



# Maximum standardized uptake value-to-tumor size ratio in fluorodeoxyglucose F18 positron emission tomography/computed tomography: a simple prognostic parameter for non-small cell lung cancer

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## PURPOSE

By correcting the effect of tumor size on metabolic activity, the maximum standardized uptake value-to-tumor size ( $SUV_{max}$ :tumor size) ratio on fluorodeoxyglucose F18 positron emission tomography ( $^{18}F$ -FDG PET)/computed tomography (CT) scans can be a prognostic parameter of non-small cell lung cancer (NSCLC). The current study evaluates the prognostic value of  $SUV_{max}$ :tumor size ratio on pretreatment  $^{18}F$ -FDG PET/CT scans in patients with NSCLC. Furthermore, the  $SUV_{max}$ :tumor size ratio is compared with other established PET parameters.

## METHODS

This study included 108 patients with NSCLC who underwent pretreatment  $^{18}F$ -FDG PET/CT scans and curative lung surgery. The associations between the  $SUV_{max}$ :tumor size ratio and other conventional PET parameters were investigated. The recurrence-free survival according to the  $SUV_{max}$ :tumor size ratio was also analyzed. In addition, the  $SUV_{max}$ :tumor size ratio was compared according to postoperative pathologic findings.

## RESULTS

In total, 72 (66.7%) of the 108 participants presented with adenocarcinoma (ADC). Nineteen (17.6%) patients experienced recurrence during a median follow-up period of 32.3 months. The median  $SUV_{max}$ :tumor size ratio was 2.37 (1.23 for ADCs and 3.90 for other histologic types). The  $SUV_{max}$ :tumor size ratio was associated with  $SUV_{max}$  and mean SUV, as well as metabolic tumor volume and total lesion glycolysis. Patients with an  $SUV_{max}$ :tumor size ratio higher than the median had a worse recurrence outcome than those with an  $SUV_{max}$ :tumor size ratio lower than the median. Participants with ADC who presented with lymphovascular invasion had a higher  $SUV_{max}$ :tumor size ratio than those without. The presence of lymph node metastasis and advanced histologic grade were associated with a high  $SUV_{max}$ :tumor size ratio in patients with ADC.

## CONCLUSION

The  $SUV_{max}$ :tumor size ratio on pretreatment  $^{18}F$ -FDG PET/CT scans was associated with aggressive tumor behavior and poor outcome in NSCLCs, particularly ADC.

## CLINICAL SIGNIFICANCE

The  $SUV_{max}$ :tumor size ratio on pretreatment  $^{18}F$ -FDG PET/CT scans has a prognostic value in patients with NSCLCs, especially ADC.

## KEYWORDS

Cancer, fluorodeoxyglucose, lung, marker, positron emission tomography, prognosis

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Despite advancement in prevention, screening, and management in recent decades, non-small cell lung cancer (NSCLC) is among the leading causes of cancer-related mortality worldwide.<sup>1</sup> Fluorodeoxyglucose F18 (<sup>18</sup>F-FDG) positron emission tomography/computed tomography (PET/CT) is a widely used imaging tool for NSCLC management. The role of <sup>18</sup>F-FDG PET/CT scanning in determining the status of solitary pulmonary nodules (malignant or not), staging of lung cancer, planning of radiation therapy, and evaluating treatment response is well established.<sup>2</sup>

The <sup>18</sup>F-FDG PET/CT technique is used for prognostic prediction in NSCLC. Studies have shown that <sup>18</sup>F-FDG uptake is related to prognosis. Among these studies, one revealed the presence of histological invasion in early-stage adenocarcinoma (ADC).<sup>3</sup> In addition, in a meta-analysis of surgically resected NSCLC, a high standardized uptake value (SUV) and other metabolic parameters [e.g., metabolic tumor volume (MTV) and total lesion glycolysis (TLG)] were poor prognosis factors of disease-free survival and overall survival.<sup>4</sup> However, the prognostic significance of the maximum SUV (SUV<sub>max</sub>), a representative parameter of <sup>18</sup>F-FDG uptake in tumors, has not as yet been completely elucidated.<sup>5</sup> The inconsistent results can be attributed to various confounding factors affecting the SUV<sub>max</sub>.

The SUV<sub>max</sub>-to-tumor size ratio (SUV<sub>max</sub>:tumor size) on <sup>18</sup>F-FDG PET/CT scans was introduced to assess the metabolic activity of NSCLC by correcting the effect of tumor size, an established prognostic factor, on the SUV. Studies have shown that it has a prognostic value in patients with NSCLC.<sup>6,7</sup> Moreover, this indicator does not correspond to the fact that thresholds are not easy to apply when measuring metabolic parameters in the early stages of NSCLC because of the generally low SUV values. However, studies supporting

the use of this indicator in clinical settings are still lacking.

The current study investigates the prognostic value of the SUV<sub>max</sub>:tumor size ratio on pretreatment <sup>18</sup>F-FDG PET/CT scans in patients with NSCLC. Furthermore, the SUV<sub>max</sub>:tumor size ratio is compared with other established PET parameters.

## Methods

### Participants

This study recruited 131 consecutive patients who underwent an <sup>18</sup>F-FDG PET/CT scan between March 2020 and December 2021 and lung surgery within 30 days after examination at our institution. Among the patients, 13 with benign postoperative pathologic results, four with small cell lung cancer, three who received neoadjuvant treatment, two with distant metastasis at the time of surgery, and one with myxofibrosarcoma were excluded from the analysis. Finally, 108 patients were included in the study (Figure 1).

The Kangbuk Samsung Hospital Institutional Review Board (decision no: KBSMC 2024-02-040, date: 03/05/2024) approved this study. The need for written informed consent from the participants was waived.

### Assessment of the medical records of the patients

The medical records of the patients were assessed for clinical and tumor characteristics, including pathologic findings after surgery, type of treatment, clinical follow-up results, and recurrence diagnosis. Cancer stage was based on the American Joint Committee on Cancer Staging Manual, 8<sup>th</sup> edition. Lung cancer recurrence was diagnosed via

pathologic examination or imaging results assessed by the attending physician. Recurrence-free survival (RFS) was defined as the date of recurrent lesion detection or last follow-up date from the date of surgery

### Fluorodeoxyglucose F18 positron emission tomography/computed tomography scan acquisition

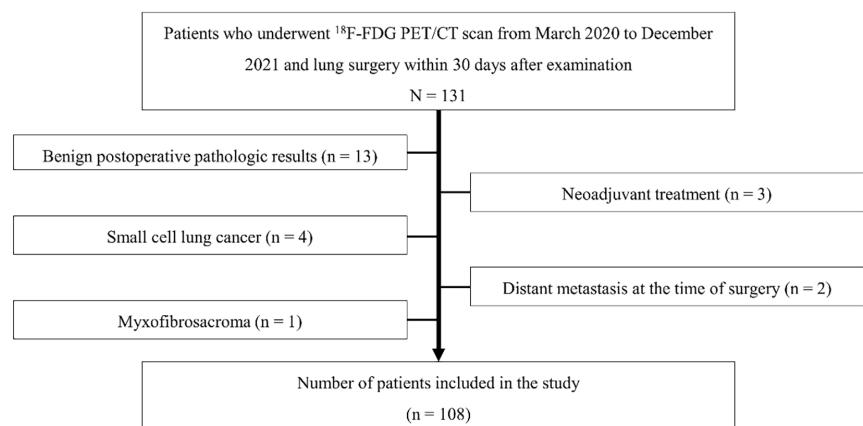
The patients fasted for at least 6 h, and each patient's blood glucose level was <200 mg/dL at the time of <sup>18</sup>F-FDG injection. PET/CT scan images were obtained approximately 60 min after the intravenous administration of <sup>18</sup>F-FDG at a dose of 2.96 MBq/kg. The Discovery MI system (GE Healthcare, Milwaukee, WI, USA) was used for <sup>18</sup>F-FDG PET/CT scan examination. Following the CT scan (120 kVp; 10–80 mA; section thickness: 3.75 mm), emission PET was performed from the thigh to the skull base (1.5 min per bed). The PET images were reconstructed using the Bayesian penalized likelihood reconstruction algorithm with attenuation-corrected images.

### Image analyses

The PET/CT scan images were reviewed on a dedicated workstation (AW; GE Healthcare, Chicago, IL, USA) by a nuclear medicine physician who can recognize lesions that would be surgically resected. A volume of interest was drawn over lung cancer lesions with an <sup>18</sup>F-FDG uptake greater than that of surrounding background activity. The semi-automatic method was used to delineate the boundaries of the tumor with the SUV-based contouring software (volume viewer software on GE AW 4.7). The SUV threshold was set to 2.5. Data on the SUV<sub>max</sub>, mean SUV (SUV<sub>mean</sub>), and MTV were recorded. TLG was defined as the product of MTV and

### Main points

- Fluorodeoxyglucose F18 positron emission tomography (<sup>18</sup>F-FDG PET)/computed tomography (CT) is a widely used imaging tool for non-small cell lung cancer (NSCLC) management.
- The maximum standardized uptake value (SUV<sub>max</sub>)-to-tumor size ratio on <sup>18</sup>F-FDG PET/CT scans was introduced to assess the metabolic activity of NSCLC by correcting the effect of tumor size.
- The SUV<sub>max</sub>:tumor size ratio on <sup>18</sup>F-FDG PET/CT scans was associated with aggressive tumor behavior and poor outcome in NSCLCs, particularly adenocarcinoma.



**Figure 1.** Flowchart of the study participants. F18-FDG, fluorodeoxyglucose F18; PET/CT, positron emission tomography/computed tomography.

SUV<sub>mean</sub>. If the SUV<sub>max</sub> of a lung cancer lesion was <2.5, only SUV<sub>max</sub> was measured, and other volumetric PET parameters were omitted. The longest diameter of the lung cancer lesion on <sup>18</sup>F-FDG PET/CT scan images was also measured. The SUV<sub>max</sub>:tumor size ratio was calculated by dividing the SUV<sub>max</sub> of the lung cancer lesion by the longest diameter of the lesion.

### Statistical analysis

The clinical characteristics and PET/CT scan parameters of the participants were compared according to histologic findings using the Mann–Whitney U test, chi-square test, or Fisher’s exact test. The association between the SUV<sub>max</sub>:tumor size ratio and other PET parameters was evaluated using Kendall’s tau-b correlation coefficient. Survival analysis was performed using the Kaplan–Meier method with subgroup survival estimates compared using the log-rank test. The Cox proportional hazards regression model was used to analyze the prognostic impact of variables. Finally, the SUV<sub>max</sub>:tumor size ratio was compared according to postoperative pathologic findings. In the analysis using SUV<sub>max</sub>:tumor size ratios in which patients had lung cancer lesions without a discernable <sup>18</sup>F-FDG uptake were treated as zero.

Jamovi version 2.3.28 was used to perform statistical analysis. A *P* value of <0.05 was considered statistically significant.

## Results

### Characteristics of the participants

Table 1 shows the clinical characteristics of all patients. Their median age was 66 years (range: 22–83) and 62 (57.4%) were men. In total, 72 (66.7%) of the 108 participants were diagnosed with ADC, whereas 36 patients presented with histologic findings other than ADC. The findings included squamous cell carcinoma [*n* = 21 (58.3%)], pleomorphic carcinoma [*n* = 9 (25.0%)], large-cell carcinoma [*n* = 4 (11.1%)], adenosquamous carcinoma [*n* = 1 (2.8%)], and atypical carcinoid [*n* = 1 (2.8%)]. Patients diagnosed with ADC had a lower median age than those with other histologic types. Furthermore, the proportion of male patients diagnosed with ADC was lower than that of male patients with other histologic types. Overall, 58 (53.7%) of the 108 patients were diagnosed with stage IA or lower lung cancer, and most of them were diagnosed with ADC. In total, 94 (87.0%) of the 108 patients underwent lobectomy, whereas 24 (22.2%) received adjuvant treatment. In

total, 19 (17.6%) patients developed recurrence during a median follow-up period of 32.3 months.

### Fluorodeoxyglucose F18 positron emission tomography/computed tomography scan parameters

The <sup>18</sup>F-FDG uptake in 101 (93.5%) of the 108 patients with lung cancer was discernable. The median SUV<sub>max</sub> was 5.71 and the median tumor size was 2.35 cm. The median SUV<sub>max</sub>:tumor size ratio was 2.37 (range: 0–25.4). More specifically, the median SUV<sub>max</sub>:tumor size ratios were 1.23 for ADCs

and 3.90 for other histologic types. Binomial logistic regression analysis of the preoperative SUV<sub>max</sub>:tumor size ratio for histologic type other than ADC returned an odds ratio of 2.13 [95% confidence interval (CI): 1.56–2.91]. The area under curve was 0.872, the sensitivity was 50.0%, and the specificity was 86.1 when the cut-off value was 0.5. There were 31 (28.7%) patients with an SUV<sub>max</sub> of <2.5, and all these patients were diagnosed with ADC. The volumetric PET parameters of 76 patients were measured. However, in one patient, the volumetric PET parameters could not be measured due to image data issues. Table 2 shows the volumetric PET pa-

**Table 1.** Characteristics of the participants

		All patients ( <i>n</i> = 108)	Patients with adenocarcinoma ( <i>n</i> = 72)	Patients with other histologic types ( <i>n</i> = 36)	<i>P</i> value
<b>Age</b>	Years, median (range)	66 (22–83)	65 (22–80)	68.5 (47–83)	0.042 <sup>a</sup>
	<b>Sex</b>	Male	62 (57.4%)	30 (41.7%)	32 (88.9%)
Female		46 (42.6%)	42 (58.3%)	4 (11.1%)	
<b>Type of surgery</b>	Lobectomy	94 (87.0%)	61 (84.7%)	33 (91.7%)	0.378 <sup>c</sup>
	Segmentectomy	7 (6.5%)	6 (8.3%)	1 (2.8%)	0.420 <sup>c</sup>
	Wedge resection	7 (6.5%)	5 (6.9%)	2 (5.6%)	1.000 <sup>c</sup>
	0	1 (0.9%)	1 (1.4%)	0	1.000 <sup>c</sup>
<b>Stage</b>	IA1	15 (13.9%)	15 (20.8%)	0	0.002 <sup>c</sup>
	IA2	28 (25.9%)	23 (31.9%)	5 (13.9%)	0.044 <sup>b</sup>
	IA3	14 (13.0%)	9 (12.5%)	5 (13.9%)	1.000 <sup>c</sup>
	IB	19 (17.6%)	11 (15.3%)	8 (22.2%)	0.372 <sup>b</sup>
	IIA	4 (3.7%)	0	4 (11.1%)	0.011 <sup>c</sup>
	IIB	16 (14.8%)	9 (12.5%)	7 (19.4%)	0.338 <sup>a</sup>
	IIIA	10 (9.3%)	4 (5.6%)	6 (16.7%)	0.081 <sup>c</sup>
	IIIB	1 (0.9%)	0	1 (2.8%)	0.333 <sup>c</sup>
<b>Tumor grade</b>	1	13 (12.0%)	12 (16.7%)	1 (2.8%)	0.056 <sup>c</sup>
	2	37 (34.3%)	27 (37.5%)	10 (27.8%)	0.316 <sup>b</sup>
	3	41 (38.0%)	27 (37.5%)	14 (38.9%)	0.888 <sup>b</sup>
	4	4 (3.7%)	0	4 (11.1%)	0.011 <sup>c</sup>
	Unspecified	13 (12.0%)	6 (8.3%)	7 (19.4%)	0.120 <sup>c</sup>
<b>Lymphovascular invasion</b>	Present	29 (26.9%)	12 (16.7%)	17 (47.2%)	<0.001 <sup>b</sup>
<b>Adjuvant treatment</b>	Chemotherapy	24 (22.2%)	12 (16.7%)	12 (33.3%)	0.050 <sup>b</sup>
	Radiotherapy only	18 (16.7%)	11 (15.3%)	7 (19.4%)	0.584 <sup>b</sup>
	Concurrent chemoradiotherapy	1 (0.9%)	0	1 (2.8%)	0.333 <sup>c</sup>
<b>Recurrence</b>	Yes	5 (4.6%)	1 (0.4%)	4 (11.1%)	0.041 <sup>c</sup>
	Censored	19 (17.6%)	7 (9.7%)	12 (33.3%)	0.002 <sup>b</sup>
<b>Recurrence-free survival</b>	Months, median (range)	89 (82.4%)	65 (90.3%)	24 (66.7%)	0.096 <sup>a</sup>
		30.3 (0.6–46.9)	32.1 (1.5–46.9)	26.9 (0.6–42.7)	

<sup>a</sup>Mann–Whitney U test; <sup>b</sup>chi-square test; <sup>c</sup>Fisher’s exact test.

rameters. Each PET parameter distribution was biased, with a significant frequency in the near-zero interval (Figure 2).

The  $SUV_{max}$ :tumor size ratio was found to be correlated with  $SUV_{max}$  and  $SUV_{mean}$  (Kendall's tau-b = 0.678 and 0.495, respectively;  $P < 0.001$ ) and MTV and TLG (Kendall's tau-b = 0.191 and 0.243;  $P = 0.015$  and 0.002, respectively). However, the correlation strength of MTV and TLG was not as strong as that of  $SUV_{max}$  or  $SUV_{mean}$ . Similar results were obtained for the ADC subgroup. Nevertheless, the  $SUV_{max}$ :tumor size ratio was not significantly associated with MTV or TLG in other patients with NSCLC.

### Maximum standardized uptake value-to-tumor size ratio and recurrence-free survival analysis

Patients with an  $SUV_{max}$ :tumor size ratio higher than the median (2.37) had a worse recurrence outcome than those with an  $SUV_{max}$ :tumor size ratio lower than the median (Figure 3). In patients with ADC, an  $SUV_{max}$ :tumor size ratio of  $>1.23$  was consistently associated with worse outcomes (Figure 4). Based on univariate analysis, the hazard ratio of a high  $SUV_{max}$ :tumor size ratio for recurrence was 6.01 (1.75–20.65,  $P = 0.004$ ) in all participants and 6.22 (0.75–51.68,  $P = 0.091$ ) in patients with ADC ( $n = 72$ ). A high  $SUV_{max}$ :tumor size ratio was associated with poor prognosis based on the multivariate analysis using clinical variables, albeit that it did not reach statistical significance (Table 3).

### Association between the maximum standardized uptake value-to-tumor size ratio and aggressive tumor behavior based on pathologic findings following surgery

The preoperative  $^{18}F$ -FDG PET/CT scan parameters according to postoperative pathologic results were compared in patients with ADC and those with other histologic types. In the ADC group, patients with lymphovascular invasion had a higher  $SUV_{max}$ :tumor size ratio than those without (3.53 vs. 0.98,  $P < 0.001$ ). Patients with lymph node metastasis had a higher  $SUV_{max}$ :tumor size ratio than those without (3.70 vs. 1.04,  $P = 0.006$ ). An advanced histological grade was associated with a high  $SUV_{max}$ :tumor size ratio in ADC (Figure 5). In patients with ADC, the odds ratios of the  $SUV_{max}$ :tumor size ratio were 1.57 (1.14–2.30,  $P = 0.010$ ) for lymphovascular invasion, 1.42 (0.99–2.09,  $P = 0.050$ ) for lymph node metastasis, and 1.92 (1.33–2.98,  $P = 0.001$ ) for histologic grade 3 lesions.

Unlike the ADC group, the other histologic type group showed no significant differences in  $SUV_{max}$ :tumor size ratio according to the lymphovascular invasion (3.80 vs. 4.50,  $P = 0.346$ ), the presence of lymph node metastasis (3.77 vs. 5.18,  $P = 0.220$ ) and histologic grade 3/4 lesions (4.15 vs. 4.82,  $P = 0.387$ ).

## Discussion

The clinical implications for  $SUV_{max}$ :tumor size ratio on pretreatment  $^{18}F$ -FDG PET/CT in surgically resected NSCLC were evaluated. The  $SUV_{max}$ :tumor size ratio was found to be

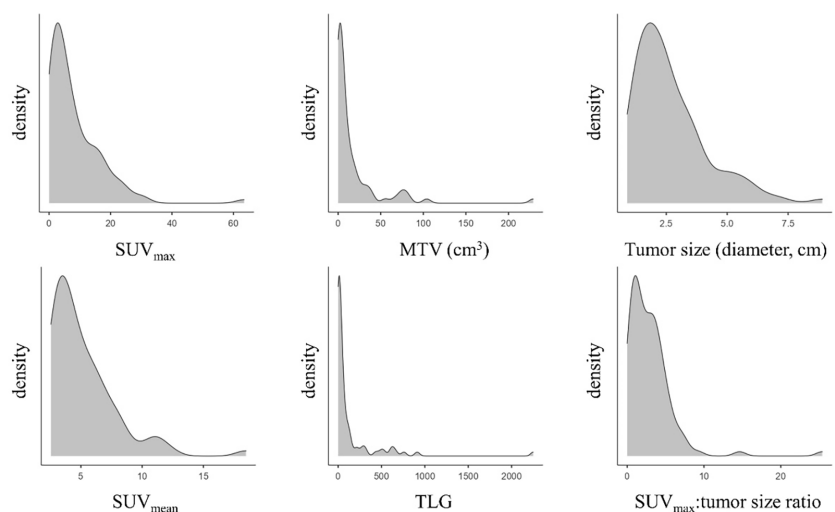
associated with conventional metabolic PET parameters in patients with ADC. An  $SUV_{max}$ :tumor size ratio higher than the median was associated with worse recurrence outcomes. Patients with ADC who presented with lymphovascular invasion, lymph node metastasis, or histologic grade 3 lesions based on the pathologic results had a higher  $SUV_{max}$ :tumor size ratio than those without. However, the results did not significantly differ in the non-ADC group.

In addition to  $SUV_{max}$ , the volumetric PET parameters, including MTV and TLG, for the

**Table 2.** Fluorodeoxyglucose F18 positron emission tomography/computed tomography scan parameters in patients with lung cancer lesions

	All patients (n = 108)	Patients with adenocarcinoma (n = 72)	Patients with other histologic types (n = 36)	P value
Median (range)				
Tumor size	2.35 (0.90–8.90)	2.15 (0.90–7.20)	2.90 (1.10–8.90)	0.006 <sup>a</sup>
No $^{18}F$ -FDG uptake	7 (6.5%)	7 (9.7%)	0	0.093 <sup>b</sup>
$SUV_{max}$	5.71 (0.69–63.48)	3.10 (0.69–5.22)	12.1 (5.22–63.48)	$<0.001^a$
$SUV_{max}$ /tumor size	2.37 (0–25.4)	1.23 (0–9.25)	3.90 (2.34–25.39)	$<0.001^a$
$SUV_{max} < 2.5$	31 (28.7%)	31 (43.1%)	0	$<0.001^b$
$SUV_{mean}$	4.37 (2.56–18.48)	3.46 (2.56–8.28)	5.20 (3.49–18.48)	$<0.001^a$
MTV (cm <sup>3</sup> )	4.21 (0.02–229)	2.08 (0.02–82.4)	10.7 (0.61–229)	$<0.001^a$
TLG	19.2 (0.05–2249)	7.60 (0.05–617)	49.8 (2.11–2249)	$<0.001^a$
Correlation coefficient of $SUV_{max}$ -to-tumor size <sup>c</sup>				
$SUV_{max}$	0.678 ( $<0.001$ )	0.709 ( $<0.001$ )	0.713 ( $<0.001$ )	
$SUV_{mean}$	0.495 ( $<0.001$ )	0.539 ( $<0.001$ )	0.654 ( $<0.001$ )	
MTV	0.191 (0.015)	0.247 (0.025)	-0.150 (0.381)	
TLG	0.243 (0.002)	0.292 (0.008)	-0.062 (0.719)	

<sup>a</sup>Mann-Whitney U test; <sup>b</sup>Fisher's exact test; <sup>c</sup>Kendall's tau-b (P value).  $SUV_{max}$ , maximum standardized uptake;  $SUV_{mean}$ , mean standardized uptake; MTV, metabolic tumor volume; TLG, total lesion glycolysis;  $^{18}F$ -FDG, fluorodeoxyglucose F18.



**Figure 2.** The fluorodeoxyglucose F18 positron emission tomography/computed tomography scan-derived parameters of patients with non-small cell lung cancer ( $n = 108$ ) were distributed considerably close to zero. The volumetric parameters, metabolic tumor volume and total lesion glycolysis, were evident.  $SUV_{max}$ , maximum standardized uptake value; MTV, metabolic tumor volume; TLG, total lesion glycolysis.

prognostic stratification of NSCLC have been evaluated.<sup>8</sup> However, there is no clear standard method for segmentation to measure the parameters, and the various methods affect the measurements.<sup>9</sup> An SUV threshold of 2.5 is widely used to delineate the tumor, and this value was also adopted in this study. However, other methods can be utilized. A specific percentage of SUV<sub>max</sub> as a threshold or a gradient method without threshold are also frequently used to define tumors. However, all these methods have a common weakness in tumors with a generally low <sup>18</sup>F-FDG uptake, such as ADC.<sup>10</sup> In the present study, the SUV<sub>max</sub> of 31 (43.1%) of 72 patients with ADCs was <2.5. Hence, volumetric PET parameters were not measured in these patients. In contrast, the SUV<sub>max</sub>:tumor size ratio could be measured in most cases and was correlated with the volumetric parameters in ADCs.

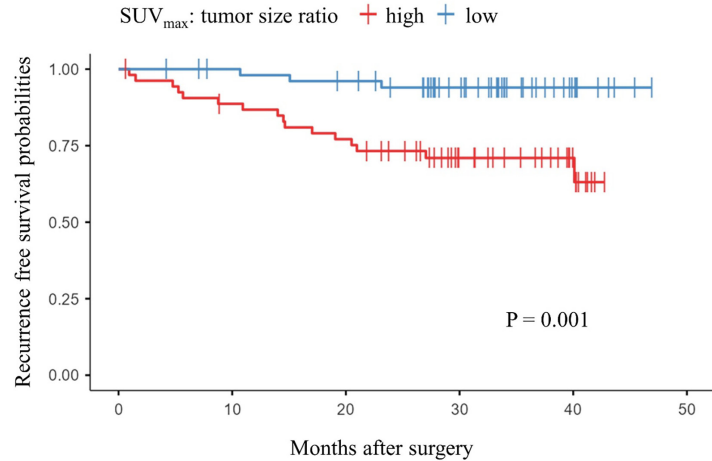
In this study, an SUV<sub>max</sub>:tumor size ratio higher than the median was associated with a poor RFS. This result is similar to that of previous studies on SUV<sub>max</sub>:tumor size ratio.<sup>6,7</sup> Furthermore, in patients with ADC, a higher SUV<sub>max</sub>:tumor size ratio was consistently related to worse outcomes. This study did not reach the level of prognostic prediction modeling via multivariate analysis. However, this outcome can be achieved in further studies with a larger number of participants and an extended follow-up period.

A higher SUV<sub>max</sub>:tumor size ratio was associated with unfavorable postoperative pathologic findings in ADCs. This is consistent with the explanation that an increase in <sup>18</sup>F-FDG uptake is related to the aggressive characteristics of tumor cells.<sup>11</sup> Tumor cell density can be another factor affecting the SUV<sub>max</sub>:tumor size ratio and is associated with tumor grade in lung ADC.<sup>12</sup> However, in the present study, no significant association was found in the remaining NSCLC group except ADC. The lack of association could not be explained based on the small number of participants alone. It seems reasonable to distinguish ADC from the other histologic types when evaluating the prognostic value of <sup>18</sup>F-FDG uptake in NSCLC.

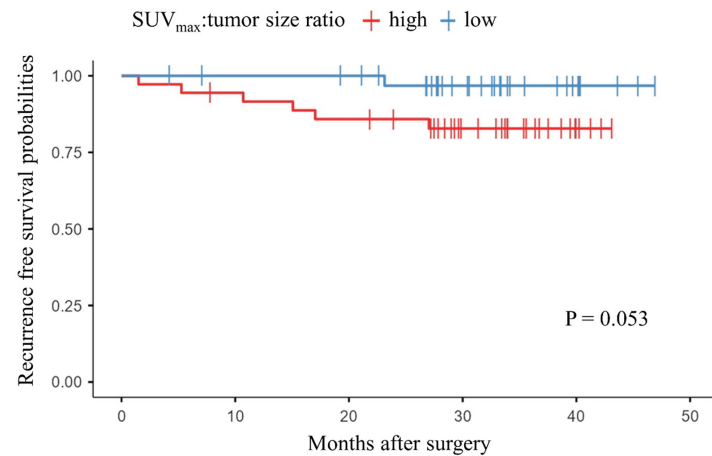
Interestingly, in a meta-analysis on the prognostic value of <sup>18</sup>F-FDG PET/CT scanning for surgically resected NSCLC, the results presented by classifying the values into lower and higher than an SUV<sub>max</sub> of 6.0 had somewhat different patterns.<sup>4</sup> The adjusted hazard ratio of the SUV<sub>max</sub> for disease-free survival was 4.63 (2.53–8.48) in the sub-threshold group and was higher than 1.68 (95% CI: 1.07–2.63) in the above threshold group.

Therefore, the association between the tumor <sup>18</sup>F-FDG uptake and prognosis may weaken following disease progress. Furthermore, acidosis can reduce <sup>18</sup>F-FDG uptake by inhibiting aerobic glycolysis with cancer progression.<sup>13,14</sup>

The current study has several limitations. First, this retrospective study focused on patients with NSCLC who underwent surgical resection, meaning selection bias could have affected the results. The potential value of predicting histologic tumor type by preop-



**Figure 3.** Patients with a maximum standardized uptake value (SUV<sub>max</sub>)-to-tumor size ratio higher than the median (2.37) had a significantly worse recurrence outcome than those with an SUV<sub>max</sub>-to-tumor size ratio lower than the median ( $P = 0.001$ ).

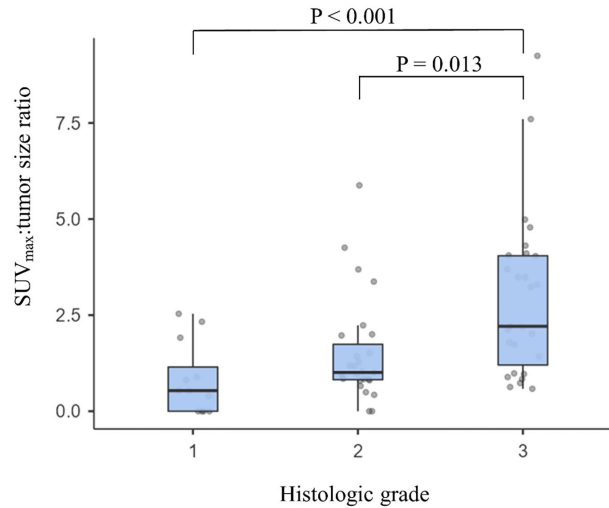


**Figure 4.** Patients with adenocarcinoma who presented with a maximum standardized uptake value (SUV<sub>max</sub>)-to-tumor size ratio higher than the median (1.23) tended to have a worse recurrence outcome than those with an SUV<sub>max</sub>-to-tumor size ratio lower than the median ( $P = 0.053$ ).

**Table 3.** Recurrence-free survival in patients with non-small cell lung cancer who underwent surgical resection based on a multivariate analysis

Variables	HR	95% CI	P value
Male sex	0.59	0.18–1.98	0.397
Age ≥70 years	0.51	0.18–1.49	0.221
pT3 or pT4	3.60	1.28–10.13	0.015
pN1 or pN2	1.14	0.36–3.57	0.824
Histology, not adenocarcinoma	2.09	0.57–7.67	0.264
SUV <sub>max</sub> -to-tumor size ratio greater than the median (2.37)	3.62	0.89–14.67	0.072

HR, hazard ratio; CI, confidence interval; SUV<sub>max</sub>, maximum standardized uptake.



**Figure 5.** The boxplot of maximum standardized uptake value (SUV<sub>max</sub>)-to-tumor size ratio according to histologic grade in 72 patients with ADC showed a higher level of SUV<sub>max</sub>-to-tumor size ratio for more advanced tumor grade. ADC, adenocarcinoma.

erative SUV<sub>max</sub>:tumor size ratio could be additionally evaluated using a larger number of participants with various histologic tumor types in the future. In addition, various factors might have influenced the clinical judgement of physicians regarding treatments, such as the type of treatment modality and adjuvant treatment following surgery. Among them, <sup>18</sup>F-FDG PET/CT scan findings might have had an influence to an uncontrolled extent. Second, the follow-up duration of this study was limited. Thus, overall survival could not be evaluated. Controlled studies with a larger number of patients and extended follow-up periods should be conducted to validate the prognostic value of the SUV<sub>max</sub>:tumor size ratio in NSCLC. Compared with other complicated parameters, the SUV<sub>max</sub>:tumor size ratio can be advantageous for multicenter research as it involves less variation based on the institution.

In conclusion, the SUV<sub>max</sub>-to-tumor size ratio on <sup>18</sup>F-FDG PET/CT scanning was associated with aggressive tumor behavior and poor outcomes in NSCLCs, particularly ADC.

#### Conflict of interest disclosure

The authors declared no conflicts of interest.

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