 4.8) was the only significant risk factor associated with occult lymph node metastasis. In cT2–4aN0 esophageal cancer, there are various primary treatment options including preoperative chemoradiotherapy, definitive chemoradiation, and esophagectomy (*20*). Our results suggest that SUV_{max} may be useful for choosing appropriate primary treatment in those groups. For example, in the case of low-risk cT2–4a disease, esophagectomy is the preferred option. If the primary tumor has an $SUV_{max} \geq 4.8$, preoperative chemoradiotherapy might be the more appropriate primary treatment because of a high risk of occult lymph node metastasis.

Theoretically, volume-based parameters are more suitable indicators of tumor burden than SUV_{max} or SUV_{mean}, because volume-based PET parameters have shown a better predictive performance for prognosis than SUV_{max} in previous studies (*21–23*). In addition, MTV demonstrated a significant correlation with occult lymph node metastasis in patients with clinically N0 tongue cancer (*8*). However, the present study revealed that SUV_{max}, but not MTV or TLG, is associated with occult lymph node metastasis. This finding suggests that the presence of malignant cells with high glucose metabolism is more important than total tumor burden in the process of lymph node metastasis in esophageal cancer.

The number of dissected lymph nodes is an important factor that might affect the results of the present study. If the number of dissected lymph nodes is insufficient, occult lymph node metastasis might be missed, resulting in an inaccurate result (*24*). The optimal number of nodes that should be dissected was reported in previous studies as at least 6–18 lymph nodes in patients with early esophageal cancer (*24–26*). In the present study, an average of 36 lymph nodes (range, 6–108) was dissected, which was a sufficient number to conduct an accurate N classification.

The pattern of occult lymph node metastasis was also investigated in this study. Patients with tumors located on the upper thoracic esophagus commonly had recurrent laryngeal lymph node metastasis. Patients with tumors located on the mid to lower thoracic esophagus or esophagogastric junction typically had left gastric lymph node metastasis. Most importantly, occult lymph node metastasis was not limited to the vicinity of the primary tumor: in 45.9% of patients (17/37), node metastasis skipped the adjacent area of primary tumor. The findings of our study suggest that lymph node dissection should be performed carefully and with sufficient range in patients at high risk of occult lymph node metastasis.

This study has several limitations. The retrospective nature of the study limits external validity of study findings. Generalization and clinical application to other populations and settings may be difficult. Another limitation is that possible risk factors, such as endoscopic findings, were not included in the analysis. The other limitation is that cT3–4 esophageal cancer patients were enrolled in this study. Because of current management guidelines, it is difficult to include these patients as preoperative chemoradiotherapy before esophagectomy is the preferred treatment for cT3–4 esophageal cancer. However, this therapeutic strategy has been established over the years. Until 2008, induction therapy was not routinely recommended in our institution. Consequently, 30 (21%; 30/143) patients who had cT3–4 esophageal cancer were included because we enrolled patients between 2003 and 2010. Further well-designed prospective studies are needed to confirm the clinical value of metabolic PET parameters in predicting occult lymph node metastasis.

CONCLUSION

The present study demonstrated that SUV_{max}, combined with clinical T classification, can be useful for predicting occult lymph node metastasis in patients with clinically N0 squamous cell carcinoma of esophagus. These parameters may allow the identification of patients at high risk of occult lymph node metastasis who might be candidates for more careful diagnostic work-up and more intensive treatment.

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DISCLOSURE

The costs of publication of this article were defrayed in part by the payment of page charges. Therefore, and solely to indicate this fact, this article is hereby marked "advertisement" in accordance with 18 USC section 1734. This study was supported by a grant from the National R&D Program for Cancer Control, Ministry of Health and Welfare, Republic of Korea (1120150). No other potential conflict of interest relevant to this article was reported.

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