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Prognostic impact of maximum standardized uptake value on ^{18}F-FDG PET/CT imaging of the primary lung lesion on survival in advanced non-small cell lung cancer: A retrospective study

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Abstract

Background: Positron emission tomography/computed tomography (PET/CT) has been recognized for diagnosing and staging lung cancer, but the prognostic value of standardized uptake value (SUV) on ^{18}F-FDG PET/CT imaging in patients with advanced non-small cell lung cancer (NSCLC) remains controversial.

Methods: We performed a retrospective analysis of patients with advanced NSCLC who had undergone ^{18}F-FDG PET/CT before systemic treatment between June 2012 and June 2016. The relationship between the maximum SUV (SUVmax) of the pulmonary lesion and lesion size was evaluated via Spearman's correlation analysis. We collected patients' clinical and pathological data. Univariate and multivariate analyses were performed to analyze the factors influencing survival.

Results: We included 157 patients with advanced NSCLC. Among these, 135 died, 13 survived, and nine were lost to follow-up (median follow-up period, 69 months). SUVmax was correlated with lesion size and was significantly greater for tumors ≥3 cm than for tumors <3 cm (10.2 ± 5.4 vs. 5.6 ± 3.3, t = −6.709, p = 0.000). Univariate analysis showed that survival was associated with gender, tumor size, epidermal growth factor receptor gene mutation or anaplastic lymphoma kinase rearrangement, SUVmax of the primary lung lesion, and treatment lines. Multivariate analysis showed a significant correlation between SUVmax of the primary lung lesion and survival. The mortality risk of patients with SUVmax ≤6 was 35% lower than that of patients with SUVmax >6 (HR = 0.651, 95% confidence interval, 0.436–0.972; Wald value, 4.400; p = 0.036).

Conclusions: The SUVmax of the primary lung lesion on PET/CT is significantly correlated with survival in treatment-naive patients with advanced NSCLC.

KEYWORDS
maximum SUV, non-small-cell lung cancer, positron-emission tomography, primary lung lesion, prognosis

INTRODUCTION

Lung cancer is the leading cause of cancer-related death worldwide in both men and women. The most common type of lung cancer is non-small cell lung cancer (NSCLC), which accounts for 80% of all cases.[1] Most patients with advanced NSCLC are diagnosed at a late stage and are thus no longer eligible for radical surgery. Accordingly, the five-year overall survival rate of patients with advanced lung cancer is only 9%–13%.[2] Several potential prognostic

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factors for NSCLC are currently recognized, such as sex, disease stage, physical status, liver or skin metastases, and driver genes.[3,4]

Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) positron-emission tomography/computed tomography (PET/CT) is based on the metabolism[5,6] and glucose uptake ability of the majority of malignant tumors.[2,4,7] The standardized uptake value (SUV) is a semiquantitative measurement of the FDG uptake in tissues. Accordingly, it can be used to evaluate tumor metabolic activity.[8–10] Several studies have shown a high sensitivity, specificity, and accuracy of PET/CT for diagnosis, staging, post-therapy assessment, and outcome prediction as well as its utility as an accurate and noninvasive modality for NSCLC patients in clinical practice, especially for early stage NSCLC.[2,3,6,7,9–19] However, the methods in these studies differ and their conclusions are not completely consistent.[11,20,21] Furthermore, the utility of SUV for predicting survival in advanced NSCLC requires further study. Thus, in this study, we aimed to explore the prognostic value of ^{18}F-FDG PET/CT in patients with advanced NSCLC.

MATERIALS

Patient population

The subjects were 269 patients who underwent PET/CT imaging between June 2012 and June 2016 at Peking Union Medical College Hospital, China. The patients were identified from the hospital's PET/CT center patient database and the Lung Cancer Center patient database. The inclusion criteria were as follows: (i) histologically/cytologically confirmed stage IV NSCLC; (ii) ineligibility to undergo radical surgery and radiotherapy; (iii) no prior systemic therapy before PET/CT; (iv) received systemic treatment within six weeks after PET/CT assessment; and (v) consent to follow-up. The exclusion criteria were as follows: patients with (i) small cell lung cancer, metastatic cancer to the lung, and other rare lung cancers or other cancer in the past five years; (ii) stage I-III NSCLC; (iii) without complete evaluation; and (iv) without systemic treatment. A total of 157 patients were included in the study. The patient selection flowchart is shown in Figure 1.

Data and evaluation

The study was approved by the Ethics Committee of Peking Union Medical College Hospital. We collected data on the patients' demographic characteristics, including sex and age. Clinical data, such as the patients' smoking history, weight loss, performance status (PS) score, tumor/node/metastasis (TNM) stage, number, and location of metastatic lesions, number of treatment regimen, and follow-up, were also collected. We also recorded the histopathological characteristics of lung cancer, including their gene signatures, histology, and the presence of mutations in the epidermal growth factor receptor (EGFR) gene or anaplastic lymphoma kinase (ALK) rearrangement. Finally, we considered the patients' PET/CT data, such as their lung lesion size as well as the maximum SUV (SUVmax) of the primary lung lesion and metastatic lesions. Patients were followed-up for a median of 69 months (range, 2–83 months). The last follow-up was in June 2018.

Overall survival was defined as the time between diagnosis and the last follow-up or death. The median age at diagnosis was 65 years which was used as a boundary value to

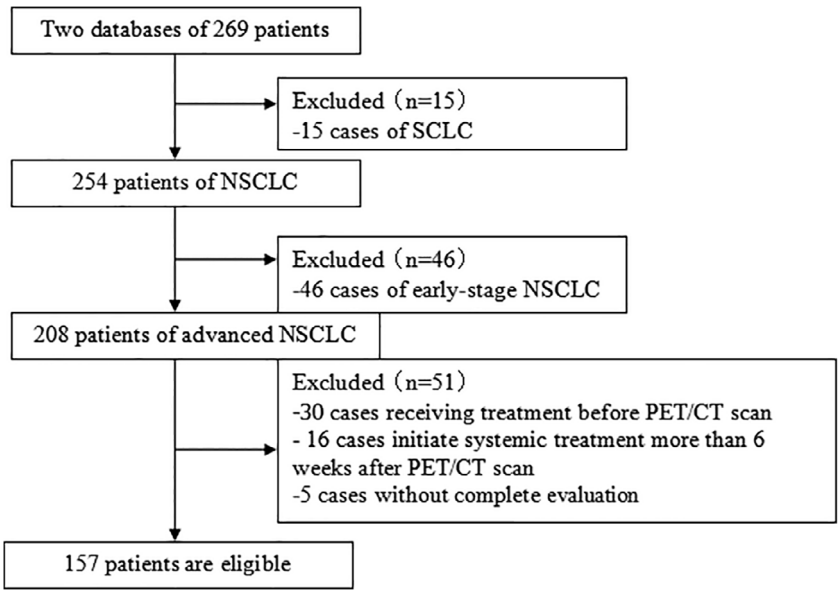

FIGURE 1 Screening flow chart of enrolled patients. NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; PET/CT, positron-emission tomography/computed tomography

divide the patients into two groups. Staging was performed according to the International Association for the Study of Lung Cancer (IASCL) TNM staging system, seventh edition. Loss of weight was defined as a 10% decline in weight within the past six months. The size of the primary lung lesion was determined according to the maximum diameter of the lesion. With respect to SUVmax, both the primary lung lesion and metastatic lesions were included. Brain metastases were not counted as PET/CT has a low sensitivity for brain metastases. For example, in this study, 33 patients had brain metastases, but only 14 were diagnosed via PET/CT. Treatment was divided into two types: receiving one treatment regimen or ≥ 2 treatment regimens. Since tests for *EGFR* mutations and ALK rearrangement, but not c-ROS oncogene 1 receptor tyrosine kinase (ROS1), were already routinely performed during the study period, *EGFR* mutations and ALK rearrangement were evaluated. In total, 46 patients with positive *EGFR* gene mutations received first-line EGFR tyrosine kinase inhibitor (TKI) treatment and five patients with ALK rearrangement received first-line ALK-TKI treatment, 106 patients received platinum-containing combination chemotherapy, and 39 patients received treatment combined with bevacizumab, while 81 patients received second-line treatment after progression.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics 25. An independent sample *t*-test was performed to explore the association between the SUVmax of the primary lung lesion or the highest SUVmax among all lesions and survival. Likewise, the differences in SUVmax between the primary lung lesion and metastatic lesion were compared using this method. The SUVmaxs were categorized into the following ranges: 0–2, 2–4, 4–6, 6–8, 8–10, 10–12, 12–14, and > 14. Survival curves were drawn to define an optimal cutoff value, and SUVmaxs were then divided into two groups according to the cutoff. Survival differences between these two groups were then evaluated using the Kaplan–Meier method. We also analyzed the survival impact of various factors, including sex, age, smoking status, loss of weight, performance status (PS) score, lung lesion size, smoking histology, *EGFR* mutation or ALK rearrangement, TNM staging, number and location of metastatic lesions, number of treatment regimen, and SUVmax of the lung lesion.

Spearman's correlation analysis was used to investigate significant relationships between the SUVmax of the primary lung lesion and tumor size. Univariate survival analysis was performed using the Kaplan–Meier method, and comparison of survival between groups was performed using the log-rank test. Multivariate analysis was performed using the Cox proportional hazards model. Hazard ratios (HR) with 95% confidence intervals (CI) were equally calculated. A p-value of <0.05 was considered statistically significant.

RESULTS

Correlation between patient clinical characteristics and SUVmax

A total of 157 patients with advanced NSCLC were included in the study. Among these patients, 135 (86%) died, 13 (8%) survived, and nine (6%) were lost to follow-up. The correlation between the clinical characteristics of the patients and the SUVmax of the primary lung lesions as well as the highest SUVmax among all lesions is shown in Table 1.

The SUVmax of the primary lung lesions was significantly correlated with tumor size. Tumors ≥3 cm in size had a significantly greater SUVmax than tumors <3 cm in size (10.2 ± 5.4 vs. 5.6 ± 3.3, $t = -6.709$, $p < 0.001$). The SUVmax of primary lung lesions was also associated with the number of treatment regimens. The SUVmax for patients receiving only first-line treatment was significantly greater than those for those receiving ≥2 treatment regimens. The factors related to the highest SUVmax among all lesions included loss of weight, lung lesion size, histology, and number of metastases. The highest SUVmax among all lesions significantly increased in patients with a lower body weight, lung lesion size ≥3 cm, squamous cell carcinoma, and number of metastases ≥2.

The SUVmax of the primary lung lesions was significantly higher than that of the metastatic lesions ($p < 0.05$) (Table 2). Further, the SUVmax of the primary lung lesions was able to better reflect the severity of the tumor ($p < 0.05$).

Correlation between SUVmax and survival

The highest SUVmax of all lesions was divided into seven groups as follows: 2–4, 4–6, 6–8, 8–10, 10–12, 12–14, and >14. According to the median survival time of patients in each group (Table 3) and the survival curve (Figure 2(a)), SUVmax = 6 was determined as the appropriate cutoff value. Patients with SUVmax >6 in all lesions had a significantly lower median survival time than patients with SUVmax ≤6 (16.7 months [95% CI: 11.691–21.709] vs. 24.3 months [95% CI: 18.32–29.02], log rank value = 5.034, $p = 0.025$) (Figure 3(a)).

The SUVmax of the primary lung lesions was divided into eight groups as follows: 0–2, 2–4, 4–6, 6–8, 8–10, 10–12, 12–14, and >14. According to the median survival time of the patients in each group (Table 4) and the survival curve (Figure 2(b)), SUVmax = 6 was determined as the appropriate cutoff value. Patients whose primary lung lesions showed SUVmax >6 had significantly lower median survival time than those who showed SUVmax ≤6 (16.4 months [95% CI: 12.465–20.335] vs. 24.3 months [95% CI: 18.685–29.848], log rank value = 5.849, $p = 0.016$) (Figure 3(b)).

The optimal SUVmax cutoff for both primary lung lesions and all lesions was six. This cutoff could be used to better distinguish patients and predict prognosis. The

TABLE 1 Correlation between patient clinical characteristics and SUVmax

Variable		No.	SUVmax of primary lung lesion	t-value	*p*-value	SUVmax of all lesions	t-value	*p*-value
Age	≥65	71	9.1 ± 6.1	1.542	0.126	10.1 ± 6.1	0.555	0.58
	<65	86	7.8 ± 4.3			9.6 ± 4.5		
Sex	Male	98	8.1 ± 5.3	0.979	0.329	9.9 ± 5.6	0.456	0.649
	Female	59	8.9 ± 4.9			9.5 ± 4.8		
Smoking history	Yes	63	8.1 ± 5.1	0.532	0.595	10.2 ± 5.6	−0.699	0.486
	No	94	8.6 ± 5.2			9.6 ± 5.1		
Weight loss	Yes	22	9.4 ± 5.5	0.945	0.346	12 ± 5.1	2.079	0.039
	No	135	8.2 ± 5.1			9.6 ± 5.3		
PS score	0–1	146	8.6 ± 5.2	1.774	0.078	9.8 ± 5.3	0.276	0.783
	≥2	11	5.7 ± 3.6			9.4 ± 5.0		
Lesion size	≥3 cm	95	10.2 ± 5.4	6.709	<0.001	11.2 ± 5.5	4.754	<0.001
	<3 cm	61	5.6 ± 3.3			7.6 ± 4.1		
Histology	Squamous	20	9.8 ± 6.8	0.995	0.33	12.1 ± 6.1	2.092	0.038
	Nonsquamous	137	8.2 ± 4.9			9.5 ± 5.1		
EGFR mutation or ALK rearrangement	Yes	51	7.9 ± 4.8	0.848	0.398	9.0 ± 4.6	1.257	0.211
	No	106	8.6 ± 5.4			10.2 ± 5.6		
TMN stage	M1a	38	8.4 ± 3.8	0.064	0.063	8.8 ± 4.4	−1.315	0.094
	M1b	119	8.4 ± 5.6			10.1 ± 5.5		
Bone metastasis	Yes	99	8.1 ± 5.4	0.897	0.371	9.6 ± 5.3	0.627	0.532
	No	58	8.9 ± 4.8			10.2 ± 5.3		
Adrenal metastasis	Yes	32	9.2 ± 6.3	0.838	0.407	11.0 ± 5.6	1.461	0.146
	No	125	8.2 ± 4.9			9.5 ± 5.2		
Pleural metastasis	Yes	49	9.0 ± 5.6	1.046	0.297	10.0 ± 5.7	0.307	0.759
	No	106	8.1 ± 5.0			9.7 ± 5.2		
Lymph node metastasis	Yes	102	8.9 ± 5.3	1.671	0.097	9.8 ± 5.5	0.025	0.98
	No	55	7.5 ± 4.8			9.8 ± 4.9		
Liver metastasis	Yes	18	10.1 ± 6.2	1.471	0.143	10.9 ± 5.7	0.952	0.342
	No	139	8.2 ± 5.0			9.7 ± 5.2		
Intrapulmonary metastasis	Yes	51	9.3 ± 5.1	1.622	0.107	10.0 ± 4.9	0.359	0.72
	No	105	7.9 ± 5.2			9.7 ± 5.5		
Metastatic numbers	≥2	78	8.9 ± 5.8	1.47	0.145	10.7 ± 5.5	2.413	0.017
	<2	77	7.7 ± 4.1			8.7 ± 4.7		
Number of treatment regimens	1	76	9.3 ± 5.5	2.227	0.027	10.5 ± 5.5	1.566	0.119
	≥2	81	7.5 ± 4.7			9.2 ± 4.7		
SUVmax of metastatic lesion higher than primary lung lesion	Yes	44	4.8 ± 3.4	6.018	<0.001	9.5 ± 5.5	0.412	0.681
	No	113	9.8 ± 5.1			9.9 ± 5.2		

Abbreviations: ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; PS, performance status; SUV, standardized uptake value; TMN, tumor/node/metastasis.

TABLE 2 Comparison between the SUVmax of primary lung lesions and metastatic lesions

Metastatic lesions	No.	SUVmax of metastatic lesion	SUVmax of primary lung lesion	t-value	*p*-value
Bone	99	6.0 ± 4.1	8.1 ± 5.4	−3.124	0.002
Adrenal	32	5.3 ± 4.5	9.2 ± 6.3	−2.872	0.006
Pleura	50	4.8 ± 4.3	9.0 ± 5.5	−4.222	<0.001
Mediastinal lymph nodes	101	6.0 ± 3.7	8.8 ± 5.3	−4.37	<0.001
Liver	17	5.9 ± 4.2	9.8 ± 6.2	−2.165	0.038
Intrapulmonary	50	3.1 ± 2.3	9.2 ± 5.1	−7.788	<0.001

TABLE 3 Correlation between the SUVmax of all lesions and overall survival

SUVmax group	Cases	Median survival time	95% CI lower limit	95% CI upper limit
2–4	15	30.0	7.118	52.815
4–6	21	24.3	9.945	38.588
6–8	35	18.1	13.044	23.089
8–10	28	23.0	11.827	34.106
10–12	15	16.5	1.318	31.615
12–14	10	18.0	3.814	32.119
>14	33	12.0	6.787	17.146

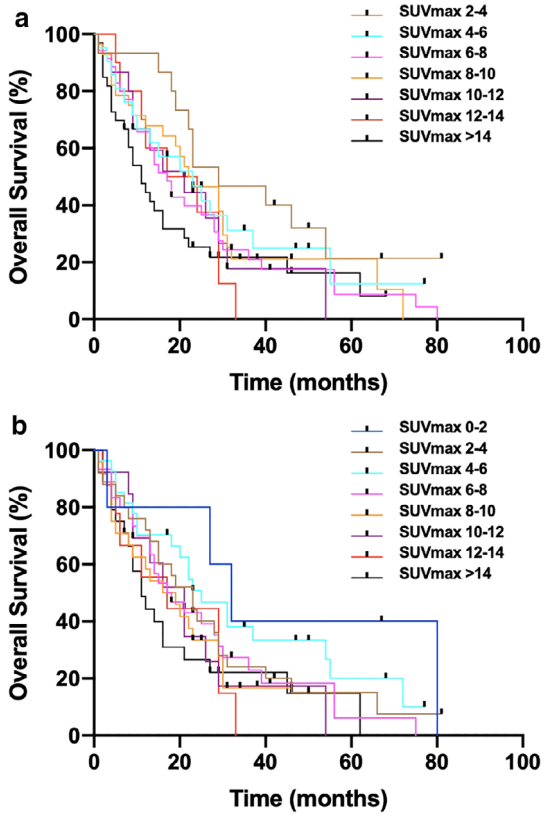

FIGURE 2 (a) The Kaplan–Meier survival estimates by SUVmax groups of all lesions. Analysis time refers to months of all lesions. (b) The Kaplan–Meier survival estimates by SUVmax groups of primary lung lesions. Analysis time refers to months

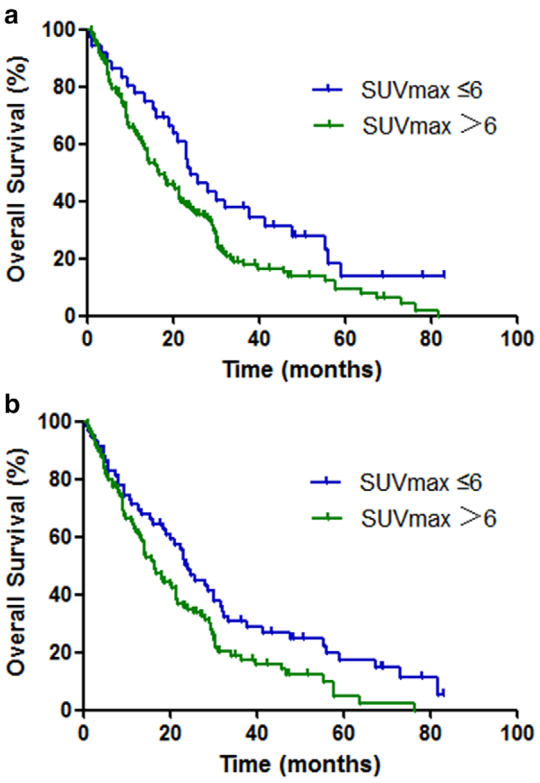

FIGURE 3 (a) Survival curves for the two subgroups of the highest SUVmax of all lesions according to the separation into SUVmax≤6/>6. (b) Survival curves for the two subgroups of the SUVmax of primary lung lesions according to the separation into SUVmax≤6/>6

TABLE 4 Correlation between the SUVmax of primary lung lesions and overall survival

SUVmax group	Cases	Median survival time	95% CI lower limit	95% CI upper limit
0–2	5	33.4	21.806	44.994
2–4	26	23.3	16.179	30.421
4–6	28	23.1	17.349	28.784
6–8	29	18.6	8.544	28.656
8–10	25	20.4	12.642	28.092
10–12	11	13.5	5.698	21.235
12–14	9	18.0	0	37.056
>14	24	12.0	6.779	17.154

SUVmax of the primary lung lesions was used for further analysis.

Analysis of factors influencing survival

Univariate analysis showed that survival was correlated with sex, size of the primary lung cancer lesion (≤3 cm vs. >3 cm), *EGFR* mutation or ALK rearrangement, the SUVmax of the primary lung cancer lesion (≤6 vs. >6), and the number of treatment regimens (Table 5). Specifically, the survival time was significantly longer among female patients ($p = 0.021$), those with *EGFR* mutations or tumors with ALK rearrangement ($p < 0.001$), size of primary lung lesions <3 cm ($p = 0.006$), SUVmax of primary lung lesions ≤6 ($p = 0.016$), and patients who received ≥2 treatment regimens ($p = 0.001$). However, survival was not correlated with age, loss of weight, smoking status, PS score, histology, TNM stage, metastatic lesions, or number of metastases ($p > 0.05$).

TABLE 5 Results of univariate analyses by log-rank test: Factors influencing effect on survival

Variable		No.	Median survival time (m)	95% CI lower limit	95% CI upperlimit	F (X^2)	*p*-value
Age	≥65	71	23.4	14.445	32.355	0.194	0.660
	<65	86	18.0	12.400	23.733		
Sex	Male	98	16.5	12.485	20.448	5.304	0.021
	Female	59	23.1	15.772	30.362		
Smoking history	Yes	63	16.7	10.506	22.894	3.104	0.078
	No	94	21.0	14.055	27.945		
Weight loss	Yes	22	16.7	11.346	22.054	1.829	0.176
	No	135	21.4	16.405	26.461		
PS score	0–1	146	20.4	15.544	25.189	3.089	0.079
	≥2	11	2.5	0	6.022		
Primary lung cancer lesion size	≥3 cm	95	16.4	12.265	20.535	7.597	0.006
	<3 cm	61	23.3	15.912	30.688		
Histology	Squamous	20	16.4	11.838	20.895	0.600	0.439
	Nonsquamous	137	20.1	15.398	24.802		
EGFR mutation or ALK rearrangement	Yes	51	29.5	25.700	33.366	18.707	<0.001
	No	106	14.0	10 337	17.730		
Stage	M1a	38	21.0	13.503	28.497	0.000	0.984
	M1b	119	18.6	13.352	23.848		
Bone metastasis	Yes	99	18.1	11.990	24.144	0.003	0.954
	No	58	21.5	18.493	24.507		
Adrenal metastasis	Yes	32	12.8	6.379	19.221	2.964	0.085
	No	125	21.5	17.495	25.505		
Pleural metastasis	Yes	49	21.0	17.114	24.886	0.000	0.993
	No	106	18.6	11.776	25.424		
Lymph node metastasis	Yes	102	16.7	11.112	22.288	3.705	0.054
	No	55	23.3	13.529	33.071		
Liver metastasis	Yes	18	10.8	6.434	15.166	0.684	0.408
	No	139	21.4	17.689	25.178		
Intrapulmonary metastasis	Yes	52	20.1	12.850	27.350	2.083	0.149
	No	105	19.0	12.930	25.070		
Metastatic numbers	≥2	78	16.4	9.837	22.963	0.003	0.955
	<2	77	21.5	17.370	25.630		
SUVmax of primary lung lesion	≤6	98	24.3	18.685	29.848	5.849	0.016
	>6	59	16.4	12.465	20.335		
Number of treatment regimens	1	76	14.0	10.412	17.654	12.070	0.001
	≥2	81	28.1	21.399	34.801		
SUVmax of metastatic lesion higher than primary lung lesion	Yes	44	18.4	6.380	30.420	0.407	0.523
	No	113	20.1	15.810	24.390		

Abbreviations: ALK, anaplastic lymphoma kinase; CI, confidence interval; EGFR, epidermal growth factor receptor; SUV, standardized uptake value.

The Spearman's correlation analysis showed an interaction between SUVmax of the pulmonary lesion and lesion size (R-value = 0.578, $p < 0.001$). Therefore, only four factors were included in the Cox multivariate analysis: sex, *EGFR* mutation or ALK rearrangement, SUVmax of the primary lung lesion, and number of treatment regimens. In the multivariate analysis, survival was still correlated with sex ($p = 0.026$), *EGFR* mutation or ALK rearrangement ($p = 0.001$), SUVmax of the primary lung cancer lesion (≤6 vs. >6) ($p = 0.036$), and number of treatment regimens ($p = 0.029$). Patients with SUVmax ≤6 had a mortality risk of 0.651 (HR = 0.651, 95% CI: 0.436–0.972, Wald value, 4.400, $p = 0.036$) compared with those with SUVmax >6.

DISCUSSION

The evaluation of SUV is intuitive and convenient, but whether SUVmax provides additional prognostic value in addition to the TNM stage remains to be explored.[11,12,21] Previous studies showed that higher SUVmax was associated with worse overall survival, but these studies were mostly based on early stage lung cancer, and results have been conflicting.[3,5,17,22] Furthermore, some studies reported that SUV has no prognostic value independent of the TNM stage in advanced lung cancer.[11,21,23] Hoang et al.[23] suggested that SUV cannot predict prognosis in patients with advanced lung cancer (stage IIIB and stage IV) because a continuous increase in SUV does not increase the risk of mortality. In contrast, Paesmans et al.[21] reported that SUV is an independent predictor for patients with stage I–III NSCLC but not for those with stage IV disease. The possible reason for this may be that the median survival for stage IV patients is only 12 months. The short survival period resulted in failure to identify any independent prognostic value for SUVmax. Our study confirmed that SUVmax is a prognostic factor for overall survival in patients with advanced lung cancer. Our analysis showed that patients with *EGFR* mutation or ALK rearrangement accounted for 32.5% of the patients in our study, and the development of targeted therapy has resulted in significantly prolonged survival in patients with advanced NSCLC.[24,25] A high SUVmax indicates a worse severity of malignancy and more aggressive tumor proliferation.[5,26] Because of these aggressive biological behavioral characteristics, patients with a high SUVmax lose the opportunity to receive second-line treatment. Thus, the benefit from a variety of treatments and the overall survival in these patients is limited.[27] Patients who received only first-line treatment had a significantly greater SUVmax than did those who received more than one treatment regimen. The results appear to support this view. Studies on the optimal SUV threshold have also reported inconsistent findings.[2,3,5,12,14,18,28,29] In this study, the median survival time and survival curves showed that an SUVmax of six was the optimal cutoff value. Meanwhile, Detterbeck et al.[30] suggested that the correlation between SUV and prognosis is a gradual association without an absolute threshold.

With regard to the association between SUVmax and clinical factors, our study found that the highest SUVmax of all lesions significantly increased among patients with loss of weight, primary lung cancer lesion size >3 cm, and number of metastases ≥2. The higher SUV may indicate more severe malignancy, shorter doubling time, and more aggressive invasion.[16,26] This would lead to a larger malignant lesion,[2,3,7,10,13,26] more extensive organ involvement, and more obvious weight loss.[2,19,31]

In addition, we also found that the SUVmax of all lesions was markedly higher in patients with squamous cell carcinoma than in patients with nonsquamous cell carcinoma. Previous studies have shown that SUV was correlated with histology, with the SUV of squamous cell carcinoma being greater than that of adenocarcinoma.[2,7,9,10,21,32] In contrast, we found no significant difference in the histology and SUVmax of primary lung cancer lesions. This may be because squamous carcinoma is a central lung cancer and thus lymph node enlargement is common and more likely to form in the cavity, mixed with obstructive pneumonia and atelectasis. Previous studies have also shown that the SUV of poorly differentiated malignant lesions was higher than that of well-differentiated tumors.[23] We could not perform a more in-depth analysis in this study because the number of cases of squamous cell carcinoma was less than that of adenocarcinoma. Further studies with a well-balanced distribution of histological tumor types are needed to evaluate the correlation between tumor histological types and SUV.

Our study has some limitations that should be considered. First, it was a retrospective study conducted only in a single center. Therefore, further studies with a larger sample size and conducted in a multicenter setting are needed to confirm our findings. Second, the estimated SUVmax of primary lung cancer lesions was influenced by various factors; including blood glucose levels of patients, imaging time, reconstruction method, maximum absorption value, and analysis by the same observer. However, it is impossible to guarantee that all patients will receive PET/CT imaging under the same conditions in the real world. Third, the inclusion of only patients who received treatment may have led to a selection bias. Fourth, this study was performed between 2012 and 2016. Immune checkpoint inhibitors (ICIs), which have been a breakthrough in the treatment of lung cancer, have not yet been approved in China, and only a few have entered clinical studies. Therefore, this study only reflects the effects of PET/CT on the prognostic effects of lung cancer in the age of chemotherapy, and the value of PET/CT in the age of immunotherapy needs to be further explored.

In conclusion, we found that pretreatment SUVmax of the primary lung lesion on PET/CT was significantly associated with prognosis in patients with advanced NSCLC. SUVmax of the primary lung lesions had a stronger relationship with survival than the highest SUVmax among all lesions. The optimal SUVmax cutoff was six, and patients with SUVmax >6 had a significantly worse prognosis than did those with a SUVmax ≤6. Thus, further prospective studies are warranted to confirm the feasibility of PET/CT imaging-guided treatments in patients with stage IV NSCLC.

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CONFLICT OF INTEREST

The authors declare no competing interests.

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