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The efficacy of positron emission tomography-CT in simultaneously detected nodules in patients with lung cancer

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Abstract:

BACKGROUND: The aim of this study is to evaluate the efficacy of positron emission tomography-computed tomography (PET-CT) in the diagnosis of ≤1 cm nodules detected during lung cancer diagnosis.

MATERIALS AND METHODS: Patients with pulmonary parenchymal nodules ≤1 cm during the diagnosis of lung cancer between January 2014 and December 2016 were included in the study. The radiologic (size, location, shape, and contour properties) and radiometabolic (presence of fluoro 2-deoxyglucose [FDG] uptake in the nodule, presence and number of PET-CT mediastinal lymphadenopathy [LAP] uptake, mediastinal LAP maximum standard uptake value [SUVmax], presence and number of PET-CT extrapulmonary metastasis) features of the nodules were recorded. Nodules that were followed for at least 6 months and unchanged in size were considered benign, and those that increased or decreased in size or completely regressed were considered malignant.

RESULTS: Of a total of 167 patients with lung cancer, 116 (69.4%) had no nodules and 51 (30.5%) had nodules. Of the 51 patients with nodules, 27 (53%) had benign and 24 (47%) had malignant nodules. Compared with patients with benign nodules, the FDG uptake rate, SUVmax values, mediastinal LAP uptake in PET-CT, SUVmax value of the mediastinal LAP with uptake, the number of mediastinal LAPs with uptake, and reported the presence and number of extrapulmonary distant organ metastases in PET-CT were statistically significantly higher in malignant nodules ($P < 0.05$). Moreover, FDG uptake of the nodule in PET-CT and the presence of mediastinal LAP uptake in PET-CT were independent predictors of malignancy of the nodules ($P < 0.05$).

CONCLUSION: PET-CT parameters other than SUVmax can be used to interpret accompanying nodules smaller than 1 cm in patients with lung cancer.

Keywords:

Lung cancer, nodule, positron emission tomography-CT

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Introduction

The presence of accompanying nodules in primary lung cancer is an important condition. The malignant or benign nature of additional nodules is important for proper planning of treatment and staging. In the 8th Edition of the tumor, TNM classification for lung cancer, a nodule in the same lobe on the same side of the lung with the primary tumor is staged as T3, a nodule in a different lobe on the same side with the primary tumor as T4, and a nodule in a contralateral lobe as M1a.[1,2] Studies conducted on nodules identified in patients with lung cancer reported that 57%–75% of the concurrently identified nodules were benign.[3,4] Relatively older studies on nodules are radiologic studies conducted using thoracic computed tomography (CT). These studies tried to distinguish benign and malignant nodules based on their many properties, including size, contour property, inner structure, density, growth rate, and contrast uptake of the nodule.[5,6] Current studies are based on metabolic imaging-positron emission tomography-computed tomography (PET-CT). These studies try to distinguish benign and malignant nodules using the maximum standard uptake value (SUVmax) calculated using the fluoro 2-deoxyglucose (FDG) uptake of the nodules. Almost all of these studies emphasize that due to the limited spatial resolution of PET scanners, the sensitivity of PET-CT decreases in nodules measuring <1 cm and hence, such a method may not be adequately reliable.[7-9]

Patients found to have additional nodules smaller than 1 cm in their lungs at the time of diagnosis of lung cancer were included in this study. Prognostic radiologic changes of the nodules in the patients were observed. The efficacies of radiologic (CT) and radiometabolic (PET-CT) imaging studies in predicting the benign or malignant nature of the nodules were assessed. The study is different from other studies on the subject in that this study investigated whether it was possible to distinguish malignant or benign nodules using parameters other than SUVmax in PET-CT scans.

Materials and Methods

Patient population

The study was planned as a retrospective, cross-sectional study in accordance with the international Helsinki Declaration, and Local Ethics Committee approval was obtained. Patients with a final diagnosis of lung cancer based on clinical, radiologic, and histopathologic findings in the chest diseases clinic of our hospital between January 2014 and December 2016 were included in the study. Thoracic CT and PET-CT scans of all patients performed at the time of diagnosis were examined. The patients were divided into two groups; patients with a parenchymal nodule identified in addition to the primary mass lesion in the parenchymal window of thoracic CT scans, patients without such nodules. Patients without a final histopathologic diagnosis of lung cancer/with suspected metastasis, patients who were not followed up after being diagnosed, patients with radiologic follow-up lasting <6 months, patients with unknown treatment characteristics, patients with a nodule larger than 1 cm, patients whose PET-CT reports were not available, and patients with a purely calcific nodules were excluded from the study [Table 1]. The clinical and demographic characteristics, cancer histopathologic types, stages, radiologic, and radiometabolic characteristics of nodules of the patients from both groups were recorded.

Table 1: Criteria for inclusion or exclusion from the study

Criteria for inclusion in the study
Patients with final histopathologic diagnosis of lung cancer
Patients found to have a nodule smaller than 1 cm in pulmonary parenchyma at the time of diagnosis
Patients whose radiologic follow-up was conducted by the same medical center/the same device/in the same section range for at least 6 months
Criteria for exclusion from the study
Patients without a final histopathologic diagnosis of lung cancer/ with suspected metastasis
Patients who were not followed up after being diagnosed
Patients with radiologic follow-up lasting<6 months
Patients with unknown treatment characteristics
Patients with a nodule larger than 1 cm
Patients whose PET-CT reports were not available
Patients with a purely calcific nodule

PET-CT: Positron emission tomography-computed tomography

CT and positron emission tomography-CT imaging and evaluation of nodules

Patients with a fasting time of not <8 h and a normal blood glucose level were undergone integrated PET-CT procedures. PET/CT scans were performed on a Philips Gemini TF ultra-high-resolution integrated PET-CT imaging system. CT sections were performed with a cross-sectional thickness of 5 mm and PET emission images were obtained between the vertex and upper femur. The scan was conducted 60 min after injection of 370–550 MBq (5–15 mCi) F-18 FDG. Oral contrast was administered concurrently with an FDG injection.

A Hitachi Pratico (1999 – Japan) device was used for thoracic CT scans. The CT examinations were performed in a caudal-cranial direction with a 1-mm slice thickness and full inspiration in the supine position. The window width was 1500 Hounsfield Units (HU) for the lung window and 400 HU for the mediastinal window. The window level was – 700 HU for the lung window and 10 HU for the mediastinal window. The measurements were

made in the axial plane; however, coronal and sagittal images were used if necessary. Intravenous contrast agents were used for all scans except for patients with acute or chronic renal insufficiency.

The additional nodule in patients diagnosed with having primary lung cancer was evaluated in accordance with the description "a single, circular or oval nodule in pulmonary parenchyma measuring ≤1 cm, surrounded by normal pulmonary tissue, which is not associated with atelectasis, pleural effusion, or lymphadenopathy."[5] Patients who underwent scans in the same CT and PET device in the same sectional range were included in the nodule assessment. The radiologic features of the identified nodules, including size, location, shape, contour properties, inner structure, and radiometabolic features, including the presence of FDG uptake in the nodule in PET-CT, SUVmax value of the nodule, presence of PET-CT mediastinal lymphadenopathy (LAP) uptake, mediastinal LAP SUVmax value, number of mediastinal LAPs with uptake, and the presence and number of PET-CT extrapulmonary metastasis were recorded. Nodules that were followed up for at least 6 months whose size did not change were considered benign [Figure 1]. Nodules that decreased in size or completely regressed with treatment or those that increased in size during follow-up were considered malignant [Figures 2-4].

Statistical analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences software package (SPSS Ver. 17.0, IBM Inc., Chicago, USA). Descriptive statistics are presented as mean ± standard deviations for continuous variables, and as percentages for categorical variables. The Kolmogorov–Smirnov test was used to check for normal distribution of the variables. Group data were evaluated using the Mann–Whitney U-test, Chi-square, and *t*-test. To estimate the independent predictors of malignancy of nodules, PET-CT variables were examined using multivariate logistic regression analysis. Logistic regression analysis was performed using the forward likelihood-ratio method, and $P < 0.05$ was considered as significant.

Results

The files of 323 patients with lung cancer were examined retrospectively for the study. Seventy-one patients who were followed up and received treatment from another medical center, 38 patients with <6 months of thoracic CT follow-up due to death or any other reason, 16 patients with unknown treatment properties, 12 patients with a nodules larger than 1 cm, 10 patients with unavailable PET-CT reports, and 9 patients with other issues were excluded from the study. The study was continued with a total of 167 patients with lung cancer [Figure 5].

One hundred and thirty-three (79.6%) patients were male and 34 (20.4%) were female. Of the total 167 patients with lung cancer, 116 (69.4%) had no nodules and 51 (30.5%) had nodules [Figure 6]. The mean age of the patients with nodule was 60.9 ± 9.4 years. The mean age of patients no nodules was 60.2 ± 9.3 years. The mean follow-up period

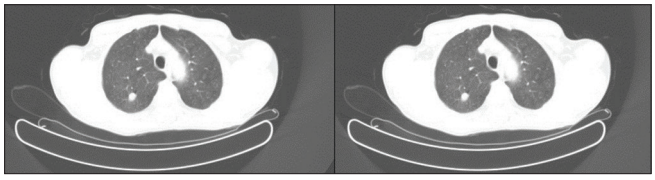

Figure 1: A nodule considered benign, which did not change in size in radiologic follow-up

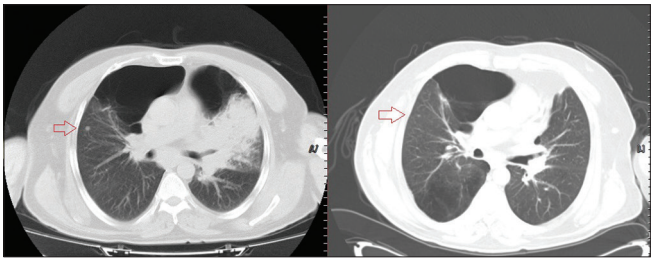

Figure 2: A nodule considered malignant, which was reduced in size after postoncologic treatment in radiologic follow-up

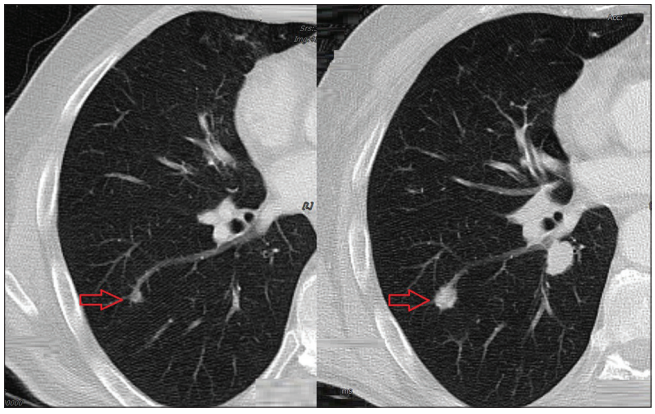

Figure 3: A nodule considered malignant, which was increased in size in radiologic follow-up

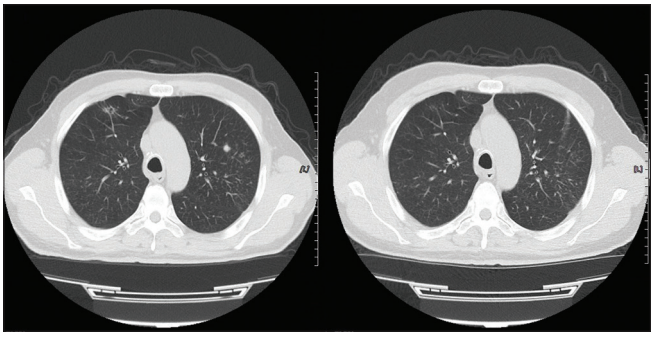

Figure 4: A nodule considered malignant, which was fully regressed in size after postoncologic treatment in radiologic follow-up

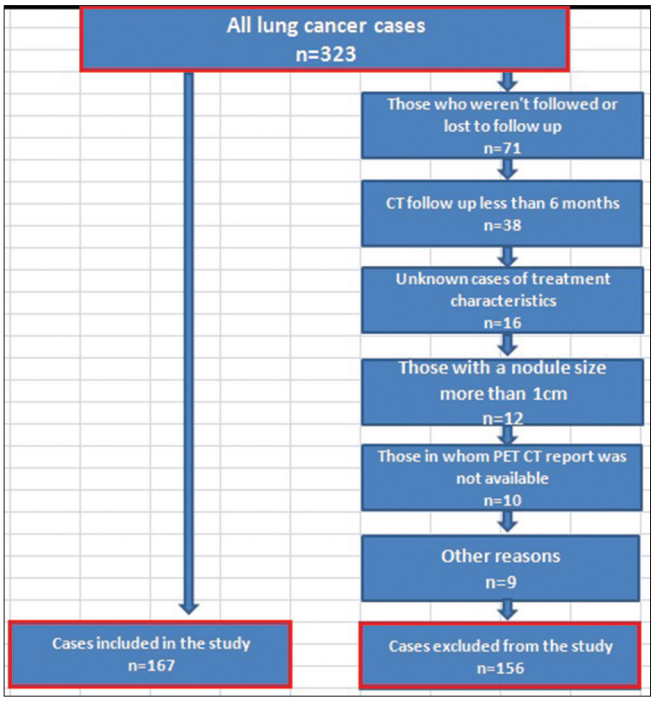

Figure 5: Patients included or excluded from the study

Table 2: Clinical and demographic characteristics of patients with lung cancer with or without identified parenchymal nodules

Demographic characteristics	Nodule present (*n*=51)	No nodule (*n*=116)	*P*
Age years±SD	60.9±9.4	60.2±9.3	0.683
Sex (female/male)	7/44	27/89	0.158
Tobacco (pack-years)	37.9±13.8	38.7±17.5	0.640
Tumor type, *n* (%)			
NSCLC	9 (17.6)	21 (17.2)	0.944
Squamous cell carcinoma	23 (45.1)	44 (37.9)	0.384
Adenocancer	13 (25.5)	27 (23.2)	0.757
SCLC	4 (7.8)	20 (17.2)	0.738
Other	2 (4)	4 (3.4)	0.880
NSCLC stage, *n* (%)			
Stage 1A-2B	14 (27.4)	46 (39.6)	0.130
Stage 3A	11 (21.5)	17 (14.7)	0.271
Stage 3B	4 (7.9)	9 (7.8)	0.602
Stage 4	16 (31.3)	20 (17.2)	0.041
SCLC stage, *n* (%)			
Limited stage	-	7 (6)	0.102
Common stage	4 (7.9)	13 (11.2)	
Surgical treatment history, *n* (%)			
Received surgical treatment	18 (35.3)	40 (34.4)	0.851
Did not receive surgical treatment	33 (64.7)	76 (65.6)	
Oncologic treatment history, *n* (%)			
Received oncologic treatment	36 (70.5)	84 (72.4)	0.809
Did not receive oncologic treatment	15 (29.5)	32 (27.6)	
The size of primary tumor (mm)	48.1±25.7	49.4±25.8	0.767

SCLC: Small cell lung cancer, NSCLC: Non-SCLC, SD: Standard deviation

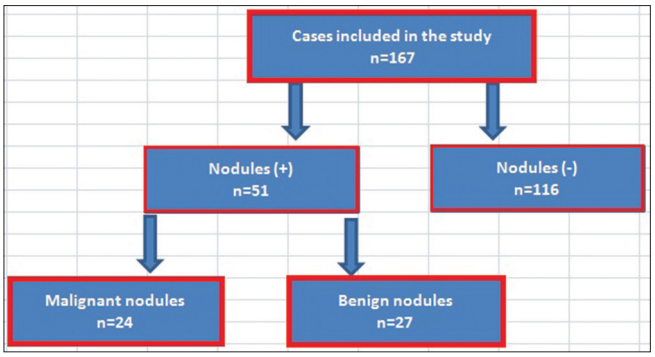

Figure 6: Flow chart of cases with nodules detected

of the nodules was 16 ± 8.2 months. The demographic, radiologic, and clinical findings of patients with or without nodules are presented in Table 2.

Regarding the 51 patients with nodules, 27 (53%) patients had benign features and 24 (47%) had malignant features. The demographic and clinical findings of nodules considered either malignant or benign are given in Table 3.

When the radiologic features of patients with malignant and benign nodules were examined, it was observed that the size of the nodule at the time of diagnosis was statistically significantly larger in patients with nodules exhibiting malignant features. At the time of diagnosis, the mean nodule size was 6.9 ± 2.1 mm in malignant nodules and 5.6 ± 1.8 mm in benign nodules ($P = 0.044$). Other radiologic features were similar between the groups ($P > 0.05$) [Table 4].

When the radiometabolic features of the patients were examined, 14 patients from the group with malignant features (14/24) and 4 patients from the group with benign features (4/27) had FDG uptake reported in their PET-CT scans. In the entire group (18/51), the FDG uptake rate in PET-CT was 35.2% for all nodules.

PET-CT scans of 14 (58.3%) patients out of 24 considered to have malignancy had FDG uptake of the nodule, whereas PET-CT scans of 23 (85.1%) patients out of 27 considered benign had no FDG uptake ($P = 0.001$). The SUVmax values of nodules with FDG uptake were significantly higher in patients considered to have malignant nodes ($P < 0.001$). In addition, compared with the patients considered to have benign nodules, mediastinal LAP uptake in PET-CT, the SUVmax value of the mediastinal LAP with uptake, the number of the mediastinal LAPs with uptake, and the presence and number of extrapulmonary distant organ metastasis reported in PET-CT were statistically significantly higher in patients considered to have malignant nodules ($P < 0.05$). The radiometabolic features of the patients are presented in Table 5.

Table 3: Clinical demographic characteristics of patients with malignant/benign nodule characteristics

Demographic characteristics	Malignant nodule (*n*=24)	Benign nodule (*n*=27)	*P*
Age (years), median (25th-75th percentile)	61 (54.5-69)	61 (57-66)	0.806
Sex (female/male)	4/20	2/25	0.402
Tobacco (pack-years), median (25th-75th percentile)	32.5 (27.2-51.5)	39 (25-47.7)	0.697
Tumor type, *n* (%)			
NSCLC	4 (16.6)	4 (14.8)	0.999
Squamous cell carcinoma	9 (37.5)	14 (51.8)	0.304
Adenocancer	8 (33.3)	5 (18.5)	0.226
SCLC	3 (12.5)	2 (7.4)	0.656
Other	-	2 (7.4)	0.492
NSCLC stage, *n* (%)			
Stage 1A-2B	4 (16.7)	10 (37)	0.104
Stage 3A	4 (16.7)	7 (25.9)	0.422
Stage 3B	3 (12.5)	1 (3.7)	0.331
Stage 4	10 (41.7)	5 (18.5)	0.070
SCLC stage, *n* (%)			
Limited stage	-	-	-
Common stage	3 (12.5)	2 (7.4)	0.656
Surgical treatment history, *n* (%)			
Received surgical treatment	5 (20.8)	13 (48.1)	0.042
Did not receive surgical treatment	19 (79.2)	14 (51.9)	
Oncologic treatment history, *n* (%)			
Received oncologic treatment	20 (83.3)	11 (40.7)	0.060
Did not receive oncologic treatment	4 (16.7)	16 (59.2)	
The size of primary tumor (mm), median (25th-75th percentile)	48 (33-60.5)	50 (20-60)	0.591

SCLC: Small cell lung cancer, NSCLC: Non-SCLC

Table 4: Radiologic characteristics of patients with malignant/benign nodule characteristics

Radiological characteristics	Malignant nodule (*n*=24)	Benign nodule (*n*=27)	*P*
Nodule size (mm)	6.9±2.1	5.6±1.8	0.044
Location, *n* (%)			
Peripheral	23 (95.8)	26 (96.2)	0.999
Central	1 (4.2)	1 (3.8)	
Contour properties, *n* (%)			
Regularly contoured	8 (33.3)	5 (18.5)	0.226
Lobular contoured	7 (29.2)	5 (18.5)	0.371
Irregularly contoured	7 (29.2)	15 (55.6)	0.058
Spicular-contoured	1 (4.2)	2 (7.4)	0.999
Inner structure, *n* (%)			
Normal	21 (91.6)	24 (88.9)	0.607
Calcification	-	2 (7.4)	0.492
Frosted glass	1 (4.2)	-	0.471
Cavitation	1 (4.2)	1 (3.7)	0.999
Lobe with nodule, *n* (%)			
The same lobe	4 (16.6)	2 (7.4)	0.402
Different lobe	20 (83.3)	25 (92.5)	
Lung with nodule, *n* (%)			
The same lung	11 (45.8)	8 (29.6)	0.232
Opposite lung	13 (54.1)	19 (70.3)	

In addition, when we examined a logistic regression model for PET-CT findings (whether the nodule had FDG uptake, presence of mediastinal LAP uptake, and presence of extrapulmonary distant organ metastasis and number of PET-CT extrapulmonary metastases), which could predict malignancy of the nodule in our study, we observed that the presence of FDG uptake in the nodule in PET-CT and the presence of mediastinal LAP uptake in PET-CT were independent predictors of malignancy of the nodule (presence of uptake in the nodule in PET-CT $P = 0.007$, odds ratio [OR]:10.6, 95% confidence interval [CI]: 1.9–58.7, and for the presence of mediastinal LAP uptake in PET-CT $P = 0.027$, OR: 9.3, 95% CI: 1.2–67.5) [Table 6].

Discussion

In this study, the clinical, radiologic, and radiometabolic features of patients who were found to have a nodule in their pulmonary parenchyma at the time of diagnosis of primary lung cancer were evaluated. One hundred and sixty-seven patients were included in the study, and 51 (30.5%) were found to have an accompanying nodule. Twenty-four (18.4%) of the identified nodules showed properties consistent with malignancy. During examinations conducted to differentiate malignant nodules from benign nodules, all nodules smaller than 1 cm (malignant + benign) were found to have a low SUVmax uptake ratio in PET-CT (35.2%). The SUVmax value of malignant nodules with uptake in PET-CT, presence of mediastinal LAP uptake, number and SUVmax values of these LAPs, and the presence and number of extrapulmonary metastases in PET-CT were statistically significantly higher ($P < 0.05$) [Table 5].

Table 5: Radiometabolic (positron emission tomography-computed tomography) features of the patients

PET-CT parameters	Malign nodule (*n*=24)	Benign nodule (*n*=27)	*P*
PET-CT revealed FDG uptake in the nodule, *n* (%)	14 (58.3)	4 (14.8)	0.001
Nodule SUVmax value	2.3±2.6	0.2±0.5	<0.001
PET-CT mediastinal LAP uptake present, *n* (%)	21 (87.5)	12 (44.4)	0.001
Mediastinal LAP SUVmax value, *n* (%)	7.9±4.9	4.8±6.7	0.007
Number of mediastinal LAPs with uptake	3.2±2.1	1.8±2.3	0.008
PET-CT extrapulmonary metastasis present, *n* (%)	14 (58.3)	5 (18.5)	0.003
Number of PET-CT extrapulmonary metastases	1.2±1.4	0.20±0.5	0.002

FDG: Fluoro 2 deoxyglucose, LAP: Lymphadenopathy, PET-CT: Positron emission tomography-computed tomography, SUVmax: Maximum standard uptake value

Table 6: The variables examined with logistic regression analysis

PET-CT parameters	*P*	OR	95% CI
PET-CT revealed FDG uptake in the nodule	0.007	10.6	1.9-58.7
PET-CT mediastinal LAP uptake present	0.027	9.3	1.2-67.5
PET-CT extrapulmonary metastasis present	0.633	1.8	0.04-6.5
Number of PET-CT extrapulmonary metastases	0.918	1	0.2-3.1

CI: Confidence interval, FDG: Fluoro 2 deoxyglucose, LAP: Lymphadenopathy, PET-CT: Positron emission tomography-computed tomography, OR: Odds ratio

In addition, the presence of uptake in the nodule and mediastinal LAPs in PET-CT were independent predictors of malignant transformation ($P < 0.05$). Other radiologic properties of the nodules (e.g., internal structure, contour properties, and location) were similar for both groups ($P > 0.05$), except for the size of the nodule ($P < 0.05$).

PET-CT is undoubtedly one of the major developments in lung cancer imaging in the recent past. When injected intravenously, 18F-FDG used in PET-CT, a metabolic imaging method, is taken up by tumor cells at a higher rate than normal cells. Metabolic images of tumor cells are obtained by the courtesy of FDG, which is not metabolized in the cell.[10] In clinical practice, PET-CT is frequently used in the evaluation of pulmonary parenchymal nodules. Especially in PET-CT, SUVmax values higher than 2.5 in nodules are recognized to be in favor of malignancy.[11] The size of the nodule is one of the factors used in the calculation of SUVmax. If the nodule size is small (<1cm), this valuable data (SUVmax >2.5) is not always reliable.[12] A meta-analysis by Gould *et al*.[7] consisting of 1474 cases reported a PET-CT sensitivity of 97% and specificity of 78% for nodules measuring in the range of 1–3 cm. A study of 136 patients with nodules measuring in the range of 1–3 cm (80 malignant/55 benign) by Nomori *et al*.[13] reported a PET-CT sensitivity of 79% and a specificity of 65%. In that study, 20 patients (8 malignant/12 benign) had nodules smaller than 1 cm, which had no uptake in PET-CT, and the authors concluded that nodules smaller than 1 cm should not be evaluated with PET-CT. Marom *et al*.[14] showed that 9 (4.6%) of 192 patients withT1 lung cancer with nodules measuring 2 cm in diameter on average had no uptake in PET-CT. These nine patients with histopathologic diagnosis of cancer had lesions measuring 1.3 cm (0.3–2.5 cm) on an average, which were smaller. The authors also added that uncertainty of PET-CT for nodules smaller than 1 cm had been maintained and further studies were needed on this subject. Similarly, Kernstine *et al*.[15] reported that PET-CT would not be beneficial in subcentimetric lung nodules, even with possible future developments in PET-CT. In view of the literature, the majority of studies have shown that the efficacy and reliability of PET-CT in nodules smaller than 1 cm are reduced. However, a few studies reported that PET-CT might be reliable. Divisi *et al*.[16] reported a PET-CT sensitivity of 95% and specificity of 73% in diagnosing 57 patients with histopathologically diagnosed nodules that ranged in size from 0.5 to 0.99 cm. Similarly, the study by Fischer *et al*.[17] is one of the few studies that argued that PET-CT might be reliable in subcentimetric nodules. Recent studies have been conducted using innovations in imaging techniques because the diagnosis of small nodules in the lungs is an important issue. Farid *et al*.[18] used four-dimensional PET-CT in small nodules but could not demonstrate its superiority over three-dimensional PET-CT. Chandarana *et al*.[19] stated that hybrid PET-magnetic resonance might be superior to PET-CT in nodules smaller than 1 cm.

In this study, there were 51 patients with lung cancer with parenchymal nodules smaller than 1 cm. In agreement with the literature, 18 (35%) of these 51 patients had uptake in PET-CT, whereas others had no reported uptake. The majority (14/18) of the patients with uptake had malignant nodules, and the SUVmax values of malignant nodules with uptake were statistically significantly higher as expected, in agreement with the literature. The study differs from other studies in the literature in that it studied SUV values and other parameters of PET-CT. In our study, the presence of mediastinal LAP uptake in PET-CT, the number of mediastinal LAPs with reported uptake, the SUVmax values of these LAPs, and the presence and number of extrapulmonary metastases to distant organs reported in PET-CT were statistically significantly higher in the group with malignant nodules.

The presence of FDG uptake in the nodule in PET-CT and presence of mediastinal LAP uptake in PET-CT were independent predictors predicting malignancy of the nodule. Uptake in the nodule increased the risk of malignancy by about ten times, and the presence of mediastinal LAP uptake increased such risk by about nine times. Nodules detected in the presence of involvement of lymphatic pathways, mediastinal lymph node metastasis and systemic metastasis in lung cancers are highly likely to be malignant.[20] Kocaturk *et al*.[21] identified N1 lymph node metastasis in 15 (57.6%) of 26 patients with synchronous multiple primary lung cancer on whom they operated. The authors reported that if a nodule was identified during surgery and the patient had no mediastinal lymph node metastasis and suspected systemic metastasis, this might be a synchronous tumor and that if the patient had lymph node metastasis and suspected systemic metastasis, this could be metastasis of the primary tumor. The result of this previous study supports our study.

In radiologic studies on lung nodules, older age of patient, history of malignancy of any organ, large nodule size, spiculated or lobular contour properties, eccentric calcifications, inner structure with ground-glass appearance, accompanying cavitation with a cavity wall of > 4 mm, and right lung and upper lobe location favor malignancy. In addition, a doubling time shorter than 400 days or longer than 20 days is considered in favor of malignancy.[22-24] In our study, radiologic features other than the size of nodules were similar in malignant and benign nodules. We ascribe this finding to the fact that all patients examined in our study were patients with lung cancer and the size of all nodules were smaller than 1 cm.[25]

There were some limitations in our study. First, this study was a retrospective study with a limited number of patients and reflected a single center's experience. Therefore, the results cannot be generalized. Second, there was no histopathologic diagnosis of accompanying nodules, and the assumption of benign or malignant nature was based on clinical/radiologic observation. During the evaluation of the study data, the likelihood of lesions that could grow very slowly, such as adenocarcinoma *in situ*, and which may not have uptake in PET, should not be overlooked, even though there was no difference between histopathologic cancer diagnoses of the two groups.

Conclusion

We conclude that in the presence of an accompanying small nodule in a patient with lung cancer, if there is both mediastinal LAP and distant organ metastasis in PET-CT, and the nodule has demonstrated uptake, it is highly likely that the nodule is malignant. In a patient with a large lung tumor, metastasis in mediastinal lymph nodes and multiple organ metastases, whether an accompanying nodule is malignant or benign is not especially meaningful in clinical practice. However, in a patient with an operable lung tumor with no mediastinal LAP uptake in PET-CT and no reported distant organ metastasis, it is very important in clinical practice to determine whether the accompanying nodule is malignant or benign. We believe that these data may be particularly useful in such cases.

We think that using PET-CT parameters other than SUVmax can be beneficial in interpreting the malignancy status of nodules smaller than 1 cm in patients with lung cancer.

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Conflicts of interest

There are no conflicts of interest.

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