Eur Radiol (2012) 22:1556–1563
DOI 10.1007/s00330-012-2395-4

CHEST

Accuracy and predictive features of FDG-PET/CT and CT for diagnosis of lymph node metastasis of T1 non-small-cell lung cancer manifesting as a subsolid nodule

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Received: 3 November 2011 / Revised: 13 December 2011 / Accepted: 21 December 2011 / Published online: 24 February 2012

Abstract
Objectives To retrospectively evaluate the diagnostic accuracy and predictive features of F-18 fluorodeoxyglucose positron emission tomography/ computed tomography (FDG-PET/CT) and CT in lymph node (LN) staging of T1 non-small-cell lung cancers (NSCLCs) manifesting as subsolid nodules.

Methods From January 2005 to May 2011, 160 patients with pathologically proven T1 subsolid NSCLCs with LN staging were included in this study. Diagnostic accuracies of FDG-PET/CT and CT for LN staging were evaluated. Maximum standardised uptake value (SUVmax) and CT features of primary tumours were evaluated to investigate predictive factors for LN metastasis.
Results LN metastases were found in nine of the 160 patients (5.6%). No LN metastasis was present in patients with a solid proportion ≤50%. Sensitivity, specificity and accuracy of FDG-PET/CT for LN staging on a per-patient basis were 11.1%, 86.1% and 81.9%; those of CT were 11.1%, 96.7% and 91.9%. Among patients with a solid proportion >50%, there were significant differences in SUVmax, solid portion size, solid proportion and lesion location between patients with and without LN metastasis. Multivariate analysis revealed that higher SUVmax, a larger solid proportion and central location were independent predictors of LN metastasis.
Conclusions FDG-PET/CT adds little value to CT in the lymph node staging of T1 subsolid NSCLCs.
Key Points
- *Lymph node (LN) metastases are important in non-small-cell lung cancer (NSCLC).*
- *Positron emission tomography (PET) helps to stage solid NSCLCs.*
- *FDG-PET/CT adds little to the LN staging of T1 subsolid NSCLCs.*
- *No LN metastasis in patients with a solid proportion ≤50%.*
- *LN metastasis is more common in solid and/or centrally sited tumours.*

Keywords NSCLC · PET/CT · CT · Lymph node · Staging

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Introduction

In patients with non-small-cell lung cancer (NSCLC), accurate lymph node (LN) staging is one of the most important factors in choices of treatment and determination of patient prognosis [1, 2]. In T1 NSCLCs, LN staging can determine whether the patient will undergo surgery or treatment using more than one technique [1].

F-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT), which provides morphological and metabolic data of malignancy, has been well established as the non-invasive investigation of choice for LN staging as well as for the assessment of the primary tumour and distant metastasis in NSCLC [3, 4]. Recent studies [5, 6] have shown that FDG-PET/CT can provide high specificity and positive predictive value in LN staging even in T1 NSCLC. However, these previous studies [3–6] on PET/CT for LN staging have been performed without considering the characteristics of the primary tumours, such as their internal attenuation.

The internal characteristics of the primary tumour, such as solid or subsolid features, have recently garnered attention as they have been suggested to be helpful in predicting the cancer's biological and clinical behaviour as well as patients' prognosis [7–12]. Lung cancers manifesting as subsolid nodules that contain an area of ground-glass opacity (GGO) within the nodule on CT [7] are typically confirmed to be bronchioloalveolar cell carcinoma (BAC) or adenocarcinoma with BAC components [7–10, 13], which exhibit very unique biological and clinical characteristics, such as a very slow growth rate, a low probability of LN or distant metastasis, and excellent prognosis [14–16]. In addition, on FDG-PET/CT, subsolid lung cancers have been reported to show lower FDG uptake than solid lung cancers [17].

In this context, the diagnostic value of FDG-PET/CT for subsolid lung cancers may be different from that for solid lung cancers regarding lung cancer staging, and thus should be more clearly evaluated as the prevalence of these lung cancers is not uncommon [18]. To our knowledge, however, there have been no studies dealing with this topic and no reports of comparisons between FDG-PET/CT and chest CT for LN metastasis in subsolid lung cancers.

Therefore, the purpose of our study was to retrospectively evaluate the diagnostic accuracy of FDG-PET/CT for LN staging in T1 subsolid NSCLCs, and to compare the accuracies of FDG-PET/CT and CT in the LN staging of T1 subsolid NSCLCs. We also investigated the predictive factors of FDG-PET/CT and CT for LN metastasis in T1 subsolid NSCLCs.

Materials and methods

This retrospective study was approved by the institutional review board of Seoul National University Hospital, which waived the requirement for patients' informed consent.

Study population

From January 2005 to May 2011, among 663 patients pathologically confirmed to have T1 NSCLCs according to the American Joint Committee on Cancer staging system [19], the study population was determined based on the following criteria:

1. Available FDG-PET/CT and thin-section chest CT (slice thickness ≤2.5 mm) before treatment.
2. An interval of no more than 2 months between FDG-PET/CT, CT and treatment.
3. NSCLCs appearing as subsolid nodules on CT with LN staging.
4. No previous chemotherapy or radiotherapy.
5. No previous or concurrent malignancy.

Out of these 663 patients, 582 patients had available FDG-PET/CT or thin-section chest CT images before treatment. Among them, 172 patients had NSCLCs manifesting as subsolid nodules on CT with LN staging. Nodules were defined as subsolid by two radiologists (H.J.L. and S.M.L., with 12 and 4 years' experience in chest CT respectively) in consensus when a nodule contained GGO within the nodule on CT [7]. Twelve patients were excluded for the following reasons; seven patients had FDG-PET/CT examinations in which the SUVmax (maximum standardised uptake value) could not be calculated, and five patients had a medical history of cancer (concurrent hepatocellular carcinomas in two, previous breast cancer in two and previous colon cancer in one). Finally, the study population comprised 160 patients with subsolid NSCLCs (Table 1). The mean intervals between PET/CT and surgery and between CT and surgery were 11.8 days (range, 1–51 days; median, 9 days) and 13.1 days (range, 0–58 days; median, 10 days) respectively.

Image acquisition

PET/CT imaging

Before intravenous administration of ^{18}F-FDG (5.2 MBq/kg of body weight), all patients fasted for at least 6 h. After administration, patients rested for 60 min before imaging. Thereafter, whole-body PET images were acquired with the conventional protocol of ^{18}F-FDG PET using a Gemini (Philips Medical Systems, Cleveland, OH, USA) equipped

Table 1 Patient characteristics

Characteristics	
Age (years) at diagnosis	
Mean	60.0
Range	29–80
Sex (male:female)	62:98
Tumour size (mm)	
Mean	18.0
Range	7–30
Internal characteristics of tumour (PSN:NS)	144:16
Histology	
BAC	25
AD with BAC	55
AD with mixed type	80

Except where indicated otherwise, data are numbers of patients

PSN part-solid nodule, *NS* non-solid nodule, *AD* adenocarcinoma, *BAC* bronchiolo-alveolar cell carcinoma

with a two-slice CT or a Biograph 40 (Siemens Medical Solutions, Knoxville, TN, USA). The resulting PET and CT images were coregistered on hardware.

Low-dose CT was performed from the skull base to the pelvis using a tube voltage of 120 kVp, 50 mA, tube-rotation time of 0.75 s per rotation and a pitch of 1.5. CT images were reconstructed with a 6.5-mm (for Gemini) or 5-mm thickness (for Biograph 40). Immediately after CT, emission PET images were acquired for 2 min per bed using the three-dimensional acquisition mode. PET data were reconstructed using iterative reconstruction algorithms.

Chest CT imaging

Chest CT was performed using various devices; Somatom Definition, Sensation-16 (Siemens Medical Solutions, Forchheim, Germany), Brilliance-64 (Phillips Medical Systems, Netherlands) and Lightspeed Ultra (GE Medical Systems, Milwaukee, WI, USA) with 120 kVp, 150–200 mAs, pitch of 0.875–1.5 and collimation of 1–2.5 mm. Images were reconstructed using the high-frequency algorithm with a thickness of 1–2.5 mm. In all patients, CT data were acquired with the patient supine and breathing suspended at full inspiration.

Image analysis

PET/CT imaging

Two nuclear medicine physicians (J.C.P. and H.J.I., with 9 and 3 years' experience in PET/CT respectively) evaluated all FDG-PET/CT images, and all decisions were reached in consensus. LN stations were evaluated and allocated into one of ten groups, according to the LN map definition for lung cancer staging proposed by Mountain and Dresler [20]. All LNs in the thorax and extrathoracic regions with abnormal FDG uptake (SUVmax >3.5) were considered positive, unless they showed high attenuation (>70 HU) or benign calcification (central nodular, laminated, popcorn or diffuse) on unenhanced CT images [4, 5, 21]. SUVmax of the primary lesions was also calculated. SUVmax threshold cut-off of 3.5 was determined according to the previous experience of our institute and other reports in a tuberculosis-endemic area [4].

Chest CT imaging

Two radiologists (C.M.P. and J.M.G. with 10 and 18 years' experience in chest CT respectively) evaluated CTs in consensus. LN assessment was based on LN size with a short-axis diameter of >10 mm defined as abnormal. The presence of necrosis within LNs was considered a sign of malignancy, regardless of LN size. Hilar LNs were considered positive for malignancy when their greatest diameter exceeded 10 mm [22]. If mediastinal or hilar nodes contained nodular or laminated calcification, they were regarded as benign, irrespective of their sizes [5].

To investigate predictive factors of LN metastasis, CT findings of each primary tumour were analysed as follows: lesion size, margin (spiculated, not spiculated), solid portion size, solid proportion, presence of pleural retraction, and location (central, peripheral). The solid proportion of the lesion was calculated by dividing the greatest diameter of the solid portion by the greatest diameter of the primary lesion. The primary lesion was determined as having a central location when it was located in the inner one third of the lung parenchyma.

Reference standard

Lymph node staging in this study was determined using the pathological results from thoracotomy only (n=32) and thoracotomy with mediastinoscopy (n=128). One hundred and fifty-four patients underwent lobectomy and six patients underwent wedge resection. There were no patients with positive results among 14 patients who underwent ultrasound-guided biopsy such as neck, oesophageal and endobronchial ultrasound.

During thoracotomy, all visible and palpable lymph nodes accessible in the mediastinum were dissected. When preoperative imaging results suggested possible LN metastasis, they were also evaluated during mediastinoscopy or thoracotomy. Contralateral hilar LN metastasis was determined using clinical and follow-up imaging studies.

Statistical analysis

Diagnostic values of FDG-PET/CT and chest CT for total and mediastinal LN staging on a per-patient basis and per-nodal-station basis were calculated. To compare the diagnostic values of the two investigations in total and mediastinal nodal staging, McNemar's test was used.

To evaluate the predictive factors for LN metastasis, statistical differences between patients with and without LN metastasis were analysed using the Mann–Whitney test and Fisher's exact test as appropriate. To identify significant predictors of LN metastasis in T1 subsolid NSCLCs, multivariate logistic regression analysis was conducted. Characteristics with a P value less than 0.10 through univariate analysis were used as input variables for multivariate logistic regression analysis. In multivariate analysis, a backward stepwise selection mode was employed with iterative entry of variables based on test results. The removal of variables was based on likelihood ratio statistics with a probability of 0.10.

Statistical analyses were performed using SPSS version 18.0 (SPSS, Chicago, IL, USA). A P value <0.05 was considered to indicate statistical significance.

Results

Total LN metastases were found in nine patients (5.6%) and mediastinal LN metastasis was observed in six (3.8%; Table 2). The distribution of LN stages was N0 in 151 patients, N1 in three and N2 in six. All LN metastases were observed in patients with NSCLCs with a solid proportion >50%. FDG-PET/CT showed 21 patients with false-positive results (three N1, six N2 and 12 N3), and CT showed five patients with false-positive results (three N2 and two N3; Fig. 1). Among the 21 patients with false-positive results on PET/CT, 14 patients had lesions with a solid proportion >50% and seven patients had lesions with a solid proportion ≤50%. In the case of false-positive CT results, four patients had lesions with a solid proportion >50% and one patient had a solid proportion ≤50%.

Accuracy of nodal metastasis

Analysis on a per-patient basis

In total LN staging, the sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of FDG-PET/CT were 11.1%, 86.1%, 81.9%, 4.6% and 94.2% respectively, and those of CT were 11.1%, 96.7%, 91.9%, 16.7% and 96.7%. CT showed significantly higher accuracy than FDG-PET/CT (P<0.001).

In mediastinal LN staging, the sensitivity, specificity, accuracy, PPV and NPV of FDG-PET/CT were 16.7%, 89.6%, 86.9%, 5.9% and 96.5% respectively. Those of CT were 16.7%, 96.8%, 93.8%, 16.7% and 96.8%. CT showed significantly higher accuracy than FDG-PET/CT (P=0.012). Table 3 summarises the comparison between FDG-PET/CT and CT on a per-patient basis.

Table 2 Patients with nodal metastasis in stage T1 subsolid NSCLCs

Patient o.	Sex/age (years)	Histology	Tumour size (cm)	Solid proportion (%)	SUVmax of tumour	N stage	Location	LN size (mm)	SUVmax of LNs
1	Male/66	AD with BAC	2.0	90.9	1.8	1	11R	4	0
2	Male/50	AD with mixed	1.8	77.8	1.1	1	12L	Unidentified	0
3	Female/58	AD with mixed	3.0	93.3	3.0	1	11R	7	0
4	Female/54	AD with BAC	1.7	88.2	3.6	2	12R	Unidentified	0
							4R	6	1.7
5	Male/42	AD with BAC	2.3	77.8	6.7	2	12L	Unidentified	0
							5	3	0
6	Male/54	AD with mixed	1.5	90.5	6.7	2	5	12	5.3
							6	8	1.8
							10L	12	4.1
7	Female/66	AD with mixed	2.1	85.0	1.9	2	7	Unidentified	0
8	Male/68	AD with mixed	2.7	85.3	3.0	2	4L	9	0
							11L	6	0
9	Female/67	AD with mixed	1.4	85.7	3.5	2	2R	5	0
							4R	7	0

NSCLC non-small-cell lung cancer, *SUVmax* maximum standardised uptake value, *AD with BAC* adenocarcinoma with bronchiolo-alveolar cell carcinoma component, *AD with mixed* adenocarcinoma with mixed subtype, *LNs* lymph nodes, *R* right, *L* left

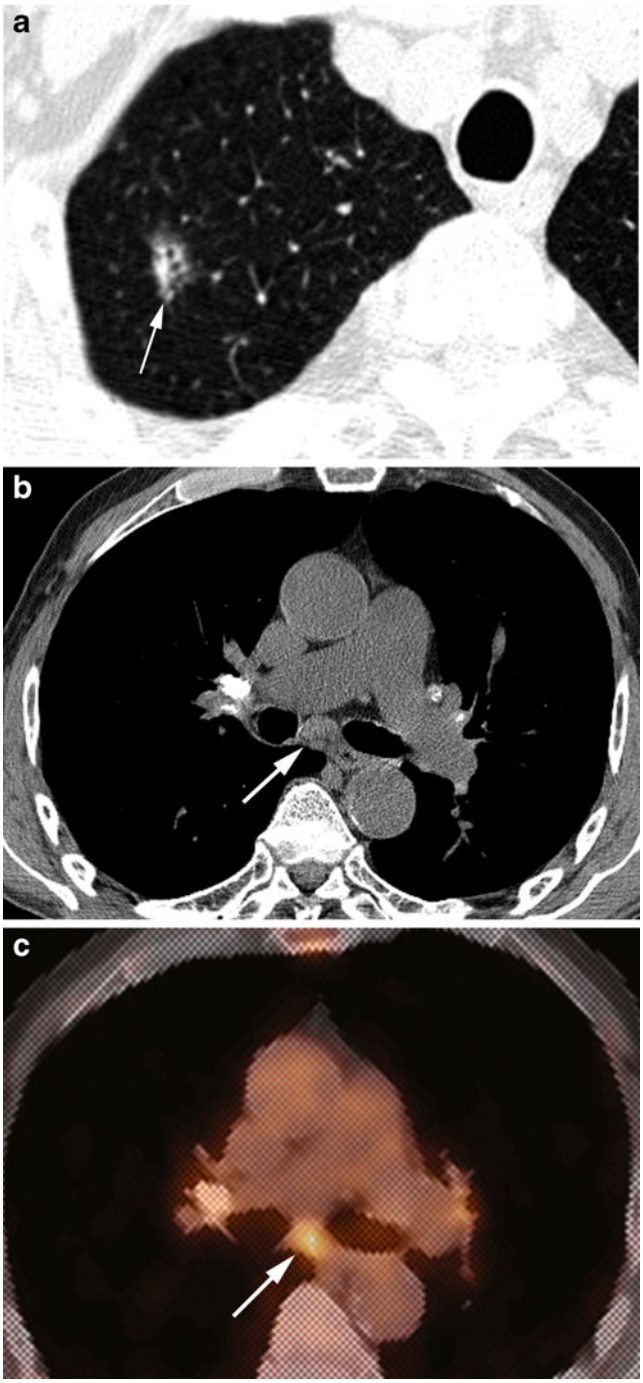

Fig. 1 Patient with N0 stage determined as N2 at thin-section CT and FDG-PET/CT. **a** Thin-section CT shows a 1.5-cm part-solid nodule (*arrow*) in the right upper lobe of a 73-year-old man. The SUVmax of the primary nodule was 2.5. **b** CT and **c** FDG-PET/CT showed a 12-mm subcarinal lymph node (LN) with an SUVmax of 3.9 (*arrow*). Pathological finding was an adenocarcinoma with no LN metastasis

Analysis on a per-nodal-station basis

The total number of evaluated LN stations was 756 and 15 LN stations showed positive results. In total LN staging, the sensitivity, specificity and accuracy of FDG-PET/CT were 13.3%, 94.2% and 92.6% respectively, and those of CT were 13.3%, 99.3% and 97.6%. CT showed higher diagnostic accuracy than FDG-PET/CT on a per-nodal-station basis with statistical significance ($P<0.001$).

In mediastinal LN staging, the total number of evaluated LN stations was 599 and 8 LN stations showed positive results. The sensitivity, specificity and accuracy of FDG-PET/CT were 12.5%, 95.9% and 94.8% respectively, and those of CT were 12.5%, 99.2% and 98.0%. CT showed higher diagnostic accuracy than FDG-PET/CT on a per-nodal-station basis with statistical significance ($P<0.001$). Table 4 summarises the comparison between FDG-PET/CT and CT on a per-nodal-station basis.

Predictive features for LN metastasis of T1 subsolid NSCLCs

As there were no LN metastases in patients with a solid proportion ≤50% ($n=83$), comparison between patients with and without LN metastasis was performed only in patients with a solid proportion >50% ($n=77$). The SUVmax of primary tumours in patients with LN metastasis was significantly higher in comparison with patients without LN metastasis (3.5±2.0 vs 2.3±1.4, $P=0.030$). The primary tumours in patients with LN metastasis showed significantly larger solid portion size and solid proportion in comparison with patients without LN metastasis ($P=0.039$, 0.013 respectively), and were more likely to be located centrally ($P=0.047$). Table 5 summarises the comparison of FDG-PET/CT and CT features in patients with and those without LN metastasis.

The SUVmax, solid portion size, solid proportion and lesion location of primary tumours were used as input variables for multivariate logistic regression analysis. Multivariate analysis revealed that SUVmax, solid proportion and lesion location were proven to be independent predictors of LN metastasis ($P=0.030$, 0.027, 0.011 respectively). Adjusted odds ratio of higher SUVmax, larger solid proportion and central location were 1.823, 1.150 and 17.902 respectively.

Discussion

In our study, total and mediastinal LN metastasis were found in 5.6% (nine out of 160) and 3.8% (six out of 160) of the study population. Previously, in T1 NSCLCs, mediastinal LN metastasis has been reported to be around 16–23% [5, 23–25], which is four- to six-times more frequent than that of the present study. One study by Matsuguma et al. [26], however, which included clinical T1 subsolid lung cancers, showed total and mediastinal LN metastasis in 10.5% and 5.3% of their study population, which was also significantly lower than in previous studies [5, 23–25]. These differences

Table 3 Comparison of diagnostic efficacies of FDG-PET/CT and CT for nodal staging on a per-patient basis

Parameters	Population	Total nodal staging			Mediastinal nodal staging		
		PET/CT	CT	*P* value [a]	PET/CT	CT	*P* value [a]
Sensitivity (%)	All	11.1 (1/9)	11.1 (1/9)	>0.99	16.7 (1/6)	16.7 (1/6)	>0.99
	≤50%	—	—	—	—	—	—
	>50%	11.1 (1/9)	11.1 (1/9)	>0.99	16.7(1/6)	16.7 (1/6)	>0.99
Specificity (%)	All	86.1 (130/151)	96.7 (146/151)	0.0009	89.6 (138/154)	96.8 (149/ 154)	0.012
	≤50%	91.6 (76/83)	98.8 (82/83)	0.031	92.8 (77/83)	98.8 (82/83)	0.063
	>50%	79.4 (54/68)	94.1 (64/68)	0.021	85.9 (61/71)	94.4 (67/71)	0.146
Accuracy (%)	All	81.9 (131/160)	91.9 (147/160)	0.0009	86.9 (139/160)	93.8 (150/160)	0.012
	≤50%	91.6 (76/83)	98.8 (82/83)	0.031	92.8 (77/83)	98.8 (82/83)	0.063
	>50%	71.4 (55/77)	84.4 (65/77)	0.021	80.5 (62/77)	88.3 (68/77)	0.146

Data *in parentheses* are numbers used to calculate percentages

Total nodal staging nodal staging for mediastinal, hilar nodes and nodes distal to hilar areas, *≤50%* patients with lesions containing a solid proportion ≤50%, *>50%* patients with lesions containing a solid proportion >50%

[a] Determined by using McNemar's test

may mainly lie in the difference between the study population of our study and those of previous studies [5, 23–25]. Previous studies [5, 23–25] have not taken into consideration the internal characteristics of the primary tumours, and their main population may have consisted of mostly solid lung cancers.

All LN metastasis in our study was observed in patients with a solid proportion >50%, and no patients with a solid proportion ≤50% had LN metastasis. These results correspond well with those of previous studies dealing with subsolid NSCLCs [16, 26]. In a study by Matsuguma et al. [26], 26 patients with a ≤50% solid proportion showed no LN metastasis. In another study by Aoki et al. [16], there was only one patient with LN metastasis among 24 patients who had a lesion with a solid proportion ≤50%. These results support the suggestion that FDG-PET/CT might be obviated for LN staging in T1 subsolid NSCLCs with a solid proportion ≤50%. By doing so, we can reduce false-positive results, unnecessary radiation dose, cost and anxiety.

Another finding of our study was that FDG-PET/CT showed very low sensitivity and significantly lower accuracy than chest CT in the LN staging of T1 subsolid NSCLCs both on a per-patient and on a per-nodal-station basis. Several reasons can be given. The first reason might be the small size

Table 4 Comparison of diagnostic efficacies of FDG-PET/CT and CT for nodal staging on a per-nodal-station basis

Parameters	Population	Total nodal staging			Mediastinal nodal staging		
		PET/CT	CT	*P* value[a]	PET/CT	CT	*P* value[a]
Sensitivity (%)	All	13.3 (2/15)	13.3 (2/15)	>0.99	12.5(1/8)	12.5 (1/8)	>0.99
	≤50%	—	—	—	—	—	—
	>50%	13.3 (2/15)	13.3 (2/15)	>0.99	12.5 (1/8)	12.5 (1/8)	>0.99
Specificity (%)	All	94.2 (698/741)	99.3 (736/741)	<0.001	95.9 (567/591)	99.2 (586/ 591)	0.0002
	≤50%	95.6 (366/383)	99.7 (382/383)	<0.001	97.4 (294/302)	99.7 (301/302)	0.0156
	>50%	92.7 (332/358)	98.9 (354/358)	<0.001	94.5 (273/289)	98.6 (285/289)	0.0075
Accuracy (%)	All	92.6 (700/756)	97.6 (738/756)	<0.001	94.8 (568/599)	98.0 (587/599)	0.0002
	≤50%	95.6 (366/383)	99.7 (382/383)	<0.001	97.4 (294/302)	99.7 (301/302)	0.0156
	>50%	89.5 (334/373)	95.4 (356/373)	<0.001	92.2 (274/297)	96.3 (286/297)	0.0075

Data *in parentheses* are numbers used to calculate percentages

Total nodal staging nodal staging for mediastinal, hilar nodes and nodes distal to hilar areas, *≤50%* patients with lesions containing a solid proportion ≤50%, *>50%* patients with lesions containing a solid proportion >50%

[a] Determined by using McNemar's test

Table 5 Comparison of features between patients with and without nodal metastasis

Characteristics	LN metastasis (n=9)	No LN metastasis (n=68)	P value
SUVmax[a]	3.5±2.0	2.3±1.4	0.030
Lesion size (mm)	21.6±6.4	19.3±5.7	0.273
Solid portion size (mm)	18.7±6.1	14.7±5.2	0.039
Solid proportion (%)	86.1±5.5	76.1±11.5	0.013
Margin (spiculated:non-spiculated)[b]	3:6	17:51	0.689
Pleural retraction (present:absent)[b]	2:7	36:32	0.154
Location (central:peripheral)[b]	3:6	5:63	0.047

SUVmax maximum standardised uptake value

[a] Data are mean ± standard deviation

[b] Data are numbers of patients per category

of metastatic LNs. All 13 false-negative LNs on FDG-PET/CT in our study were less than 10 mm on CT and four of them could not even be identified. Current PET/CT examinations definitely have a limitation in detecting and estimating metastatic LNs of subcentimetre size because of spatial resolution [5, 27]. The second reason may be that primary lung cancers appearing as subsolid nodules show very low FDG uptake [17, 28]. In the case of adenocarcinomas appearing as subsolid nodules, the SUVmax has been reported to be relatively low, ranging from 0.4 to 2.6 (mean SUVmax, 1.3) [28]. This phenomenon was also found in the present study; the mean SUVmax of primary lesions in our study was 1.8. Thus, FDG uptake values of metastatic LN cannot be expected to be high in the case of subsolid NSCLCs, and this may make it difficult to accurately evaluate subcentimetre LN metastases. The third reason may be related to the lower prevalence of LN metastasis in the study population. The lower sensitivity of FDG-PET/CT in detecting LN metastasis was previously reported in a smaller LN metastasis population with early uterine cervix cancer [29]. The authors of that study insisted that the lower the ratio of histological LN metastasis, the lower the sensitivity of FDG-PET/CT [29]. This explanation could be applied similarly to our results. In addition, FDG-PET/CT examinations are known to be very sensitive to non-specific inflammation, especially in a tuberculosis-endemic country such as South Korea [30], which may have led to the lower specificity of FDG-PET/CT than that of CT in the detection of metastatic LNs in our study.

Among patients with a solid proportion >50%, the SUVmax, solid portion size, solid proportion and lesion location of primary tumours were significantly different between patients with and those without LN metastasis. Furthermore, multivariate analysis revealed that higher SUVmax, larger solid proportion and central location of primary tumours were significant predictors of LN metastasis in T1 subsolid NSCLCs. According to the studies by Higashi et al. [31] and Bille et al. [32], the higher SUVmax of the primary lesion was a strong predictor of concurrent intratumoral lymphatic vessel invasion and LN involvement. This corresponds well with our results. In subsolid lung cancers, the appearance of GGO is considered to reflect replacement growth of a tumour without invasion of the stroma [9]. The solid component usually represents areas of fibroblastic proliferation or invasive components of the tumour, which increase the probability of LN metastasis [9]. Thus, it may be reasonable that lesions with larger solid proportions have a higher probability of LN metastasis, and correspond to this radio-pathological background. Our results showed that a central tumour location was a significant predictor of LN metastasis. Bille et al. [32] also reported that central location of lung cancers was an independent predictor of LN metastasis, although they did not consider the internal characteristics of the primary tumours. This can be explained by the fact that centrally located lung cancers are closer to the axial bronchovascular bundles and thus may have a higher chance of involving the lymphatic vessels and LNs. Based on our results, we believe it may be reasonable to recommend invasive staging work-ups such as mediastinoscopy for LN staging when a T1 subsolid NSCLC with a solid proportion >50% shows higher SUVmax, a larger solid proportion and central location even in the case of negative LN results on imaging studies.

Our study has several limitations. First, our study was of retrospective design. Therefore, there may have been bias. Second, although we had included 160 patients with subsolid NSCLCs, there were only nine patients with nodal metastasis. Third, the decision on whether contralateral hilar LNs or non-resected mediastinal LNs had metastasis was based on the results of clinical and imaging follow-up studies for confirming N0 stage. Although theoretically all LNs should be pathologically investigated, it may be impossible and unnecessary in routine practice.

In conclusion, FDG-PET/CT adds little value compared with CT alone in the LN staging of T1 NSCLCs manifesting as subsolid nodules. Higher SUVmax, larger solid proportion and central location of primary tumours are independent predictors of LN metastasis in T1 subsolid NSCLCs with a solid proportion >50%.

Acknowledgements This study was supported by the Research Grant of the Korean Foundation for Cancer Research (grant number: CB-2011-02-01) and Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (grant number: 2011-0022379).

Conflicts of interest None.

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