^{18}F-FDG Uptake by Primary Tumor as a Predictor of Intratumoral Lymphatic Vessel Invasion and Lymph Node Involvement in Non-Small Cell Lung Cancer: Analysis of a Multicenter Study

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Intratumoral lymphatic vessel invasion and lymph node involvement are important factors in the planning of therapeutic strategies, particularly limited surgical resection in patients with non-small cell lung cancer. ^{18}F-FDG uptake within the primary lesion correlates with aggressiveness on PET studies. The more metabolically active the tumor, the more aggressive are the findings. The aim of this multicenter study was to determine whether ^{18}F-FDG uptake of the primary tumor is a predictor of intratumoral lymphatic vessel invasion and lymph node metastasis in patients with non-small cell lung cancer. **Methods:** One hundred thirty-two patients with lung cancer were studied. All patients underwent a thoracotomy within 4 wk of the ^{18}F-FDG PET study. A 3-point visual scoring system (low, moderate, or high grade in comparison with mediastinal activity) was used to interpret ^{18}F-FDG uptake within the primary lesions. The degree of ^{18}F-FDG uptake in the primary tumor was correlated with the incidence of intratumoral lymphatic vessel invasion and lymph node involvement. Multivariate analysis was performed with logistic multivariate analysis to assess the joint effects and interactions of the variables (age, sex, tumor size, histology, and ^{18}F-FDG uptake) on intratumoral lymphatic vessel invasion and lymph node involvement. **Results:** Intratumoral lymphatic vessel invasion and lymph node involvement were found in 7.1% and 5.9%, respectively, of the patients classified in the low-grade group, and in 14.3% and 10.0%, respectively, of the patients classified in the moderate-grade group. In contrast, of the patients classified in the group with high ^{18}F-FDG uptake, intratumoral lymphatic vessel invasion and lymph node involvement were found in 39.7% and 38.9%, respectively. Multivariate analysis showed that only ^{18}F-FDG uptake was a significant factor for intratumoral lymphatic vessel invasion and that tumor size and ^{18}F-FDG uptake were significant factors for lymph node involvement. Of the patients in the high-grade group whose tumors were classified as ≥3 cm in size, lymph node involvement was found in 51.5%. In contrast, of the patients in the low- to moderate-grade group whose tumors were classified as <3 cm in size, lymph node involvement was found in only 9.1% ($P < 0.0001$). **Conclusion:** Patients with a low to moderate ^{18}F-FDG uptake in the primary lesion had a significantly lower risk of concurrent intratumoral lymphatic vessel invasion and nodal involvement than did patients with a high ^{18}F-FDG uptake. In patients with non-small cell lung cancer, ^{18}F-FDG uptake by the primary tumor is a strong predictor of intratumoral lymphatic vessel invasion and lymph node metastasis.

Key Words: lung cancer; ^{18}F-FDG PET; nodal involvement

J Nucl Med 2005; 46:267–273

Lymph node involvement is an important prognostic factor in lung cancer without distant metastases (*1*). Patients without metastatic lymph nodes, or with only intrapulmonary or hilar lymph nodes, are generally considered candidates for straightforward resection. Intratumoral lymphatic vessel invasion is also important in the evaluation of lung cancer, because intratumoral lymphatic vessel invasion reflects tumor aggressiveness and is directly associated with lymph node involvement. Patients with intratumoral lymphatic vessel invasion had recurrence of the disease, and died earlier, than did those without (*2*). Thus, intratumoral

Received Apr. 5, 2004; revision accepted Sep. 17, 2004.

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lymphatic vessel invasion was also associated with a poor prognosis (*3,4*).

Both intratumoral lymphatic vessel invasion and lymph node involvement are important factors in the planning of therapeutic strategies, particularly limited surgical resection in patients with non-small cell lung cancer (*5*). Ichinose et al. (*5*) reported that 44% of tumors showed lymphatic vessel invasion in patients with resected non-small cell lung cancer classified as pathologic stage I located at the periphery of the lung. If we could select patients with tumors without intratumoral lymphatic vessel invasion and lymph node involvement, limited resection might successfully be performed without local recurrence (*5*).

Matsuguma et al. (*6*) reported that the area of ground-glass opacity on thin-section CT scans is a strong predictor of intratumoral lymphatic vessel invasion and lymph node metastasis in patients with clinical T1 N0 M0 adenocarcinoma and thus could be a useful index for planning a limited surgical resection for these patients. This excellent strategy is, however, applicable only to patients with lung adenocarcinoma.

^{18}F-FDG uptake within the primary lesion has been shown to correlate with aggressiveness (*7*) and survival (*8*) on PET studies of patients with non-small cell lung cancer. The more metabolically active the tumor, the more aggressive it is, and the worse the outcome. Recently, Vesselle et al. (*9*) reported that the metabolic activity of the primary tumor and tumor size are important variables in ^{18}F-FDG PET interpretation for non-small cell lung cancer, as they affect the likelihood of malignant involvement in nodes. However, the relationship between the metabolic activity of the primary tumor and intratumoral lymphatic vessel invasion is unknown.

The aim of this study was to determine whether a correlation exists among the incidence of intratumoral lymphatic vessel invasion, nodal involvement, and ^{18}F-FDG uptake in primary lung cancer and to determine whether ^{18}F-FDG uptake by primary tumor is a predictor of intratumoral lymphatic vessel invasion and lymph node metastasis in patients with non-small cell lung cancer. We conducted a multicenter study to increase the sample size and to decrease bias.

MATERIALS AND METHODS

Patient Preparation

In this retrospective study, we included 132 patients who were referred for PET for preoperative staging of their suspected or proven lung cancer. None of the patients had received prior treatment. All patients underwent CT of the chest within 4 wk of the PET study for the staging of lung cancer. All 132 patients were considered to be potential candidates for surgical resection. Seventy-six men and 56 women (age range, 42–84 y) were enrolled in this study. All patients underwent sampling of multiple mediastinal lymph nodes on thoracotomy within 4 wk after the PET study. Written informed consent was obtained from all patients.

Imaging Protocol

In this multicenter study, PET was performed with 3 types of dedicated PET camera, either the Headtome IV (Shimazu) (n = 62), at Kanazawa Cardiovascular Hospital; the Advance (General Electric Medical Systems) (n = 56), at the Medical and Pharmacologic Research Center Foundation; or the ECAT HR (Siemens/CTI) (n = 14), at the National Institute for Longevity Sciences. All patients fasted for 6 h before the scanning. Blood (1 mL) was drawn for estimation of baseline blood glucose levels, and the data were recorded. ^{18}F-FDG was administered intravenously. The average injected dose of ^{18}F-FDG was 370 MBq. After a 40- to 50-min uptake period, an emission scan was acquired. Two-dimensional acquisition was used at 2 of the PET centers (Kanazawa Cardiovascular Hospital and the Medical and Pharmacologic Research Center Foundation), and 3-dimensional acquisition was used at the third PET center (National Institute for Longevity Sciences). Transmission scans of all subjects were obtained for attenuation correction. At 2 of the PET centers (Kanazawa Cardiovascular Hospital and National Institute for Longevity Sciences), filtered backprojection with measured attenuation correction was used for reconstruction. At the third PET center (the Medical and Pharmacologic Research Center Foundation), iterative reconstruction with segmented attenuation correction was used, applying the expectation maximization algorithm with ordered subsets (28 subsets and 2 iterations).

Data Analysis

^{18}F-FDG accumulation within the primary lung tumor on the attenuation- and decay-corrected images was graded independently. A 3-point visual scoring system (low, moderate, or high grade) was used to interpret the ^{18}F-FDG uptake within the primary lesions: low grade = less than mediastinal blood-pool activity, moderate grade = equal to mediastinal blood-pool activity, and high grade = much greater than mediastinal blood-pool activity. This is a modified method of Lowe et al. (*10*) and Vansteenkiste et al. (*1*).

Histologic Study

The nodal status was determined for each patient on the basis of the thoracotomy findings. Ipsilateral hilar and mediastinal sampling was performed during the thoracotomy. The surgically resected specimens were routinely fixed in 10% formalin and embedded in paraffin. All 5-mm sections were stained with hematoxylin–eosin and then examined by light microscopy for histology. The histologic sections of the primary tumor were also studied for evidence of intratumoral lymphatic vessel invasion using hematoxylin–eosin staining. To distinguish intratumoral lymphatic vessel invasion from blood vessel invasion, an elastica van Gieson's stain was also used. In 96 patients, the existence of intratumoral lymphatic vessel invasion in the primary tumor was confirmed histopathologically.

The degree of tracer uptake in the primary lesion was correlated with the existence of pathologic intratumoral lymphatic vessel invasion and nodal staging.

Statistical Analysis

Statistical analysis was performed using the SPSS software system (version 10.0; SPSS Inc.) for Windows (Microsoft). Univariate analysis was used to analyze the associations among the pathologic variables and age (≤60 y or >60 y), sex, tumor size (≤3 cm or >3 cm), histology (adenocarcinoma or nonadenocarci-

TABLE 1
Patient and Tumor Characteristics

Variable	*n*	%
Age		
≤60 y	34	25.8
>60 y	98	74.2
Sex		
Male	76	57.6
Female	56	42.4
Tumor size		
<3 cm	77	58.3
≥3 cm	55	41.7
Histology		
Adenocarcinoma	103	78.0
Squamous cell carcinoma	21	15.9
Adenosquamous cell carcinoma	5	3.8
Large cell carcinoma	2	1.5
Carcinoid	1	0.8
Pathologic N stage		
pN0	92	69.7
pN1	14	10.6
pN2	26	19.7
Pathologic stage		
IA	64	48.5
IB	24	18.2
IIA	3	2.3
IIB	10	7.6
IIIA	26	19.7
IIIB	5	3.8
Intratumoral lymphatic vessel invasion		
Negative	66	68.8
Positive	30	31.2
^{18}F-FDG uptake		
Low	17	12.9
Moderate	20	15.1
High	95	72.0

noma), and ^{18}F-FDG uptake by the primary tumor (low to moderate grade or high grade). Multivariate analysis was performed with logistic multivariate analysis to assess the joint effects and interactions of the variables on intratumoral lymphatic vessel invasion and lymph node involvement. Cox proportional-hazards regression was used to calculate the multivariate-adjusted relative risks of incidence and the corresponding 95% confidence intervals for baseline ^{18}F-FDG uptake categories. The multivariate-adjusted relative risks were adjusted for sex, age, lesion size, and histology.

RESULTS

In the diagnosis of the N stage, the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value for ^{18}F-FDG PET were 76.9%, 89.1%, 85.5%, 75.0%, and 90.1%, respectively.

Tumor characteristics are shown in Table 1. The tumor size was measured pathologically. The diameters of the primary lung tumors ranged from 0.8 to 12.0 cm. Fifty-five (41.7%) of the lung tumors were ≥3 cm in diameter (Table 1). Of the remaining 77 lung tumors (58.3%), 48 (36.4%) were 2.0–2.9 cm and 29 (21.9%) were <2 cm. Regarding the degree of ^{18}F-FDG uptake in the primary lesions, 17 tumors (12.9%) were classified as low grade, 20 (15.1%) as moderate grade, and 95 (72.0%) as high grade (Table 1).

Intratumoral lymphatic vessel invasion and lymph node involvement were found in 7.1% and 5.9%, respectively, of the patients classified in the low-grade group and in 14.3% and 10.0%, respectively, of the patients classified in the moderate-grade group (Table 2). In the patients classified in the low- and moderate-grade groups, the lymph node involvement was microscopic. In contrast, of the patients classified in the group with high ^{18}F-FDG uptake, intratumoral lymphatic vessel invasion and lymph node involvement were found in 39.7% and 38.9%, respectively (Table 2). Thus, patients with a low ^{18}F-FDG uptake in the primary lesion had a significantly decreased risk of concurrent intratumoral lymphatic vessel invasion and lymph node metastasis than did patients with a high ^{18}F-FDG uptake (P = 0.028 and P = 0.010, respectively) (Table 2).

In univariate analysis, sex and ^{18}F-FDG uptake (low- to moderate-grade group or high-grade group) were factors significantly associated with intratumoral lymphatic vessel invasion (Table 3). However, in multivariate analysis, only ^{18}F-FDG uptake was significantly associated with intratumoral lymphatic vessel invasion (Table 3).

In univariate analysis, sex, tumor size (≤3 cm or >3 cm), histology (adenocarcinoma or nonadenocarcinoma), and ^{18}F-FDG uptake (low- to moderate-grade group or high-grade group) were factors significantly associated with lymph node involvement (Table 4). However, in multivariate analysis, tumor size and ^{18}F-FDG uptake were factors significantly associated with lymph node involvement (Ta-

TABLE 2
Risk for Intratumoral Lymphatic Vessel Invasion and Lymph Node Involvement Based on ^{18}F-FDG Uptake

Uptake	Intratumoral lymphatic vessel invasion			Significance (vs. low)	Lymph node involvement			Significance (vs. low)
	−	+	%		−	+	%	
Low	13	1	7.1		16	1	5.9	
Moderate	12	2	14.3	NS	18	2	10.0	NS
High	41	27	39.7	P = 0.028	58	37	38.9	P = 0.010

− = negative; + = positive; NS = not statistically significant.

TABLE 3
Univariate and Multivariate Analysis of Factors Associated with Intratumoral Lymphatic Vessel Invasion

Variable	Intratumoral lymphatic vessel invasion			Univariate		Multivariate	
	−	+	%	RR (95% CI)	Significance	RR (95% CI)	Significance
Age							
≤60 y	15	9	37.5	0.69 (0.26–1.81)	NS	0.32 (0.08–1.23)	NS
>60 y	51	21	29.2				
Sex							
Male	28	21	42.9	3.17 (1.26–7.95)	$P = 0.014$	2.40 (0.86–6.71)	NS
Female	38	9	19.1				
Tumor size							
<3 cm	42	13	26.3	2.29 (0.95–5.51)	NS	1.39 (0.49–3.98)	NS
≥3 cm	24	17	41.5				
Histology							
Adenocarcinoma	52	24	31.6	1.08 (0.37–3.14)	NS	1.79 (0.52–6.13)	NS
Nonadenocarcinoma	14	6	30.0				
^{18}F-FDG uptake							
Low–moderate	25	3	10.7	5.49 (1.51–20.0)	$P = 0.010$	7.43 (1.51–36.5)	$P = 0.014$
High	41	27	39.7				

− = negative; + = positive; RR = relative risk; CI = confidence interval; NS = not statistically significant.

ble 4). Of the patients in the high-grade group whose tumors were classified as ≥3 cm in size, lymph node involvement was found in 51.5% (Table 5). In contrast, of the patients in the low- to moderate-grade group whose tumors were classified as <3 cm in size, lymph node involvement was found in only 9.1% ($P < 0.0001$) (Table 5).

The multivariate-adjusted relative risks for the incidence of intratumoral lymphatic vessel invasion and lymph node metastases were 7.43 and 4.46 for the low- to moderate-grade group and high-grade group, respectively (Tables 3 and 4).

Thus, a significant correlation exists among the incidence of intratumoral lymphatic vessel invasion, nodal involvement, and ^{18}F-FDG uptake in primary lung cancer. Patients with a low to moderate ^{18}F-FDG uptake in the primary lesion had a significantly decreased risk of concurrent intratumoral lymphatic vessel invasion and lymph node metastasis than did patients with high ^{18}F-FDG uptake.

TABLE 4
Univariate and Multivariate Analysis of Factors Associated with Lymph Node Involvement

Variable	Lymph node involvement			Univariate		Multivariate	
	−	+	%	RR (95% CI)	Significance	RR (95% CI)	Significance
Age							
≤60 y	25	9	26.5	1.28 (0.54–3.08)	NS	0.55 (0.19–1.60)	NS
>60 y	67	31	31.6				
Sex							
Male	47	29	38.2	2.52 (1.13–5.65)	$P = 0.024$	1.42 (0.57–3.49)	NS
Female	45	11	19.6				
Tumor size							
<3 cm	63	14	18.2	4.03 (1.84–8.84)	$P < 0.0001$	2.51 (1.05–5.99)	$P = 0.037$
≥3 cm	29	26	47.3				
Histology							
Adenocarcinoma	78	26	25.0	0.33 (0.14–0.79)	$P = 0.013$	0.49 (0.18–1.32)	NS
Nonadenocarcinoma	14	14	50.0				
^{18}F-FDG uptake							
Low–moderate	34	3	8.1	7.23 (2.07–25.2)	$P = 0.002$	4.46 (1.14–17.5)	$P = 0.032$
High	58	37	38.9				

− = negative; + = positive; RR = relative risk; CI = confidence interval; NS = not statistically significant.

TABLE 5
Risk for Lymph Node Involvement Based on Tumor Size and ^{18}F-FDG Uptake

Group	Tumor size		^{18}F-FDG uptake	Lymph node involvement			Significance (vs. a)
				−	+	%	
a	≥3 cm	and	High	25	26	51.5	
b	≥3 cm	and	Low–moderate	4	0	0	NS
c	<3 cm	and	High	33	11	25.0	0.012
d	<3 cm	and	Low–moderate	30	3	9.1	$P < 0.0001$

− = negative; + = positive; NS = not statistically significant.
c vs. d: $P = 0.084$.

DISCUSSION

The principal finding of this study is that a significant correlation exists among the incidence of intratumoral lymphatic vessel invasion, nodal involvement, and ^{18}F-FDG uptake by the primary tumor. This study indicated that low to moderate ^{18}F-FDG uptake by the primary tumor led to a significantly and independently decreased risk of intratumoral lymphatic vessel invasion and lymph node metastases. Patients whose lung cancer showed high ^{18}F-FDG uptake had a 4.46- to 7.43-fold higher risk of intratumoral lymphatic vessel invasion and lymph node metastases after multivariate adjustment than did patients whose lung cancer showed low to moderate ^{18}F-FDG uptake. These phenomena can be explained by the fact that the greater the ^{18}F-FDG uptake is, the higher is the malignant grade. ^{18}F-FDG is avidly taken up by tumor cells because cancer tissue consumes a large amount of glucose as an energy source. ^{18}F-FDG uptake reflected cell dedifferentiation (*11*), proliferative potential (*12*), aggressiveness (*7*), and prognosis (*8*) in patients with lung adenocarcinoma.

The Lung Cancer Study Group reported the results of a prospective randomized trial comparing limited resection with lobectomy for the management of patients with T1 N0 (*13*). A total of 247 patients were eligible for analysis. The limited-resection group had a significantly higher local recurrence rate than did the lobectomy group. The Lung Cancer Study Group therefore concluded that limited resection should not be recommended as the resection of choice for patients with T1 N0 disease. Ichinose et al. (*5*) reported that 44% of tumors showed intratumoral lymphatic vessel invasion in patients with resected non-small cell lung tumors classified as pathologic stage I located at the periphery of the lung. They speculated that this was the main reason that the limited-resection group had a higher local recurrence rate in the Lung Cancer Study Group trial. Others reported that intratumoral lymphatic vessel invasion correlated with a poor prognosis in patients with non-small cell lung cancer (*2–4*). This finding suggested that intratumoral lymphatic vessel invasion reflected tumor aggressiveness. Therefore, if we could select patients with tumors without lymphatic invasion, limited resection might successfully be performed without local recurrence. In our series, tumors with a low to moderate ^{18}F-FDG uptake had a low incidence of intratumoral lymphatic vessel invasion, and multivariate analysis showed that only ^{18}F-FDG uptake was a significant factor for intratumoral lymphatic vessel invasion. Among patients with non-small cell lung cancer, ^{18}F-FDG uptake by lung cancer was related to the aggressiveness of the tumor, independent of tumor size. This finding suggests that ^{18}F-FDG uptake is an important factor in the planning of appropriate surgical treatment, especially less invasive surgical intervention. Limited resection might successfully be performed without recurrence on patients whose lung cancer shows low ^{18}F-FDG uptake.

Several studies have shown that ^{18}F-FDG PET is superior to CT in the staging of mediastinal disease, with a reported sensitivity and specificity of 67%–91% and 82%–96%, respectively (*14*). Although ^{18}F-FDG PET may accurately establish lymph node staging in lung cancer patients, there are drawbacks to PET staging. ^{18}F-FDG PET staging of the mediastinum remains challenging because of the decreased specificity caused by ^{18}F-FDG accumulation in inflamed lymph nodes and silicotic nodes, which can lead to a false-positive interpretation (*15*). Conversely, the lack of sufficient ^{18}F-FDG in lymph nodes with minimal metabolic involvement can result in a false-negative interpretation. Gupta et al. (*16*) reported that the false-negative rate was 8% and the false-positive rate was 13%. Vansteenkiste et al. (*1*) demonstrated that the range of ^{18}F-FDG uptake overlaps significantly for both inflammatory and malignant nodes. Therefore, mediastinoscopy is still used for decisions on resectability status, as it depends on the presence of N2/N3 disease.

Recently, Vesselle et al. (*9*) reported that ^{18}F-FDG uptake by the primary tumor and tumor size are important variables in ^{18}F-FDG PET interpretation for non-small cell lung cancer, as they affect the likelihood of malignant involvement in hypermetabolic nodes. The size of a non-small cell lung tumor significantly influenced the incidence of malignant mediastinal adenopathy, with larger tumors being more likely to have nodal involvement than smaller tumors (*9*). These data appear to agree with many previous studies that generally showed a higher risk with increased T stage (*17,18*). The larger the primary tumor, the greater is the

likelihood that it has spread to the lymph nodes (*17,18*). ^{18}F-FDG uptake of the primary tumor is a variable that depends on the aggressiveness of lung adenocarcinoma (*7*). In our current study, ^{18}F-FDG uptake and tumor size were found to be significant factors for lymph node involvement in both univariate and multivariate analyses. Of the patients in the high-grade group whose tumors were classified as ≥3 cm in size, lymph node involvement was found in 51.5%; in contrast, of the patients in the low- to moderate-grade group whose tumors were classified as <3 cm, lymph node involvement was found in only 9.1% ($P < 0.0001$). These phenomena support the results of Vesselle et al. (*9*) and suggest that a small lesion with a low ^{18}F-FDG uptake may obviate mediastinoscopy.

This study had several limitations. First, a visual grading system was used to interpret ^{18}F-FDG uptake within the primary lesions, and the SUV threshold was not used. We selected a multicenter study to increase the sample size and to decrease bias, but the disadvantage of this strategy was the difficulty of obtaining unity in methodology. This was the main reason that the data were not analyzed using SUV threshold in the current study. SUV measurements are affected by the applied methods for both image reconstruction and attenuation correction (*19,20*). Iterative reconstruction with segmented attenuation correction resulted in significantly higher mean SUVs and maximum SUVs than those resulting from filtered backprojection with measured attenuation correction (*19,20*). This finding should be considered when serial PET studies are performed on cancer patients. Moreover, if SUV is used for tissue characterization, different cutoff values should be applied, depending on the chosen method of acquisition, image reconstruction, and attenuation correction. In the current multicenter study, filtered backprojection with measured attenuation correction was used for reconstruction at 2 of the PET centers. However, iterative reconstruction with segmented attenuation correction was used at the third PET center. In addition, the use of 3-dimensional acquisition rather than 2-dimensional acquisition also could potentially influence the accuracy of SUV measurements (*20*). In the current multicenter study, 2-dimensional acquisition was used at 2 of the PET centers, and 3-dimensional acquisition was used at the third PET center. Finally, it is uncertain whether and to what degree the geometry and specifications of different PET tomographs from different manufacturers might affect the accuracy and reproducibility of SUV measurements (*20*). In the current multicenter study, PET was performed with 3 types of dedicated PET cameras. Therefore, the SUV threshold was not adequate in the current multicenter study, and the data were analyzed using a visual grading system. Lowe et al. (*10*) reported that SUV and visual evaluations are equally accurate methods of ^{18}F-FDG PET data analysis in the differentiation of malignant from benign focal pulmonary abnormalities. This study showed that ^{18}F-FDG uptake in the mediastinum can be used as an accurate reference for visual interpretation. The researchers evaluated lesion uptake relative to mediastinal uptake to provide a distinct reference for assessment. Lesion uptake greater than mediastinal uptake most likely represents a malignant process. In the current study, a modified method of Lowe et al. was used to interpret the ^{18}F-FDG uptake within the primary lesions. Vansteenkiste et al. (*1*) also reported that a visual scale is as accurate as the use of an SUV threshold in distinguishing between benign and malignant lymph nodes. Therefore, in this multicenter study, a visual scale was found to be more adequate than the SUV threshold.

Second, the area of ground-glass opacity on thin-section CT scans was reported to be a strong predictor of intratumoral lymphatic vessel invasion and lymph node metastasis in patients with clinical T1 N0 M0 adenocarcinoma (*6*) and thus could be a useful index for planning a limited surgical resection for these patients. It is necessary to compare the ^{18}F-FDG uptake of primary tumors on PET with the area of ground-glass opacity in the primary tumor on CT as predictors of intratumoral lymphatic vessel invasion and lymph node metastasis.

In our series, tumors with a low to moderate ^{18}F-FDG uptake had a low incidence of intratumoral lymphatic vessel invasion, and small lesions (<3 cm) with a low to moderate ^{18}F-FDG uptake had a low incidence of lymph node involvement. These results suggest that limited resection might successfully be performed without recurrence in patients whose lung cancer shows low ^{18}F-FDG uptake and that a small lesion with a low ^{18}F-FDG uptake may obviate mediastinoscopy. Further studies will be necessary to clarify this issue.

CONCLUSION

A significant correlation exists among the incidence of intratumoral lymphatic vessel invasion, nodal involvement, and ^{18}F-FDG uptake by the primary tumor in patients with non-small cell lung cancer. Patients with a low to moderate ^{18}F-FDG uptake in the primary lesion had a significantly decreased risk of concurrent intratumoral lymphatic vessel invasion and lymph node metastasis than did those with a high ^{18}F-FDG uptake. In patients with non-small cell lung cancer, ^{18}F-FDG uptake by the primary tumor is a strong predictor of intratumoral lymphatic vessel invasion and lymph node metastasis.

ACKNOWLEDGMENTS

This work was supported by a grant for collaborative research from Kanazawa Medical University (C2003-2); by a grant-in-aid for cancer research (12-4,16-5) from the Ministry of Health and Welfare, Japan; and by a grant-in-aid (50189750) for scientific research from the Ministry of Education.

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J Nucl Med. 2005;46:267-273.

The Journal of Nuclear Medicine is published monthly.
SNMMI | Society of Nuclear Medicine and Molecular Imaging
1850 Samuel Morse Drive, Reston, VA 20190.
(Print ISSN: 0161-5505, Online ISSN: 2159-662X)

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