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Maximum standardized uptake value on ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography improves outcome prediction in retroperitoneal liposarcoma

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While ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG PET/CT) has been investigated in extremity sarcomas, there is no evidence on its usefulness in retroperitoneal sarcoma. This study was designed to evaluate the usefulness of ^{18}F -FDG PET/CT in predicting aggressiveness of retroperitoneal liposarcoma. Patients experienced surgery for retroperitoneal liposarcoma from November 2007 to February 2018 and underwent preoperative ^{18}F -FDG PET/CT were included. Preoperative maximum standardized uptake value (SUV_{max}) was calculated. To evaluate the predictability of SUV_{max} for Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grade 3, receiver operating characteristics (ROC) curve analysis was performed. To analyze whether SUV_{max} can be a risk factor for prognosis, multivariable Cox regression was performed including potential risk factors regarding operation and histopathology. A total of 133 patients were included. ROC curve showed area under the curve of 0.877 ($P < 0.001$), with a cut-off point of 4.5 SUV_{max} showing 85.7% sensitivity and 78.3% specificity. Cox analyses showed that $\text{SUV}_{\text{max}} > 4.5$ was a significant factor for recurrence-free survival (HR = 2.148, CI 1.301–3.546, $P = 0.003$) and overall survival (HR = 5.052, CI 1.854–13.766, $P = 0.002$). SUV_{max} is highly predictive of FNCLCC grade 3 and $\text{SUV}_{\text{max}} > 4.5$ can be used as a prognostic factor before obtaining the histopathology.

Liposarcoma (LPS) is a mesenchymal origin malignancy that can occur wherever fat is present. LPS typically occurs in the retroperitoneum (up to 40% of cases)¹, although it can also be found in the mesentery or peritoneum². Besides LPS, other soft tissue sarcomas (STS) including leiomyosarcoma can occur in the retroperitoneum. Although STS accounts for only 1% of all malignancies, it is associated with high mortality and requires specialized management³.

Complete surgical resection of retroperitoneal STS is the most important factor related to prognosis^{4–7}. However, STS is a highly recurrent disease and its aggressiveness can be well categorized by the Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system^{4–8}. Evaluating the aggressiveness of a tumor before treatment may offer clinical advantages with regard to determining the surgical extent and whether neoadjuvant radiation therapy can be an option^{9–12}. Computed tomography (CT) has limited value for the evaluation of tumor aggressiveness¹³, and the usefulness of ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG PET/CT) was recently reported in several studies on STS in the extremities^{14–17}. ^{18}F -FDG PET/CT is frequently used for functional imaging by evaluating tumor glucose metabolism and

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proliferation¹⁵. Several studies have reported correlations of hypermetabolic STSs with histopathologic characteristics and their clinical implications for prognosis^{18,19}.

However, these previous studies only included limb sarcoma. Since retroperitoneal STSs locate in the deepest region of the abdomen and cause minimum symptoms, they are often discovered incidentally and have an even poorer prognosis than extremity STS. Their close anatomical relationship to vital retroperitoneal structures makes complete surgical resection difficult and has a major impact on survival. Nonetheless, despite the different disease course of retroperitoneal STS compared with extremity STS, the biological characteristics are the same. Therefore, we designed this study to evaluate the usefulness of ¹⁸F-FDG PET/CT in predicting tumor aggressiveness in retroperitoneal LPS and whether it has clinical implications for prognosis.

Methods

Patients. Data on patients who underwent surgery for retroperitoneal LPS from November 2007 to February 2018 were reviewed from the center's sarcoma database. Among these patients, those who underwent ¹⁸F-FDG PET/CT before surgery and were proven to have a histopathology of LPS were considered eligible for inclusion. Patients whose FNCLCC grades were unclassifiable were included. Patients who had STS other than LPS were excluded from the study.

Data collection. Demographic data, treatment history, preoperative CT and ¹⁸F-FDG PET/CT, operative data, postoperative course, histopathology, and follow-up data regarding recurrence and death were collected. A detailed review of ¹⁸F-FDG PET/CT images was performed by a nuclear medicine specialist and the preoperative maximum standardized uptake value (SUV_{max}) of the tumor was re-evaluated for this study. Medical records were thoroughly reviewed to obtain data on surgical procedures.

¹⁸F-FDG PET/CT imaging and measurement of maximum SUV. All patients fasted for at least 6 hours before the PET/CT study. Blood glucose levels were required to be less than 200 mg/dL. Whole-body PET and unenhanced CT images were acquired using a PET/CT scanner (Discovery STE, GE Healthcare, Waukesha, WI, USA). Whole-body CT was performed using a 16-slice helical CT with 30 to 170 mAs adjusted to the patient's body weight at a 140-kVp and 3.75-mm section width. After the CT scan, an emission scan was performed from the thigh to the basal skull for 2.5 min per frame in three-dimensional mode 60 minutes after intravenous injection of ¹⁸F-FDG (5.0 MBq/kg). PET images were reconstructed using CT for attenuation correction with the ordered subsets expectation maximization algorithm (20 subsets, 2 iterations) with matrix of 128×128 and voxel size of $3.9 \times 3.9 \times 3.3$ mm. Standardized uptake value (SUV_{max}) was normalized to patient body weight.

For measurement of SUV_{max} , we placed a spherical volume of interest of 3 cm in diameter at a location where the LPS tissue had highest metabolic activity on PET using the volume viewer software on a GE Advantage Workstation 4.4.

Data analysis. The study was designed for analysis of two main outcomes. First, we analyzed whether preoperative SUV_{max} can be predictive of FNCLCC grade, which is representative of tumor aggressiveness and has been proven to be related to the prognosis of STS. Second, we analyzed whether a high SUV_{max} can be predictive of the prognosis of the patient.

We performed receiver operating characteristics (ROC) curve analysis for medical diagnostic test evaluation using SUV_{max} of the tumor to predict FNCLCC grade 3 LPS. We also calculated the cut-off point based on the maximum Youden index.

Median SUV_{max} was compared between different histopathologic categories (FNCLCC grade, tumor differentiation, mitotic count, and necrosis) using the Kruskal Wallis test.

To analyze whether the cut-off point of SUV_{max} can be a risk factor for prognosis, survival analyses were performed including data from the first set of PET/CT scans, operation procedures, and histopathology of patients with non-metastatic LPS. Recurrence-free survival and overall survival were analyzed using Kaplan–Meier survival analysis. Potential risk factors for recurrence and death were analyzed using a multivariable Cox proportional hazard model including the cut-off point of SUV_{max} . We designed three survival models based on different time points of evaluation. Model 1 contains preoperative variables including the SUV_{max} . Model 2 includes operative variables such as specific details of the surgery together with SUV_{max} and other preoperative variables. Model 3 includes the histopathology of the tumor and does not include SUV_{max} .

All statistical analyses were performed using SPSS 20.0 (SPSS Inc., Chicago, IL). This study was approved by the institutional review board of Samsung Medical (IRB No. 2018-05-047). The need for informed consent was waived by the institutional review board of Samsung Medical Center due to the retrospective nature of the study. The data can be available on individual investigator's request.

Ethical approval. This study was approved by the institutional review board of Samsung Medical (IRB No. 2018-05-047).

Informed consent. The need for informed consent was waived by the institutional review board of Samsung Medical Center due to the retrospective nature of the study.

Results

A total of 133 patients met the inclusion criteria of available SUV_{max} data from ¹⁸F-FDG PET/CT scan, subsequent surgery, and histopathology of LPS. One hundred and nine patients had single data set of PET/CT scans, while 23 patients had two data sets of PET/CT scans after recurrence and 1 patient had three data sets of PET/CT scans after two recurrent episodes. Among these patients, 158 sets of data on PET/CT scan, operation, and histopathology were reviewed.

Factors	No. of patients	%
Patient number	133	
Number of PET/CT and operations performed	158	
Sex, male/female	73/60	54.90%
Mean age (years)	55.9 ± 11.8	
Disease status		
Primary	74	46.8
Remnant	17	10.8
Recurrent	66	41.8
Metastatic	1	0.6
SUV _{max} median (IQR)	3.3 (4.4)	
Minimum-maximum	0.4–41.3	
0–4.9	106	67.1
5–9.9	31	19.6
10–14.9	15	9.5
>15	6	3.8
Anatomy		
Retroperitoneal		
Right		
Suprarenal	5	3.2
Infrarenal	15	9.5
Perirenal	45	28.5
Pelvis	6	3.8
Left		
Suprarenal	3	1.9
Infrarenal	11	7
Perirenal	34	21.5
Pelvis	7	4.4
Intraperitoneal	32	20.3
Histology		
FNCLCC grade		
G1	40	25.3
G2	80	50.6
G3	35	22.2
missing	3	1.9
Tumor differentiation		
WDLPS	37	23.4
DDLPS	113	71.5
Myxoid/round cell LPS	7	4.4
Pleomorphic LPS	1	0.6
Mitosis count, (per 10 HPF)		
0–9	123	77.8
10–19	24	15.2
≥20	11	7
Necrosis		
Absent	73	52.1
<50%	62	44.3
≥50%	5	3.6

Table 1. Demographic, clinical, surgical, and histopathologic data of the study patients.

Table 1 shows the baseline characteristics of the study population. There were 73 males and 60 females with a mean age of 55.9 ± 11.8 years at the initial presentation. Nearly half of the patients (n = 74, 46.8%) had primary LPS while 10.8% and 41.8% had remnant LPS from a previous operation and recurred LPS, respectively. The median SUV_{max} was 3.3 with an interquartile range (IQR) of 4.4. The SUV_{max} of the entire patient population ranged from 0.4 to 41.3. Nearly two-thirds (n = 106, 67.1%) of the PET/CT scans showed a SUV_{max} less than 5. Regarding disease aggressiveness, 40 (25.3%), 80 (50.6%), and 35 (22.2%) patients were classified as FNCLCC grade 1, 2, and 3 respectively. Regarding histology, 37 (23.4%), 113 (71.5%), 7 (4.4%), and 1 (0.6%) patients had well-differentiated LPS (WDLPS), dedifferentiated LPS (DDLPS), myxoid/round cell LPS, and pleomorphic LPS,

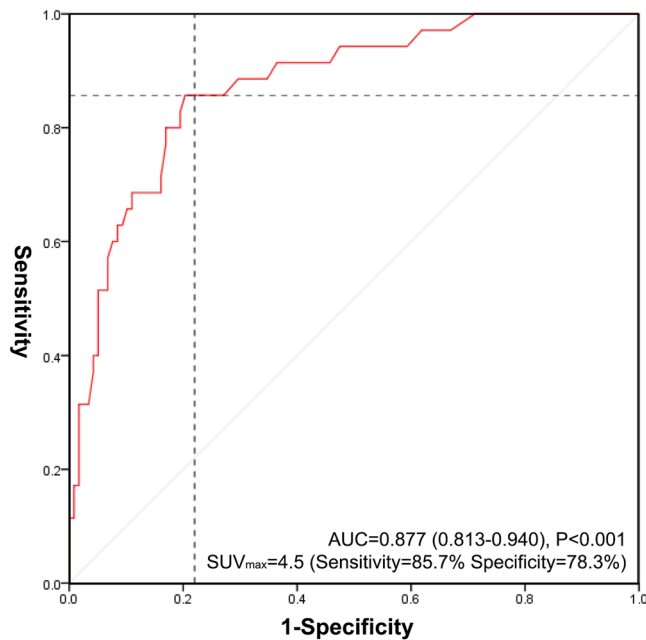


Figure 1. ROC curve for prediction of FNCLCC grade 3 by SUV_{max} .

respectively. Number of mitoses per 10 high power fields was 0–9, 10–19, and ≥ 20 in 123 (77.8%), 24 (15.2%), and 11 (7.0%) patients, respectively. Necrosis was absent in 73 patients (52.1%), while 62 (44.3%) and 5 (3.6%) patients had $< 50\%$ and $\geq 50\%$ necrosis, respectively.

SUV_{max} based on histopathology. Kruskal Wallis test showed significant differences in SUV_{max} between different pathologic features. FNCLCC grade 1, 2, and 3 had median SUV_{max} of 2.25 (IQR 1.5), 3.3 (IQR 2.7), and 9.1 (IQR 8.4), respectively ($P < 0.001$). WDLPS, myxoid/round cell LPS, and DDLPS had median SUV_{max} of 2.20 (IQR 1.7), 2.8 (IQR 4.2), and 4.3 (IQR 5.4), respectively ($P < 0.001$). Cases with mitotic count 0–9, 10–19, and ≥ 20 per 10HPF had median SUV_{max} of 3.0 (IQR 2.7), 5.35 (IQR 7.1), and 13.3 (IQR 9.4), respectively ($P < 0.001$). Cases with no necrosis, $< 50\%$ necrosis, and $\geq 50\%$ necrosis had median SUV_{max} of 2.8 (IQR 2.1), 5.25 (IQR 6.1), and 5.4 (IQR 5.7), respectively ($P < 0.001$).

ROC curve of SUV_{max} predicting FNCLCC grade 3. Figure 1 shows the ROC curve of SUV_{max} predicting FNCLCC grade 3. The area under the curve (AUC) was calculated to be 0.877 (confidence interval [CI] 0.813–0.940, $P < 0.001$). By setting the cut-off point as SUV_{max} of 4.5, sensitivity and specificity were calculated to be 85.7% and 78.3%, respectively.

Table 2 shows the comparisons of characteristics between the $SUV_{max} \leq 4.5$ group and $SUV_{max} > 4.5$ group. There were no differences in sex ($P = 0.623$), age ($P = 0.362$), disease status ($P = 0.920$), and median tumor size ($P = 0.514$). However, linear-by-linear association analysis showed a significant difference in the distribution of cases according to FNCLCC grade ($P < 0.001$). There were only five cases with FNCLCC grade 3 in the $SUV_{max} \leq 4.5$ group whereas more than half ($n = 30$, 53.6%) of the $SUV_{max} > 4.5$ group were FNCLCC grade 3 and there were no grade 1 cases. Differentiation ($P < 0.001$), mitosis ($P < 0.001$), and necrosis ($P < 0.001$) were significantly unfavorable in the $SUV_{max} > 4.5$ group.

$SUV_{max} > 4.5$ as a prognostic factor of recurrence-free survival. Survival analyses were based on the first surgical procedure performed in our center for each patient. The 1-, 3-, and 5-year recurrence-free survivals were 64.9%, 43.2%, and 28.1%, respectively. Multivariable Cox regression analyses were performed for three different models. Potential risk factors for recurrence in the univariable analyses were used for multivariable adjusted models. (Table 3)

Model 1 was composed of preoperative variables including $SUV_{max} > 4.5$. Multivariable Cox analysis showed that $SUV_{max} > 4.5$ (hazard ratio [HR] = 2.183, CI 1.257–3.793, $P = 0.006$), remnant or recurrent LPS (HR = 2.590, CI 1.534–4.372, $P < 0.001$), perinephric location (HR = 0.514, CI 0.300–0.882, $P = 0.016$), and suspected invasion on preoperative radiology (HR = 1.824, CI 1.003–3.319, $P = 0.049$) were related to recurrence-free survival.

Model 2 used preoperative variables including $SUV_{max} > 4.5$ and operative variable. Multivariable Cox analysis showed that $SUV_{max} > 4.5$ (HR = 2.148, CI 1.301–3.546, $P = 0.003$), male sex (HR = 1.725, CI 1.030–2.889, $P = 0.038$), remnant or recurrent LPS (HR = 2.478, CI 1.490–4.122, $P < 0.001$), and gross incomplete resection (HR = 3.233, CI 1.909–5.474, $P < 0.001$) were related to recurrence-free survival.

Model 3 added histopathology but excluded $SUV_{max} > 4.5$. The multivariable model showed that male sex (HR = 1.895, CI 1.099–3.268, $P = 0.021$), remnant or recurrent LPS (HR = 2.317, CI 1.381–3.888, $P = 0.001$), gross incomplete resection (HR = 2.941, CI 1.696–5.102, $P < 0.001$), LPS other than WDLPS (HR = 2.241,

	SUV _{max} ≤ 4.5 (n = 101)	SUV _{max} > 4.5 (n = 57)	P
Sex, male/female	59/42	31/26	0.623
Mean age (years)	55.6 ± 12.2	57.2 ± 10.3	0.362
Disease status (primary vs. other)			0.920
Primary	47 (46.5%)	27 (47.4%)	
Remnant	14 (13.9%)	3 (5.3%)	
Recurrent	40 (39.6%)	26 (45.6%)	
Metastatic	—	1 (1.8%)	
Median size (cm)	16 (20)	14 (12)	0.514
FNCLCC grade			<0.001
G1	38 (38.4%)	2 (3.6%)	
G2	56 (56.6%)	24 (42.9%)	
G3	5 (5.0%)	30 (53.6%)	
Differentiation (WD vs. other)			<0.001
WDLPS	35 (34.7%)	2 (3.5%)	
DDLPS	60 (59.4%)	53 (93.0%)	
Myxoid/round cell	6 (5.9%)	1 (1.8%)	
Pleomorphic	—	1 (1.8%)	
Mitosis (/10 HPF)			<0.001
0–9	91 (90.1%)	32 (56.1%)	
10–19	8 (7.9%)	16 (28.1%)	
≥20	2 (2.0%)	9 (15.8%)	
Necrosis			<0.001
Absent	58 (67.4%)	15 (27.8%)	
<50%	27 (31.4%)	35 (64.8%)	
≥50%	1 (1.2%)	4 (7.4%)	

Table 2. Comparison of demographic, medical, and histopathologic data between SUV_{max} ≤ 4.5 group and SUV_{max} > 4.5 group.

CI 1.082–4.639, $P = 0.030$), and FNCLCC grade 3 (HR = 2.117, CI 1.161–3.860, $P = 0.014$) were related to recurrence-free survival.

SUV_{max} > 4.5 as a prognostic factor of overall survival. The 1-, 3-, and 5-year overall survival rates were 95.5%, 80.9%, and 75.2%, respectively. Multivariable Cox regression analyses were performed for three different models following the principle described above (Table 4).

Model 1, which included preoperative variables including SUV_{max} > 4.5, showed that SUV_{max} > 4.5 (HR = 5.441, CI 2.055–14.411, $P = 0.001$) and male sex (HR = 3.177, CI 1.051–9.605, $P = 0.041$) were related to overall survival.

Model 2, which added operative variables to model 1, showed that SUV_{max} > 4.5 (HR = 5.052, CI 1.854–13.766, $P = 0.002$) and gross incomplete resection (HR = 6.347, CI 2.238–18.001, $P = 0.001$) were related to overall survival.

Model 3, which added histopathology but excluded SUV_{max} > 4.5 from model 2, showed that gross incomplete resection (HR = 6.415, CI 2.023–20.346, $P = 0.002$), and FNCLCC grade 3 (HR = 3.023, CI 1.119–8.167, $P = 0.029$) were related to overall survival. Figure 2 shows the survival curves according to SUV_{max} > 4.5 in model 1 and model 2, and FNCLCC grade 3 in model 3.

Discussion

This study analyzed the usefulness of ¹⁸F-FDG PET/CT in predicting tumor aggressiveness represented by FNCLCC grade and yielded promising results. To date, there are only a few studies evaluating ¹⁸F-FDG PET/CT for extremity STS^{16,20–22}. Furthermore, these studies had a heterogeneous background through inclusion of various STSs. Our study focused only on retroperitoneal LPS, which is the most common STS in the retroperitoneum, and showed a high predictability of SUV_{max} for FNCLCC grade 3 and a significant relationship to recurrence and survival when using a cut-off point of SUV_{max} 4.5.

In our sarcoma center, the goal of surgery is to perform gross complete resection for the purpose of obtaining a negative margin. To achieve this goal, we perform radical nephrectomy in cases with a tumor invading or abutting the perirenal fat. Other organs are resected only when tumor invasion is evident and combined resection is inevitable. Previously, we reported the importance of achieving gross complete resection and performing radical nephrectomy when the tumor is abutting perirenal fat^{8,23}. The patients undergo ¹⁸F-FDG PET/CT preoperatively for metastasis work-up, but it also gives information on the metabolic status of the tumor.

		Recurrence-free survival											
		Univariable			Multivariable								
					Model 1			Model 2			Model 3		
Variables	No	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Male (vs. female)	73	1.764	1.061–2.932	0.029	1.406	0.831–2.379	0.204	1.725	1.030–2.889	0.038	1.895	1.099–3.268	0.021
Remnant or recurrent	55	3.026	1.835–4.991	<0.001	2.590	1.534–4.372	<0.001	2.478	1.490–4.122	<0.001	2.317	1.381–3.888	0.001
SUV _{max} >4.5	48	2.509	1.535–4.103	<0.001	2.183	1.257–3.793	0.006	2.148	1.301–3.546	0.003		Not included	
Perinephric location	76	0.513	0.317–0.832	0.007	0.514	0.300–0.882	0.016			NS			NS
Suspected invasion	77	1.796	1.077–2.993	0.025	1.824	1.003–3.319	0.049			NS			NS
Gross incomplete resection	42	4.188	2.516–6.970	<0.001		Not included		3.233	1.909–5.474	<0.001	2.941	1.696–5.102	<0.001
Differentiation				0.001									0.030
WDLPS	36					Not included			Not included				
Other LPS	94	3.052	1.610–5.784								2.241	1.082–4.639	
FNCLCC G1/G2	102			<0.001									0.014
G3	29	3.223	1.924–5.399			Not included			Not included		2.117	1.161–3.860	

Table 3. Three separate multivariable Cox proportional hazard models analyzing risk factors for recurrence-free survival. *Model 1 is modeled based on preoperative variables while model 2 and 3 added operative variables and tumor histopathology to model 1, respectively. Age >60 (P = 0.954), multiplicity (P = 0.635), size >20 cm (P = 0.272), nephrectomy (P = 0.052) and resection of three or more organs (P = 0.424) were excluded from multivariable adjusted modeling due to an insignificant relationship in the univariable analysis.

		Overall survival											
		Univariable			Multivariable								
					Model 1			Model 2			Model 3		
Variables	No	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Male (vs. female)	73	3.327	1.103–10.034	0.033	3.177	1.051–9.605	0.041			NS			NS
SUV _{max} >4.5	48	5.642	2.124–14.987	0.001	5.441	2.055–14.411	0.001	5.052	1.854–13.766	0.002		Not included	
Nephrectomy	77	0.288	0.109–0.760	0.012		Not included				NS			NS
Gross incomplete resection	42	7.537	2.698–21.057	<0.001		Not included		6.347	2.238–18.001	0.001	6.415	2.023–20.346	0.002
FNCLCC G1/G2	102			0.002				—	—	—			0.029
G3	29	4.611	1.758–12.096			Not included					3.023	1.119–8.167	

Table 4. Three separate multivariable Cox proportional hazard models analyzing risk factors for overall survival. *Model 1 is modeled based on preoperative variables while model 2 and 3 added operative variables and tumor histopathology to model 1, respectively. Age >60 (P = 0.738), remnant or recurrent (P = 0.114), suspected invasion (P = 0.078), multiplicity (P = 0.540), size >20 cm (P = 0.717), perinephric location (P = 0.258), resection of three or more organs (P = 0.073), and differentiation (P = 0.377) were excluded from the multivariable adjusted modeling due to insignificant relationship in the univariable analysis.

The ¹⁸F-FDG PET/CT scan showed a variable range of SUV_{max} with a median value of 3.3 (range 0.4–41.3). ROC curve analysis showed an AUC of 0.877, and SUV_{max} > 4.5 showed 85.7% sensitivity and 78.3% specificity. Nearly one-third (36.1%) of cases were above 4.5 SUV_{max}, and there were no differences in the baseline characteristics except for tumor histopathology between cases above or below 4.5 SUV_{max}. Therefore, setting a cut-off point of 4.5 seems appropriate not only due to the high SUV but also based on the data distribution.

In particular, in multivariable Cox regression analyses SUV_{max} > 4.5 showed a significant relationship to poor recurrence-free survival and overall survival. In analysis using three models, SUV_{max} > 4.5 showed usefulness as a prognostic factor comparable to FNCLCC grade. These results might be useful as they allow surgical oncologists to predict tumor aggressiveness by SUV_{max} even before the surgery. The information can be crucial in planning the extent of resection. Surgical oncologists can plan radical resection with combined organ resection when a tumor is predicted to be aggressive. However, a well-designed study is required for making a conclusion on the topic.

The usefulness of ¹⁸F-FDG PET/CT in STS has been addressed by numerous studies. In 2005, Schwarzbach *et al.* reported that mean SUV can be a useful prognostic parameter by analyzing 55 STSs of the entire body. In their study, 31.1% (n = 23) of patients had retroperitoneal STS, and LPS accounted for 52.7% (n = 39) of total STSs¹⁷. In 2013, Choi *et al.* published a study on 91 extremity STSs and reported the usefulness of total lesion glycolysis, showing an AUC of 0.833 for predicting disease progression within 2 years²¹. In 2015, Fendler *et al.* reported that metabolic response by ¹⁸F-FDG PET predicts progression-free survival and time to local and distant progression after neoadjuvant chemotherapy for STS²². In their study, half of the patients (n = 36, 49%) had STSs

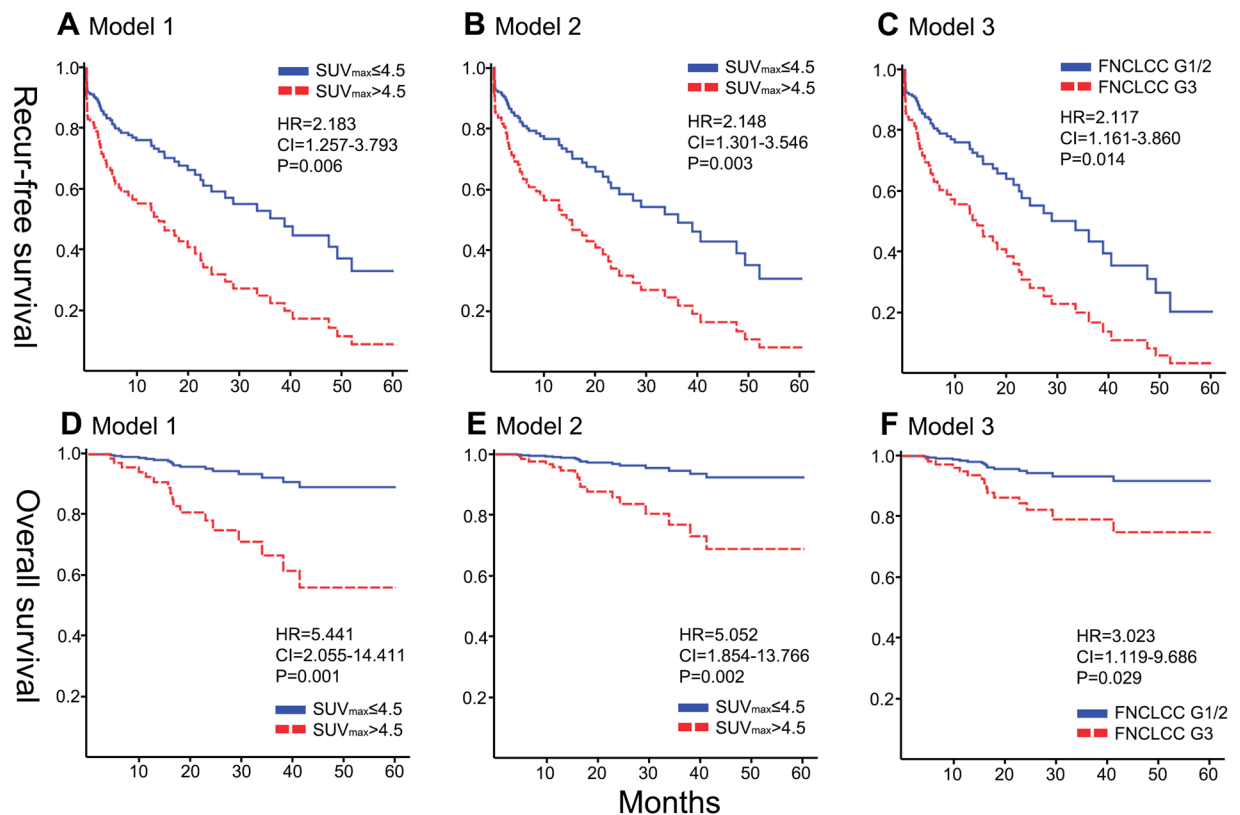


Figure 2. Survival curves analyzed with multivariable Cox proportional hazard models. (A–C) $SUV_{max} > 4.5$ was a significant risk factor for recurrence in models 1 and 2 (A,B) whereas FNCLCC grade 3 was a significant risk factor for recurrence in model 3 (C). (D–F) $SUV_{max} > 4.5$ was a significant risk factor for survival in models 1 and 2 (D,E) whereas FNCLCC grade 3 was a significant risk factor for survival in model 3 (F). Model 1 is modeled based on preoperative variables while model 2 and 3 added operative variables and tumor histopathology to model 1, respectively.

in the abdomen or retroperitoneum, and LPS accounted for 18% ($n = 13$) of patients. However, no previous study focused on retroperitoneal STS, especially LPS.

There are some limitations that must be overcome in future studies. The study only included retroperitoneal LPS and therefore our results cannot be generalized to the other types of STS. However, retroperitoneal LPS can be distinguished by radiologic findings when evaluated by a radiologist specialized in STS. When a retroperitoneal tumor is suspected to be LPS, the ^{18}F -FDG PET/CT scan can add valuable information on the aggressiveness of the tumor.

We only used SUV_{max} as a prognostic tool, although SUV_{avg} or metabolic tumor volume (MTV) were also evaluated for practicality. LPSs are usually giant tumors and there is heterogeneity within the tumor mass regarding aggressiveness. Even if a mass is composed of mainly WDLPS, a single solid portion can beDDLPS with high grade. Consequently, the patient may possess a small but high-grade tumor content. These characteristics are in accordance with ^{18}F -FDG PET/CT findings that the most fat-containing portion shows low SUV uptake while a single solid portion can be hypermetabolic. Adjusting SUV_{avg} in a giant tumor can deviate the result because grade, not size, is the most important prognostic factor. Therefore, we concluded that SUV_{max} better reflects the clinical situation.

Figure 3 shows an example of different aggressiveness within a mass. A 56-year old male patient underwent mass excision for retroperitoneal LPS. Preoperatively, the patient had a LPS with a solid portion that showed hypermetabolic features ($SUV_{max} = 5.0$) and a fatty mass on the medial side with small FDG uptake ($SUV = 1.8$). During the first operation the solid mass was completely removed and histopathology revealedDDLPS with FNCLCC grade 2. However, the 1-week postoperative CT scan showed that a mass similar to normal fat remained on the medial side near the inferior vena cava. After the second operation, the fatty mass was found to be WDLPS with FNCLCC grade 1. Unfortunately, on the 8-month postoperative CT scan the patient was discovered to have a peritoneal carcinomatosis with several solid masses in the entire abdomen. The patient died 4 months later. This is a typical case that shows the heterogeneous characteristics of a mass in a single patient showing a spectrum from low-grade to high-grade tumor. The small but high FDG-uptake spot that showed SUV_{max} of 5.0 can represent the patient's prognosis more precisely than the bulk WDLPS with no uptake. For this reason, we consider SUV_{max} to be the key indicator of prognosis in patients with retroperitoneal LPS.

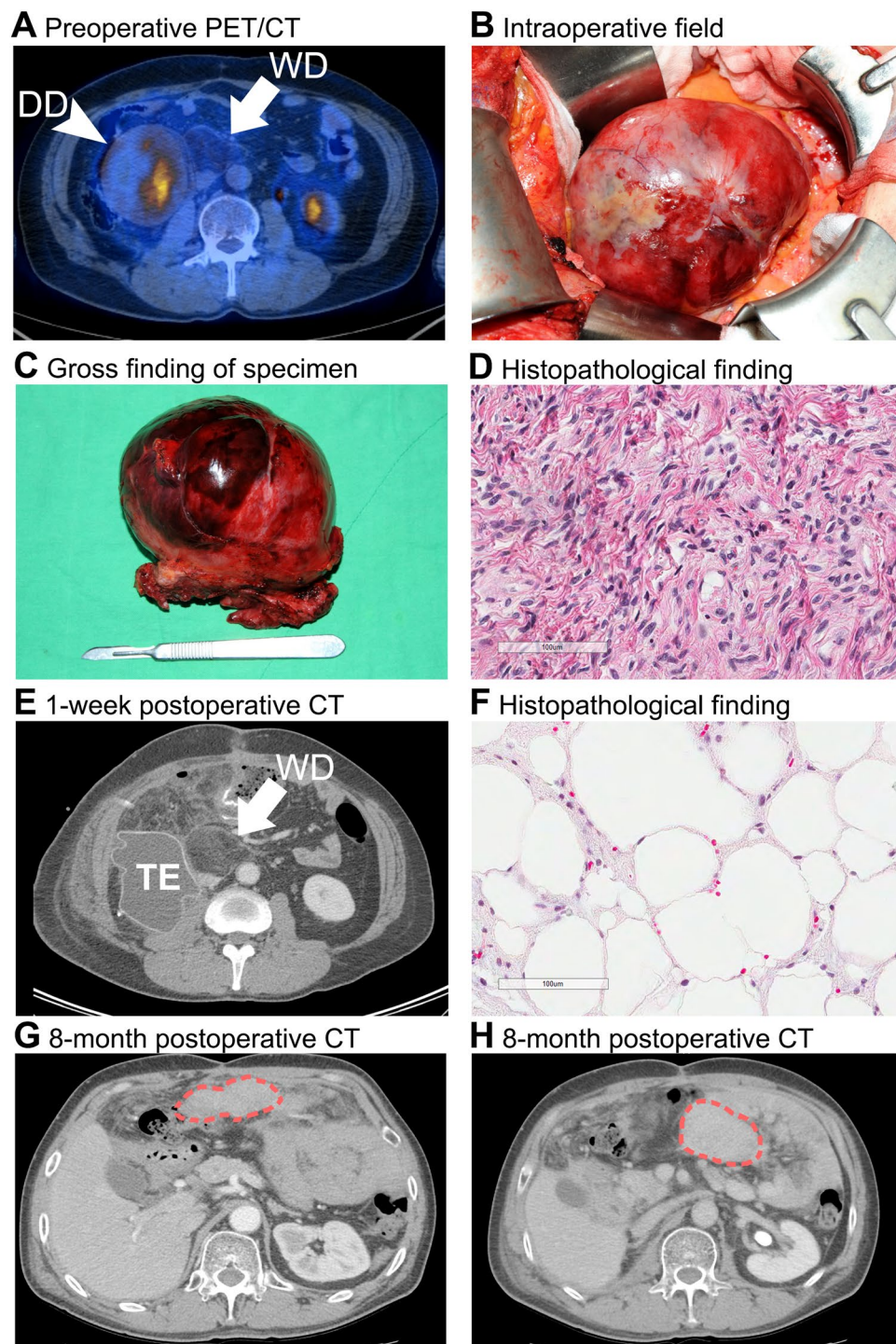


Figure 3. A 56-year-old male patient underwent surgical resection of retroperitoneal LPS. On the preoperative PET/CT scan (A), a hypermetabolic solid mass and a fatty mass with no FDG uptake located on the medial side were detected. A solid LPS was resected (B) and confirmed as DDLPS with FNCLCC grade 2 (C,D). However, the 1-week postoperative CT revealed remnant fatty mass on the medial side (E). After reoperation, the fatty mass was confirmed as WDLPS, FNCLCC grade 1 tumor (F). CT scan performed 8 months after the initial operation revealed peritoneal carcinomatosis with a relatively solid mass (G,H). The patient died 4 months later. Arrowhead indicates DDLPS, arrow indicates WDLPS, red dotted line indicates solid tumor with peritoneal carcinomatosis. **DD** dedifferentiated liposarcoma, **WD** well-differentiated liposarcoma, **TE** tissue expander.

In cases similar to Fig. 3, the clinical significance of preoperative needle biopsy can be limited. In a huge mass, a single site biopsy cannot represent the tumor's aggressiveness properly. Measuring the SUV_{max} can give valuable information in those cases.

This study including the largest cases of retroperitoneal LPS to date showed that SUV_{max} is highly predictive of FNCLCC grade 3 (AUC = 0.877), and $SUV_{max} > 4.5$ can be used as a key prognostic factor before obtaining the histopathology report. For clinicians, this can provide vital guidance in planning the treatment strategies for the patient. For example, based on the SUV_{max} of retroperitoneal sarcoma suspected to be liposarcoma, surgeons can plan whether to perform radical resection such as compartmental resection or to preserve adjacent organs while taking effort to obtain gross complete resection. For radiologists, this study provides important guidance for investigating the usefulness of ^{18}F -FDG PET/CT in other type of STSs.

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Additional Information

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