Is there a cut-off value for standardized uptake values in positron emission tomography for predicting response to treatment and survival in patients with advanced non-small cell lung cancer? Single center experience

B.B. Oven Ustaalioglu¹, M. Gumus¹, A. Bilici¹, M. Seker¹, R. Ustaalioglu², U. Kefeli¹, T. Salepci¹, N. Canpolat³, A. Mayadagli⁴, I. Dogusoy²

¹Department of Medical Oncology, ⁴Department of Radiation Oncology, Dr. Lutfi Kirdar Kartal Education and Research hospital, Istanbul; ²Department of Thoracic Surgery, Dr. Siyami Ersek Cardiothoracic Surgery Hospital, Istanbul; ³Department of Nuclear Medicine, Kosuyolu Education and Research hospital, Istanbul, Turkey

Summary

Purpose: Positron emission tomography (PET) is an important imaging technique for the diagnosis and staging of patients with non-small cell lung cancer (NSCLC). In this study, we evaluated the standardized uptake values (SUV) of PET in NSCLC patients to determine whether there was a cut-off value for predicting response to treatment and survival.

Methods: We retrospectively analyzed 149 patients with locally advanced NSCLC. All the patients were staged by PETcomputerized tomography (CT) after diagnosis. ¹⁸ fluoro-2deoxyribose (FDG) was used as the PET tracer. Univariate and multivariate analyses were performed to detect whether any prognostic factors were related to response to treatment.

Results: The median patient age was 60 years and the median follow-up time 10.3 months. One-year progression-free survival (PFS) and overall survival (OS) rates were 31%

Introduction

Lung cancer is the leading cause of cancer-related deaths among both men and women [1-4]. Most patients present with advanced stage and a 5-year survival rate of 14% [5,6]. Two-thirds of patients with NSCLC are usually diagnosed at advanced stage (IIIB and IV) [3,6,7]. PET is the most important radiological imaging technique for staging and evaluation of response to treatment of patients with NSCLC [1,4,8,9]. In an effort to improve survival, many prognostic factors such as stage at presentation, Eastern Cooperative Oncology Group (ECOG) performance status (PS), weight loss and molecular markers have been used [5]. NSCLC is characterand 58.7%, respectively. The median OS was 15.4 months. Stage, sex and response to treatment were important factors for OS and PFS. We defined a cut-off value for SUVmax (the highest standardized uptake value for all cross sectional areas) as 10.8 by using ROC analysis. Multivariate analysis identified response to treatment as the most significant (p<0.05) prognostic factor for OS. Logistic regression analysis showed that SUVmax and weight loss were important for response to treatment.

Conclusion: Multivariate analysis indicated that whilst response to treatment was an important factor for predicting survival, the SUVmax was also significant for determining response to therapy and a cut-off value for SUVmax was defined as 10.8.

Key words: cut-off value, metastasis, non-small cell lung cancer, PET, prognosis, SUVmax

ized by carbohydrate metabolic derangement, which is a poor prognostic factor for survival [10]. PET measures increased glycolysis in the tumor quantitatively after administration of FDG [11]. The FDG uptake in NSCLC cells, which is measured semi-quantitatively as SUV, correlates with the growth rate and proliferation capacity of the tumor [5,6,10,12]. The prognostic importance of SUV has been reported previously [1,2,11,13,14] and different retrospective studies also showed that there was significant relationship between FDG uptake within the primary tumor and survival [15]. In all of these studies patients were at an early stage of the disease and could be treated with surgery or radiotherapy.

In our study we attempted to find out whether

Correspondence to: Bala Basak Oven Ustaalioglu, MD. Selimiye Mah, Sair Nesimi sok, Kardesler Apt, No: 1, Daire:4, 34668, Uskudar, Istanbul, Turkey. Tel: +90 505 540 16 30, E-mail: basakoven@yahoo.com

there was any cut-off value for SUVmax of the primary tumor that could predict response to treatment or survival in patients with advanced NSCLC. In addition, we evaluated whether there was any association between the SUV cut-off value and prognostic factors such as stage, PS, histological type and weight loss.

Methods

Patients

One hundred and forty-nine patients with NSCLC treated and followed up between September 2005 and August 2008, at the Department of Medical Oncology, Dr. Lutfi Kirdar Research and Education hospital were retrospectively analyzed. Patients were included in the study if PET/CT had been performed for NSCLC staging. The following patient and disease characteristics were recorded and analyzed as possible prognostic factors for response to treatment and survival: age, sex, weight loss, smoking history, tumor cell type, disease clinical stage, type of chemotherapy and PS. The patients were evaluated by physical examination, complete blood count, renal and liver function tests, thoracic CT and bronchoscopy or transthoracic needle biopsy followed by PET/CT for staging. Bone scanning and magnetic resonance imaging (MRI) of the brain were only performed in case where the symptoms were suggestive of specific metastases.

PET/CT

Whole-body imaging was carried out using a combined PET/CT scanner (Biograph, Sensation 16 PET/ CT system, Siemens Dual, LSO). All patients fasted for 12 hours before PET imaging and their blood glucose levels were obtained prior to tracer injection. Patients with a fasting glucose level >200 mg/dl before PET were excluded from the analysis. After injection of 6.5 MBq/kg (370-555 MBq) FDG, the patients rested on a comfortable chair during the FDG uptake period. Between 60 and 120 min after tracer injection, attenuationcorrected images were acquired with a scanner (axial field of view of 10.1 cm and resolution of approximately 5 mm). A CT scan was performed prior to the acquisition of PET data in a single step with the patients in the supine position for accurate anatomical localization. CT scanning was carried out from the top of the skull through the upper thighs in a single imaging procedure. During the scan, patients were asked to maintain shallow respiration. Thereafter, an emission PET scan was acquired in the two-dimensional mode over the same anatomical regions. Attenuation-corrected PET images, CT scans and co-registered PET/CT images were interpreted using a dedicated image fusion workstation and a final consensus was reached for each patient. The interpretation was performed by a nuclear medicine physician. For the determination of SUV, the ROI (region of interest) was automatically placed on the transaxial, coronal and vertical sections around the focal FDG uptake zone in the primary tumor. The FDG uptake in this ROI was semi-quantified by calculating the SUV in each pixel according to the following formula: SUV=mean ROI uptake (mCi/mL)/injected dosemCi/body weight (g) by a computer program [5,10]. The highest standardized uptake value for all cross sectional areas (vertical, coronal or transaxial) was termed as SUVmax.

Staging, treatment and follow-up

All tumors were staged by PET/CT according to the tumor-node-metastasis (TNM) system adopted by the American Joint Committee on Cancer Staging [16]. The clinical stage was used because all patients were inoperable or metastatic so surgery could not be performed.

After PET/CT most of the patients were treated with platinum-based chemotherapy. All of the patients underwent PET/CT for staging when diagnosis of NSCLC was confirmed pathologically and were followed for a median of 10.3 months (range of 2-36). Follow-up data were registered and a chest CT was performed every 3 months. OS was defined as the time between the date of pathological diagnosis to the date of death from all causes. Living patients were censored at the last follow-up visit. PFS was defined as the date on which response to chemotherapy was first registered to the date of disease progression or recurrence or to the date of death or last known contact. Using the Response Evaluation Criteria in Solid Tumors (RECIST) criteria, the response to therapy was assumed as partial when the tumor size decreased by 30%, as assessed radiologically. If the tumor size had not changed after treatment the disease was defined as stable and if the tumor size increased by 20%, the disease was defined as progressive [17].

Statistical analysis

Statistical analysis was performed using SPSS-15 (SPSS Inc., Chicago, IL). Survival was calculated using the Kaplan-Meier method and the prognostic factors were compared using the log-rank test in univariate analysis. Hazard ratios (HR) with 95% confidence intervals (CI) were also calculated. All p-values were two-sided in the tests and p-values ≤0.05 were considered statistically significant. Multivariate analysis was carried out using the Cox proportional hazards model

to assess the effect of prognostic factors on survival. In addition, binary logistic regression analysis in the multivariate analysis was performed to detect independent factors predicting response to treatment. A receiver operating characteristics (ROC) curve was used to indicate the variability of sensitivity and specificity for cut-off points of the SUV values of PET.

Results

A total of 149 patients with advanced (IIIB or IV) NSCLC, staged using PET/CT, were retrospectively analyzed. Their median age was 60 years (range 38-83). Ninety-three (62%) patients were younger than 65 years and 84% of the patients were male. Approximately 84% of the patients were smokers. When lung cancer was diagnosed, over 80% of patients had an EC-OG PS of 0-1. Fifty-six (38%) patients complained of weight loss before diagnosis. According to TNM classification, 50% of the patients had stage IV and 50% stage IIIB disease. The median SUVmax of the primary tumor, mediastinal lymph nodes and metastases were 13.9, 10 and 12.2, respectively. While approximately half of the NSCLC subtypes could not be determined, the others were squamous cell carcinoma (27%) and adenocarcinoma (28%). The median follow-up time was 10.3 months (range 2-35). The patients were treated with a median of 6 cycles of chemotherapy (range 2-8) with carboplatin or cisplatin-based combination chemotherapy (carboplatin-paclitaxel, carboplatin-docetaxel, cisplatin-paclitaxel, cisplatin-docetaxel, cisplatin-gemcitabine) (43% vs. 57%, respectively). In addition, concomitant (68%) and sequential (32%) radiotherapy was given to 72% of stage IIIB patients. Partial



Figure 1. ROC curve at different cut-off points of SUVmax.



Figure 2. Kaplan-Meier curves for overall survival of patients with advanced stage NSCLC according to SUVmax > 10.8 and ≤ 10.8 .

response was obtained in 62% of the patients, whereas the remaining (38%) had stable or progressive disease. One- and 2-year PFS rates were 31.2% and 11.3%, respectively. The median PFS time was 6.4 months. One- and 2-year OS rates were 58.7% and 29.5%, respectively. The median OS was 15.4 months.

Two types of analysis were performed. The correlations between SUVmax and the other known prognostic factors, such as age, sex, weight loss, PS, chemotherapy regimen and survival, were firstly examined by univariate analysis. After this, the most discriminative cut-off point of SUVmax was calculated using ROC analysis as 10.8 in patients with advanced NSCLC (AUC=0.610; p=0.018; Figure 1). The sensitivity and specificity of 10.8 as the SUV cut-off value to predict response to treatment were 76.1% and 54.4%, respectively (95% CI 52.7-68.9). The results of univariate



Figure 3. Kaplan-Meier curves for progression-free survival of patients with advanced stage NSCLC according to SUVmax > 10.8 and ≤ 10.8 .

analysis for OS and PFS are listed in Table 1. Stage, response to treatment and sex proved to be significant for OS (p < 0.05). In addition, sex, weight loss and response to treatment were significantly related to PFS (p < 0.05). However, the cut-off SUV max value (>10.8 vs. \leq 10.8) was not related to OS (p=0.41) or PFS (p=0.81) (Figures 2 and 3). Although patients with a SUVmax >10.8 had better PFS than those with a SUVmax <10.8 (8.1 vs. 6.3 months), this was not statistically significant (p=0.81). In addition, better response rates were detected for primary tumor with SUV max >10.8 than for SUV max ≤ 10.8 (p < 0.05). Another factor found to predict response to treatment was stage (IIIB vs. IV) (p=0.024; Table 2). In multivariate logistic regression analysis, weight loss and SUVmax were found to be important factors for predicting response to treatment (p < 0.05; Table 3). On the other hand, when using Cox regression analysis no factor predicted survival, except response to treatment (p=0.0009; Table 4).

Discussion

To the best of our knowledge, this is the first study to have investigated whether there was a cut-off value of SUVmax in PET/CT which could predict response to treatment and survival of NSCLC patients. Our results indicated that while response to treatment was an important factor for predicting survival by multivariate analysis, the SUVmax was also a significant factor for determining response to therapy with a cut-off value of 10.8.

Most patients with NSCLC present at an advanced stage (III or IV) [7,9] and their median survival ranges from 4 to 6 months. Recently, with new chemotherapy regimens, the median OS reached 7-10 months and the 1-year survival increased to 35-40%. The platinum-based regimens are standard for chemotherapy [9]. Most of the patients with NSCLC who were referred to our department were at an advanced stage (IIIB 45% and IV 55%) and were staged using PET/CT.

Characteristics	n (%)	OS (months)	p-value	PFS (months)	p-value
Age (years)			0.13		0.32
<65	93 (62.4)	16.2		7.7	
≥65	56 (37.6)	13.3		5.5	
SUV of tumor mass	()		0.41		0.81
≤ 10.8	53 (35.6)	12.1		6.3	
>10.8	96 (64.4)	16.5		8.1	
Gender			0.024		0.047
Female	23 (15.4)	25.6		12.6	
Male	126 (84.6)	13.3		6	
Smoking			0.70		0.64
Smoker	125 (83.9)	15.4		7.0	
Non-smoker	24 (16.1)	25.6		6.0	
ECOG PS			0.12		0.52
0-1	126 (84.6)	16		7.1	
≥ 2	23 (15.4)	9.4		6	
Weight loss			0.142		0.032
Present	56 (37.6)	15.4		5.5	
Absent	93 (62.4)	14.1		8.3	
Histopathology			0.70		0.59
Squamous cell	40 (26.8)	13.1		7.5	
Adenocarcinoma	42 (28.2)	16.6		5.3	
Non-small cell, NOS	67 (45.0)	15.4		6.3	
Stage			0.022		0.21
IIIB	57 (38.3)	21.1		9.8	
IV	92 (61.7)	11.9		5.9	
Platinum			0.61		0.84
Cisplatin	61 (43.0)	16.6		6.8	
Carboplatin	81 (57.0)	13.1		6.4	
Response			0.000		< 0.001
PR	92 (61.7)	23.8		11.2	
PD/SD	57 (38.3)	6.4		3.7	

Table 1. Univariate analysis of the patient and disease characteristics in relation to OS and PFS

OS: overall survival, PFS: progression free survival, PD: progressive disease, SD: stable disease, PR: partial response, NOS: not otherwise specified, PS: performance status

Age (years) < 65 $34 (59.6)$ $59 (64.1)$ ≥ 65 $23 (40.4)$ $33 (35.9)$ SUV of tumor mass ≤ 10.8 $31 (54.4)$ $22 (23.9)$ > 10.8 $26 (45.6)$ $70 (76.1)$ Sex $Female$ $6 (10.5)$ $17 (18.4)$ Male $51 (89.5)$ $75 (81.6)$ Smoking $5moker$ $77 (8.7)$	p-value	
< 65 $34 (59.6)$ $59 (64.1)$ ≥ 65 $23 (40.4)$ $33 (35.9)$ SUV of tumor mass $= 10.8$ $31 (54.4)$ $22 (23.9)$ > 10.8 $26 (45.6)$ $70 (76.1)$ Sex $=$ $=$ Female $6 (10.5)$ $17 (18.4)$ Male $51 (89.5)$ $75 (81.6)$ Smoking $=$ $=$ Smoker $=$ $48 (84.2)$ $=$	0.6	
$ \ge 65 \qquad 23 (40.4) \qquad 33 (35.9) \\ SUV of tumor mass \\ \le 10.8 \qquad 31 (54.4) \qquad 22 (23.9) \\ > 10.8 \qquad 26 (45.6) \qquad 70 (76.1) \\ Sex \\ Female \qquad 6 (10.5) \qquad 17 (18.4) \\ Male \qquad 51 (89.5) \qquad 75 (81.6) \\ Smoking \\ Smoker \qquad 48 (84.2) \qquad 77 (8.7) \\ \end{cases} $		
SUV of tumor mass ≤ 10.8 $31 (54.4)$ $22 (23.9)$ > 10.8 $26 (45.6)$ $70 (76.1)$ Sex $76 (10.5)$ $17 (18.4)$ Male $51 (89.5)$ $75 (81.6)$ Smoking $77 (8.7)$		
$ \leq 10.8 \qquad 31 (54.4) \qquad 22 (23.9) \\ > 10.8 \qquad 26 (45.6) \qquad 70 (76.1) \\ Sex \\ Female \qquad 6 (10.5) \qquad 17 (18.4) \\ Male \qquad 51 (89.5) \qquad 75 (81.6) \\ Smoking \\ Smoker \qquad 48 (84.2) \qquad 77 (8.7) \\ \end{cases} $	0.000	
> 10.8 26 (45.6) 70 (76.1) Sex Female 6 (10.5) 17 (18.4) Male 51 (89.5) 75 (81.6) Smoking Smoker 48 (84.2) 77 (8.7)		
Sex 6 (10.5) 17 (18.4) Male 51 (89.5) 75 (81.6) Smoking 77 (8.7)		
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Male 51 (89.5) 75 (81.6) Smoking 75 (84.6) 77 (8.7)		
Smoking Smoker 48 (84 2) 77 (8 7)		
Smoker 48 (84 2) 77 (8 7)	0.93	
Non-smoker 9 (15.8) 15 (16.3)		
ECOG PS	0.16	
0-1 45 (78.9) 81 (88.0)		
≥ 2 12 (21.1) 11 (12.0)		
Weight loss	0.05	
Present 27 (47.4) 29 (31.5)		
Absent 30 (52.6) 63 (68.5)		
Histopathology	0.229	
Squamous cell carcinoma 11 (19.3) 29 (31.5)		
Adenocarcinoma 19 (33.3) 23 (25.0)		
Non-small cell, NOS 27 (47.4) 40 (43.5)		
Stage	0.024	
IIIB 15 (26.3) 42 (45.7)		
IV 42 (73.7) 50 (54.3)		
Type of platinum	0.38	
Cisplatin 20 (37.7) 41 (46.1)		
Carboplatin 33 (62.3) 48 (53.9)		

Table 2. Univariate analysis of the patient and disease characteristics in relation to response to treatment

CR: complete response, PR: partial response, PD: progressive disease, NOS: not otherwise specified, PS: performance status

Table 3. Multivariate binary logistic regression analysis of various clinicopathological factors in the prediction of response to treatment in patients with advanced NSCLC

95% CI
0.51-32.7
0.53-4.12
0.09-1.79
0.14-4.16
0.26-3.98
0.13-0.92
0.78-5.88
0.43-2.99

HR: hazard ratio, CI: confidence interval, PS: ECOG performance status

 Table 4. Multivariate Cox regression analysis of various clinicopathological factors in the prediction of overall survival in patients with advanced NSCLC

Factors	Wald	Р	HR	95% CI
Gender (male vs. female)	2.02	0.15	0.30	0.61-1.56
Age ($<65 \text{ vs.} \ge 65 \text{ years}$)	0.00	0.99	1.00	0.51-1.94
SUVmax (≤10.8 vs. >10.8)	2.2	0.13	0.59	0.30-1.16
Smoking (present vs. absent)	1.03	0.30	0.50	0.13-1.89
PS (0-1 vs. >2)	0.15	0.69	0.83	0.33-2.06
Weight loss (present vs. absent)	1.10	0.29	1.38	0.75-2.56
Stage (IIIB vs. IV)	0.14	0.70	0.87	0.43-1.74
Chemotherapy (cisplatin vs. carboplatin)	0.09	0.75	0.90	0.49-1.66
Response to treatment (PR vs. SD/PD)	27.64	0.00	6.56	3.25-13.23

HR: hazard ratio, CI: confidence interval, PR: partial response, PD: progressive disease, SD: stable disease, PS: ECOG performance status

The role of PET/CT has increased in the diagnosis and staging of lung cancer [6]. Apart from staging, the SUVmax value in PET imaging is an important factor, predicting survival in NSCLC [6,15]. The increased glucose metabolism related to the biological aggressiveness of the tumor is measured by SUVmax on the PET [6]. Patients who bear more metabolically active tumors, as measured by SUV, are considered to have short survival times without treatment [6]. In the current study, we investigated if the SUVmax predicted survival or response to treatment in our patient population with advanced-stage NSCLC.

As several studies have suggested, the FDG uptake measured on the PET correlated with survival, although the cut-off values of SUV were different (Table 5). The importance of the SUVmax for primary tumors has been previously evaluated by several investigators [1,10,17-19]. In our study, the median SUVmax of the primary tumor, mediastinal lymph nodes and metastases were 13.9, 10 and 12.2, respectively. Our median SUVmax of the primary tumor was compatible with those reported in the literature. This study addressed the prognostic role of SUV cut-off values in patients with NSCLC. In a previous review, Jeong et al. showed that the cut-off value for SUV was 7 for survival. Using multivariate analysis the authors found that staging and a SUVmax higher than 7 were independent prognostic variables but histology was not a prognostic factor [6]. We found 10.8 as the cut-off value of SUVmax by using ROC analysis. Dhital et al. reported no significant correlation between tumor histology and SUV, and a SUV >20 was associated with worse prognosis. The authors noted that the 1-year survival rate was 75% when the SUV was <10 and 16% when the SUV was >20 [20]. We did not find any significant relationship between OS and the SUVmax value by univariate analysis (p=0.41). The 2-year OS rate was 42.4% and 38.6% for primary tumor with SUVmax <10.8 and >10.8, respectively. Higashi et al. also found that a SUV<5 was a better prognostic variable than stage in surgically resected NSCLC patients and that SUV was the most important independent factor for DFS by using multivariate analysis [21]. Van Baardwijk et al. showed that in operable NSCLC the best discriminative value of SUVmax was 8 and that patients with SUVmax >8 had a worse prognosis [22]. Vansteenkiste et al. retrospectively reviewed 82 patients with NSCLC treated by surgery. With resected tumors <3 cm and a SUVmax <7, the 2-year survival rate was 86%; in contrast, when the tumor had SUVmax >7, the 2-year survival was only 60% [10]. In the largest study to date, Cerfolio et al. retrospectively evaluated 315 patients and reported that a SUV max ≥10 was associated with a reduction in DFS in patients with stage IB NSCLC [19]. Although we showed that the tumor of patients with SUVmax >10.8 had a better PFS than those with SUV max ≤ 10.8 (8.1 vs. 6.3 months, respectively; p=0.81), this relationship was not confirmed by univariate analysis. Downey et al. showed that an one unit increase in SUVmax corresponded to a 7% increase in the risk of death and that the 2-year survival rates were 68 vs. 96% for SUVmax > 9 or < 9, respectively [12]. Inour study, multivariate Cox regression analysis showed that neither stage nor SUVmax were related to survival, which is incompatible with the results in the literature. This may have been due to the fact that our patients were at an advanced stage of disease, whereas the patients in the literature were mostly at an early stage of NSCLC. No studies in the English literature have analyzed inoperable NSCLC to define the relationship between response to treatment and the SUVmax of the primary tumor.

On the other hand, Sugawara et al. showed that FDG uptake of the tumor did not independently predict survival in 38 NSCLC patients [23]. Also, Vesselle

Study	No. of patients	Stage	SUV	Follow-up (mo)	2-year survival (%)	p-value	Reference
1	98	Ι	3.3	31	95 vs.80	0.008	7
2	125	I-III	7	19	83 vs.45	0.001	8
3	155	I-IV	10	21	52 vs.23	0.005	9
4	262	I-III	5	17	94 vs.65	0.02	10
5	315	IB-IIIA	10	26	84 vs.55	0.001	11
6	102	I-II	8	NA	NA	NA	14
7	100	I-IIIB	9	16	96 vs.68	< 0.01	15
8	73	I-IIIA	7	NA	NA	NA	16
9	57	I-IIIA	5	14	88 vs. 17 (5 yr)	0.0002	17
10	77	I-IIIA	20	NA	NA	NA	18
11	176	I-IV	15	NA	NA	NA	1
Present study	y 149	IIIB-IV	10.8	7.7	42.4 vs.38.6	0.412	

Table 5. Previous studies correlating SUV to survival

No: number, mo: month, NA: not available

et al. analyzed 208 potentially resectable NSCLC and did not find a relationship between SUVmax and poor outcome in patients undergoing resection [3]. No relationship was found between SUVmax and OS in 149 advanced stage NSCLC patients in the present study.

Ahuja et al. evaluated 155 patients with NSCLC imaged by PET. Using multivariate analysis, patients with a lesion > 3 cm with a SUV > 10 had a median survival less than 6 months, which was worse than those with a SUV <10 [5]. In a retrospective study of stage I-IIIB NSCLC patients separated into surgery and radiotherapy groups, Sasaski et al. found a prognostic significance of SUVmax if it was > 5 for OS and DFS, regardless of treatment modality or stage. The authors showed that 2-year OS and DFS rates were significantly better in patients with a low SUVmax (<5) than those with a high SUVmax (2-year OS rates 94 vs. 65%, respectively). Other factors including tumor size, N stage and clinical stage, but not weight loss, were also important prognostic factors for OS and DFS, but the SUVmax showed a stronger prognostic ability [24]. In the present study, although univariate analysis showed that sex, stage (IIIB vs. IV) and response to treatment predicted OS, in the multivariate analysis these factors were not significantly related to survival, except for response to treatment. The recent study performed by Al Sarraf et al. assessed 176 patients with NSCLC and reported that an early-stage tumor and adenocarcinoma had a lower SUVmax than an advanced stage squamous cell cancer, and that following resection, patients with a SUVmax <15 had significantly longer survival than those with a SUVmax ≥ 15 [1]. We did not find any relationship between histological type and survival. Our data remains consistent with previously published works, as summarized in Table 1. One important factor illustrated in Table 1 is the differences in the SUVmax cut-off values used for predicting survival. This variability can be a result of differences among NSCLC subtypes, stage, follow-up times and treatment modalities. In our study, we retrospectively analyzed patients with advanced NSCLC and we excluded patients who had undergone curative surgery or neoadjuvant chemotherapy. Moreover, we included patients with NSCLC if PET had been performed before treatment, so these selection criteria could have been responsible for the differences between our results and those from the literature.

Up until now, all of the studies had evaluated the relationship between SUVmax and OS or PFS in NSCLC. It is noteworthy that we also evaluated factors that affect the response to treatment by using logistic regression analysis. Stage and SUVmax values were significantly related to response to treatment (p < 0.01). While patients with a primary tumor SUVmax >10.8 had a partial response (PR) rate of 70%, those with a SUVmax ≤ 10.8 had a PR rate of 22% only. In addition, patients with a primary tumor SUVmax > 10.8 vs. ≤ 10.8 had progressive or stable disease rates of 26 vs. 31%, respectively (p <0.01).

In the literature, other prognostic factors such as age, weight loss, presence of mediastinal lymph nodes, PS and stage were also analyzed and Kramer et al. reported that stage and PS were the most significant prognostic factors for survival in NSCLC and that the others were not significant (p=0.051) [13]. Another study showed that patient age, tumor histology and tumor size had no impact on OS, however, a SUV>5 and the presence of mediastinal lymph nodes affected recurrence of the disease [25]. Although we did not show any correlation between histological type, age, weight loss or PS with OS, we found significant correlations between sex and weight loss for predicting PFS (p < 0.05). On the other hand, these relationships could not be confirmed with multivariate analysis. Also, there was no known standard cut-off value for SUVmax, and a further problem was which SUV value to use (mean or maximum SUV of primary tumor) [26]. We used the SUVmax for primary tumor in the present study.

This study showed that in advanced stage and metastatic NSCLC patients, a SUVmax >10.8 (obtainable by noninvasive imaging before treatment) was important for predicting response to treatment. This might be due to the higher proliferation rate of a primary tumor with a greater SUVmax, therefore these patients responded better to chemotherapy. Our study was limited by the number of available patients and did not allow the analysis of more variables. Additional larger and prospective studies are needed to avoid the biases inherent in retrospective studies. These results indicated that PET remains an accurate tool for the staging of lung cancer, but also that the SUV of primary tumors could be an important guide in decision making by providing information about response to treatment for patients with NSCLC. However, the best cut-off value which could be used universally remains unknown.

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