Evaluation of a diagnostic ^{18}F-FDG PET/CT strategy for differentiating benign from malignant retroperitoneal soft-tissue masses

C.H. Lim [a], H.Y. Seok [b], S.H. Hyun [a], S.H. Moon [a], Y.S. Cho [a], K.-H. Lee [a], B.-T. Kim [a], J.Y. Choi [a],*

[a] Department of Nuclear Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, South Korea
[b] Department of Radiology, Seoul Medical Center, South Korea

ARTICLE INFORMATION

AIM: To investigate the optimal combined 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG) positron-emission tomography (PET)/computed tomography (CT) diagnostic criteria for distinguishing between benign and malignant retroperitoneal soft-tissue masses (RPMs).

MATERIALS AND METHODS: A total of 74 patients (M:F=34:40; age, 53±13.2 years) who underwent FDG PET/CT for the initial work-up of RPMs were included. The maximum standardised uptake value (SUV_{max}), tumour size, presence of fat or calcifications and separated hypermetabolic lesions were included as PET/CT diagnostic parameters. Receiver-operating characteristic (ROC) curves were used to compare the diagnostic performance.

RESULTS: The final pathological diagnoses included 52 malignant and 22 benign tumours. High SUV_{max} (>4.8) and large size (>13 cm) favoured malignancy, and yielded a diagnostic accuracy and AUC of 64.9%, 0.820±0.059, and 68.9%, 0.738±0.061, respectively. In a subgroup of RPMs with a fat component, both SUV_{max} and size were significantly different between benign and malignant RPM, which yielded a diagnostic accuracy and AUC of 91%, 0.977±0.024 (cut-off, 1.9 cm) and 87.9%, 0.865±0.072 (cut-off, 13 cm), respectively. In a subgroup without a fat component, only SUV_{max} was significantly different with an accuracy of 90.2% and AUC of 0.919±0.043. The optimal diagnostic flow by combining SUV_{max} and tumour size after dividing patients into two groups according to the presence of fat showed a sensitivity of 90.4%, a specificity of 95.5%, and an accuracy of 91.9%.

CONCLUSIONS: The combination of SUV_{max} and size according to the presence of a fat component may be the optimal PET/CT diagnostic criteria for distinguishing benign and malignant RPMs.

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* Guarantor and correspondent: J. Y. Choi, Department of Nuclear Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 06351, 81, Irwon-Ro, Gangnam-gu, Seoul, South Korea. Tel.: +82-2-3410-2648; fax: +82-2-3410-2639.
E-mail address: jynm.choi@samsung.com (J.Y. Choi).

Introduction

The retroperitoneum is subject to a broad spectrum of diseases, including diverse benign tumours and malignant neoplasms (of either primary or metastatic nature).

Approximately 70–80% of primary retroperitoneal soft-tissue masses (RPMs) are malignant; however, these only account for 0.1–0.2% of all malignancies.[1] Metastatic tumours may occur in the retroperitoneal space as a consequence of local extension or lymph node involvement.[2] There are various treatment options for these malignancies, which differ according to the specific pathology. Therefore, it is important to non-invasively differentiate these masses at an early stage.[3]

Computed tomography (CT) and magnetic resonance imaging (MRI) play important roles in the differentiation of benign and malignant retroperitoneal lesions. These imaging methods are also important in lesion characterisation and assessment of disease extent and involvement of adjacent/distant structures.[4,5] One study suggested that tumours of a large size with irregular margins and an absence of calcifications are more likely to be malignant compared to other masses without these characteristics.[6] It was reported that interpreting RPM with fat separately could help to narrow the differential diagnosis.[7,8] Regardless, it remains difficult to differentiate masses in the retroperitoneum given their heterogeneity and the substantial overlap of imaging findings.[4,9]

Combined positron-emission tomography (PET)/CT using 2-[18F]-fluoro-2-deoxy-D-glucose (FDG) has been used extensively to differentiate malignant tumours from benign lesions in many organ systems. Semiquantitative analyses with standardised uptake value (SUV) cut-off values have been reported in many studies on discerning malignant lesions in individual organ systems[10–13]; however, to the authors' knowledge, there have been no published studies dealing with the diagnostic criteria required to differentiate between benign and malignant lesions in patients with RPMs. In clinical practice, a maximum SUV (SUV_{max}) of 2.5 has been used as a cut-off to separate benign from malignant lesions[14,15]; however, one previous study reported that a lower SUV_{max} of 0.81 was the best cut-off for differentiating between benign and malignant fat-containing soft-tissue masses in the extremities.[16] Thus, when analysing the best SUV cut-off for discerning benign and malignant RPMs, including fat-containing masses such as liposarcoma, the presence of a fat component may be considered as one component of the optimal diagnostic PET/CT criteria. Additional information provided by the CT portion of PET/CT studies may be useful for lesion characterisation.

Therefore, the aim of the present study was to investigate the optimal FDG PET/CT diagnostic criteria showing the best efficacy for distinguishing benign and malignant RPMs.

Materials and methods

Patients

The medical records of 90 consecutive patients who underwent FDG PET/CT for the characterisation of RPMs and/or initial staging of malignant RPMs detected using other imaging methods (CT and/or MRI, etc.) between January 2013 and July 2016 were reviewed retrospectively. Of these, 16 patients with a history of cancer were excluded from analysis. A total of 74 patients were thus finally included for analysis. All FDG PET/CT examinations were performed prior to tissue diagnosis for pretreatment evaluation. The final diagnoses were histopathologically determined. This retrospective study was approved by the institutional review board. The requirement for written consent was waived.

FDG PET/CT protocol

All patients fasted for at least 6 h and had a blood glucose level <150 mg at the time of PET/CT. Imaging was performed 60 min after the injection of 5 MBq/kg FDG (without intravenous or oral contrast medium) on a Discovery LS (GE Healthcare, Waukesha, WI, USA) or a Discovery STe PET/CT system (GE Healthcare Waukesha, WI, USA). Continuous spiral CT was performed using an eight-slice helical CT (140 keV; 40–120 mA; Discovery LS) or with 16-slice helical CT (140 keV; 30–170 mA; Discovery STe). An emission scan was then performed from head to thigh for 4 minutes per frame in two-dimensional (2D) mode. Reconstruction of these attenuation-corrected PET images (4.3×4.3×3.9 mm) was performed using an ordered-subset expectation maximisation algorithm (28 subsets, two iterations; Discovery LS system). Alternatively, the emission scan was performed for 2.5 minutes per frame in three-dimensional (3D) mode with reconstruction of the attenuation-corrected PET images (3.9×3.9×3.3 mm) using a 3D ordered-subset expectation maximisation algorithm (20 subsets, two iterations; Discovery STe system).

Imaging analyses

FDG uptake in all retroperitoneal tumours was quantified by calculating the SUV_{max} from 3D volumes of interest in the lesion with the highest FDG uptake (visual assessment). The CT portion of the PET/CT images was assessed by an experienced radiologist and a nuclear medicine physician, both of whom were blinded to the clinical information. Decisions regarding tumour characteristics were reached in consensus. The tumour size and presence of fat and calcifications were evaluated. The tumour size was determined by measuring the longest diameter on the CT images. Tumours were classified using the CT attenuation characteristics as having a mainly fatty component (attenuation, less than −20 HU) or as being a mainly soft-tissue mass. Hypermetabolic lesions separated from RPMs were considered as suspicious for metastasis.

Statistical analysis

The significance of differences between groups was assessed by the Mann–Whitney U-test or the Pearson chi-square tests. Independent two-sample t-tests and receiver-operating characteristic (ROC) curves were applied for comparative analyses. Areas under the ROC curves

(AUCs) were calculated non-parametrically and compared using the method derived by Hanley and McNeil.[17] The diagnostic sensitivity, specificity, accuracy, and positive and negative predictive values were calculated using standard formulas, which were compared by chi-square test and McNemar's test. All calculations were performed with SPSS (version 23.0; SPSS Chicago, IL, USA, SPSS Inc.) and MedCalc (version 15.5; MedCalc Software Mariakerke, Belgium, MedCalc) statistical software. A *p*-value of <0.05 was considered significant. Data were expressed as mean-±2×standard error of the mean, unless otherwise mentioned.

Results

Baseline characteristics and final diagnosis

The characteristics of the 74 patients are summarised in Table 1. There were 34 men and 40 women, ranging in age from 18 to 85 years (mean±SD, 53±13.2 years). Fifty-two malignant and 22 benign lesions were included. The malignant lesions included 21 dedifferentiated liposarcomas, nine differentiated liposarcomas, six leiomyosarcomas, four undifferentiated sarcomas, four lymphomas, and others. Two retroperitoneal lesions in case of biopsy-confirmed metastatic carcinoma were ultimately found to be metastases from prostate cancer. The benign lesions included four cases of fat necrosis, three leiomyomas, three schwannomas, three angiomyolipomas, and others. Thirty-three cases (44.6%) had a fat component on CT, which included 26 cases of liposarcomas, three angiomyolipomas, two fat necrosis,

one lipoma, and one myelolipoma. The final diagnoses of all lesions were histopathologically confirmed after surgical resection (*n*=70) or biopsy (*n*=4) within 1 month of FDG PET/CT.

Differential imaging findings of malignant and benign RPMs

RPMs in the entire study population had an average SUV_{max} of 6.7±1.8 with a range between 0.3 and 41.4. The mean SUV_{max} of the malignant masses (8.5±2.5; range, 0.9−41.4) was significantly higher than that of benign lesions (2.2±0.6; range, 0.3−4.8; *p*<0.001; Table 2). The mean size of the malignant masses (16±2.4 cm; range, 3.2−30 cm) was also significantly larger than that of benign lesions (9.4±2.4 cm; range, 2.2−28.9 cm; *p*<0.001; Table 2). All RPMs with additional hypermetabolic lesions highly suspicious for malignancy were proven to be malignant lesions including two lymphomas and two cases of prostate cancer. The proportion of calcification in malignant RPMs was not significantly different from that in benign RPMs (30.8% versus 27.3%; *p*=0.764; Table 2). Although the frequency of fat-containing masses was not different between malignant and benign RPMs, the degree of FDG uptake was significantly different in both benign and malignant RPMs according to the presence of fat. In other words, both benign (2.8±0.6 versus 1±0.4; *p*=0.001) and malignant (13.2±4.1 versus 3.9±1.1; *p*<0.001) RPMs without a fat component had a significantly higher SUV_{max} than those with a fat component.

Differential imaging findings of malignant and benign RPMs according to the presence of fat

Patients were divided into two subgroups according the presence of a fat component for image analysis (Table 3). In both subgroups, malignant RPMs had a significantly higher SUV_{max} than benign RPMs. The tumour size was significantly different between benign and malignant RPMs with a fat component (20.3±3.1 versus 9.8±4.2, respectively; *p*=0.003), but not between malignant and benign RPMs without a fat component (11.7±2.7 versus 9.2±3.1, respectively; *p*=0.144). There were no significant differences in the

Table 1
Baseline patient' characteristics.

Characteristics	*n* (%)
Age (years)	
Range	18−85
Mean	53±13.2
Sex	
Male	34 (46%)
Female	40 (54%)
Tumour pathology	
Malignant	
Dedifferentiated liposarcoma	21 (28.4%)
Differentiated liposarcoma	9 (12.2%)
Leiomyosarcoma	6 (8.1%)
Undifferentiated sarcoma	4 (5.4%)
Lymphoma	4 (5.4%)
Prostate cancer metastasis	2 (2.7%)
Other	6 (8.1%)
Benign	
Fat necrosis	4 (5.4%)
Leiomyoma	3 (4.1%)
Schwannoma	3 (4.1%)
Angiomyolipoma	3 (4.1%)
Other	9 (12.2%)
Fat component on PET/CT	
Present	33 (44.6%)
Absent	41 (55.4%)
Histopathological confirmation by	
Surgical resection	70 (94.6%)
Biopsy	4 (5.4%)

Table 2
Differential PET/CT findings of malignant and benign RPMs.

Findings	Malignant (*n*=52)	Benign (*n*=22)	*p*-Value
Size (cm, range)	16±2.4 (3.2−35)	9.4±2.4 (2.2−28.9)	<.001
SUV_{max} (range)	8.5±2.5 (0.9−41.4)	2.2±0.6 (0.3−4.8)	<.001
Presence of a fat component	26 (50%)	7 (31.8%)	0.150
Presence of calcifications	16 (30.8%)	6 (27.3%)	0.764
Suspicious for metastasis	4 (7.7%)	0 (0%)	0.311

SUV_{max}, maximum standard uptake value; RPMs, retroperitoneal masses.

Table 3
Differential PET/CT findings between malignant and benign RPMs according to the presence of fat component.

Findings	RPMs without a fat component			RPMs with a fat component		
	Malignant (n=26)	Benign (n=15)	p-Value	Malignant (n=26)	Benign (n=7)	p-Value
Size (cm, range)	11.7±2.7 (3.2–35)	9.2±3.1 (4.5–28.9)	0.144	20.3±3.1 (4–33)	9.8±4.2 (2.2–19)	0.003
SUV$_{max}$ (range)	13.2±4.1 (2.8–41.4)	2.8±0.6 (0.3–4.8)	<0.001	3.9±1.1 (0.9–13.3)	1±0.4 (0.4–1.9)	<0.001
Presence of calcifications	9 (34.6%)	6 (40%)	0.730	7 (26.9%)	0 (0%)	0.299
Suspicious for metastasis	4 (15.4%)	0 (0%)	0.278	0 (0%)	0 (0%)	1.000

SUV$_{max}$, maximum standard uptake value; RPMs, retroperitoneal masses.

presence of calcifications and additional hypermetabolic malignant lesions between any of the groups.

Comparison of diagnostic efficacy of PET/CT imaging criteria for differentiating benign and malignant RPMs

Both SUV$_{max}$ and the size of the primary tumour were significantly different between benign and malignant RPMs (Table 2). The AUC from a ROC curve analysis of the SUV$_{max}$ was 0.820±0.059 (Fig 1). With the best cut-off of 4.8, the SUV$_{max}$ showed a sensitivity of 50% (26/52), a specificity of 100% (22/22), an accuracy of 64.9% (48/74), a positive predictive value (PPV) of 100% (26/26), and a negative predictive value (NPV) of 45.8% (22/48) to diagnosis malignant RPMs. The AUC from a ROC curve analysis of size was 0.738±0.061. With the best cut-off of 13 cm, tumour size showed a sensitivity of 61.5% (32/52), a specificity of 86.4% (19/22), an accuracy of 68.9% (51/74), a PPV of 91.4% (32/35), and a NPV of 48.7% (19/39) to diagnose malignant RPMs.

When evaluating the subgroup of RPM with a fat component, both SUV$_{max}$ and size of primary tumour were significantly different between benign and malignant RPMs (Table 3). The AUC from a ROC curve analysis of the SUV$_{max}$ was 0.967±0.024 (Fig 1). With the best cut-off of 1.9, SUV$_{max}$ showed a sensitivity of 88.5% (23/26), a specificity of 100% (7/7), an accuracy of 91% (30/33), a PPV of 100% (23/23), and a NPV of 70% (7/10) to diagnose malignant RPMs. The AUC from a ROC curve analysis of size was 0.865±0.072 (Fig 1). With the same best cut-off of 13 cm, tumour size showed a sensitivity of 88.5% (23/26), a specificity of 85.7% (6/7), an accuracy of 87.9% (29/33), a PPV of 95.8% (23/24), and a NPV of 66.7% (6/9) to diagnose malignant RPMs.

In a subgroup without fat, only SUV$_{max}$ was significantly different between benign and malignant RPMs (Table 3). The AUC from ROC curve analysis of SUV$_{max}$ was 0.919±0.043 (Fig 1). With the same best cut-off of 4.8, SUV$_{max}$ showed a sensitivity of 84.6% (22/26), specificity of 100% (15/15), accuracy of 90.2% (37/41), PPV of 100% (22/22), and NPV of 79% (15/19) to diagnose malignant RPMs.

Optimal diagnostic flow for differentiating malignant from benign RPMs

The optimal diagnostic flow for differentiating malignant from benign RPMs is suggested in Fig 2. In the first step, because both AUCs of SUV$_{max}$ in subgroups with or without fat were higher than that in all subjects groups (0.967 versus 0.820, p=0.011; 0.919 versus 0.820, p=0.132; Fig 1), subjects are divided into two groups according to the

presence of a fat component. In the second step, in RPM patients with a fat component, the differentiation between benign and malignant RPMs can be done based on the combination of both SUV$_{max}$ and tumour size, because these two variables showed significant differences between benign and malignant RPMs. Because both parameters showed a high specificity (SUV, 100%; size, 85.7%) and PPV (SUV, 100%; size, 95.8%) for detecting malignant RPMs, RPMs with higher FDG uptake (SUV$_{max}$ >1.9) or a larger tumour size (>13 cm) could be considered malignant (Fig 3). In RPM patients without a fat component, the differentiation between benign and malignant RPMs can be done based on the SUV$_{max}$, because the SUV$_{max}$ was significantly different between benign and malignant RPMs (Fig 4).

Table 4 demonstrates the comparisons of diagnostic performance according to the different PET/CT criteria. This optimal diagnostic flow showed a high sensitivity of 90.4% (47/52), specificity of 95.5% (21/22), accuracy of 91.9% (68/74), PPV of 97.9% (47/48), and NPV of 80.8% (21/26) to diagnose malignant RPMs in all patients. This combined criteria of SUV$_{max}$, tumour size and presence of fat component showed significantly better sensitivity and accuracy than any single criteria using SUV$_{max}$ (90.4% versus
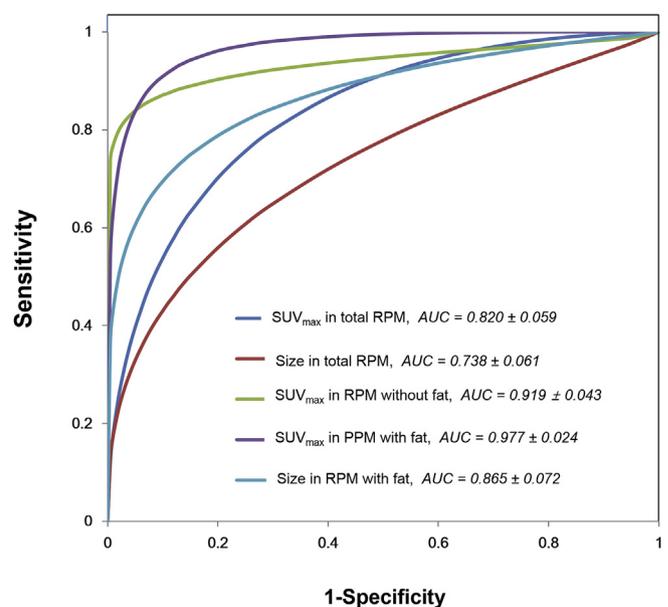

Figure 1 ROC curves illustrating performance of SUV$_{max}$ and size for differentiating benign from malignant retroperitoneal masses.
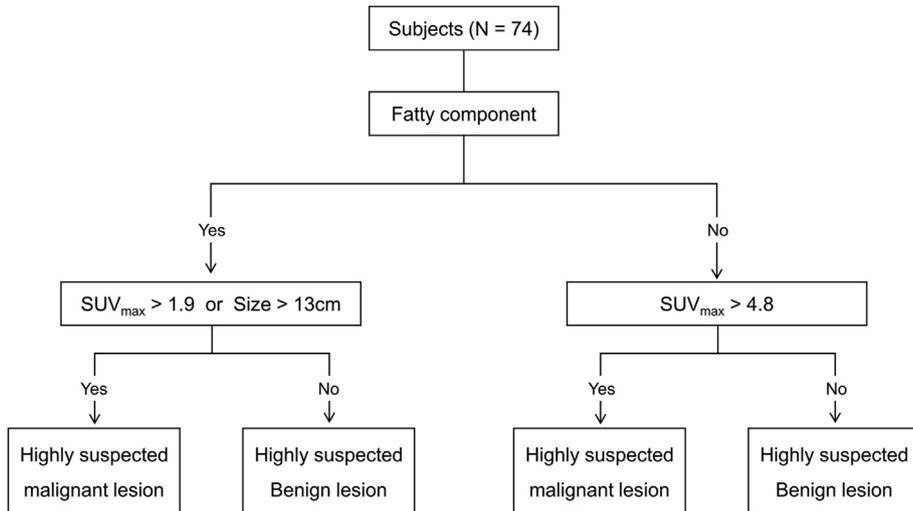
Figure 2 Suggested optimal diagnostic flow chart for differentiating benign and malignant retroperitoneal masses in all patients.

50%, $p < 0.001$; 91.9% versus 64.9%, $p < 0.001$) or tumour size (90.4% versus 61.5%, $p < 0.001$; 91.9% versus 68.9%, $p < 0.001$), respectively, in all patients.

PET/CT findings according to RPM histological tumour type

The PET/CT findings of each histological tumour type are shown in Table 5. In RPMs originated from retroperitoneal fat tissue, FDG accumulation was highest in dedifferentiated liposarcomas ($n=21$; $SUV_{max}=6.6\pm3.7$), followed by differentiated liposarcomas ($n=9$; $SUV_{max}=2.6\pm0.7$), angiomyolipomas ($n=3$; $SUV_{max}=1.1\pm0.7$), and lipoma ($n=1$; $SUV_{max}=0.4$). Four cases of the 31 liposarcomas did not have a fat component, and eight cases had calcifications, all of which were dedifferentiated liposarcomas. Among fat-containing tumours, malignant liposarcomas (dedifferentiated liposarcomas, 19.3±3.5 cm; differentiated liposarcomas, 19.4±5.7 cm) were significantly larger than both benign lipoma (9.6 cm) and angiomyolipomas (12.4±7.6
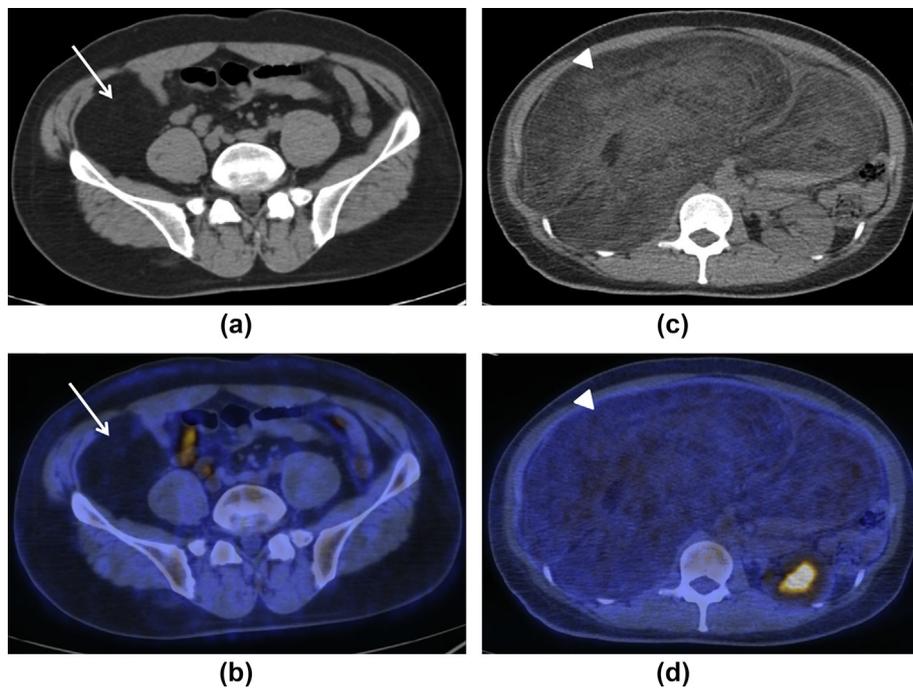

Figure 3 Representative case showing differentiation between benign and malignant retroperitoneal masses with fat component. Axial CT (a) and fused PET/CT (b) images of a 46-year-old male patient showing a 9.6 cm fat-containing mass with faint FDG uptake ($SUV_{max}=0.4$) in the right pelvis (white arrow), which was histopathologically shown to be a benign lipoma. Axial CT (c) and fused PET/CT (d) images of a 37-year-old female patient showing a 29 cm sized fat-containing mass with mild FDG uptake ($SUV_{max}=2.3$) in the right abdomen (white arrowhead), which was shown to be a malignant differentiated liposarcoma.
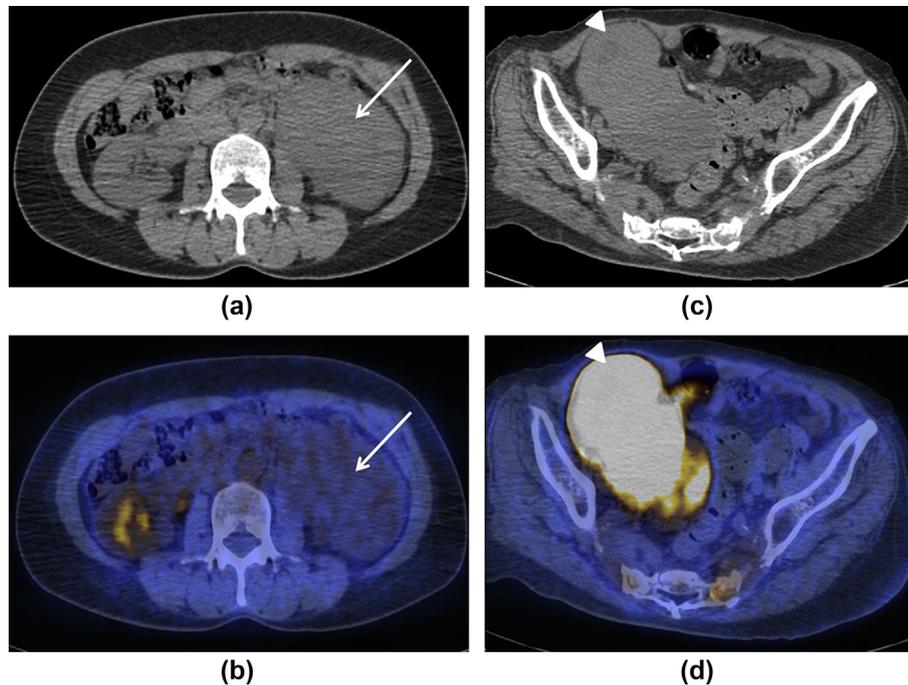
Figure 4 Representative case showing differentiation between benign and malignant retroperitoneal masses without a fat component. Axial CT (a) and fused PET/CT (b) images of a 44-year-old female patient shows a 9.6 cm sized non-fatty mass with mild FDG uptake (SUV_{max}=2.2) in the left abdomen (white arrow), which was shown to be a benign leiomyoma pathologically. Axial CT (c) and fused PET/CT (d) images of a 78-year-old female patient showing an 11 cm non-fatty mass with high FDG uptake (SUV_{max}=27.6) in the right pelvis (white arrowhead), which was shown to be a malignant leiomyosarcoma.

cm). Among RPMs originating from muscular tissues, leiomyosarcomas (n=6; SUV_{max}=17.1±6.4) had the highest FDG accumulation, followed by undifferentiated sarcomas (n=4; SUV_{max}=7.5±3.4) and leiomyoma (n=3; SUV_{max}=2.5±0.8). Undifferentiated sarcomas (20.7±10.3 cm) were larger than both leiomyosarcomas (10.4±1.8 cm) and leiomyomas (7.4±2.2 cm). Although lymphomas had intense FDG accumulation (n=4; SUV_{max}=18.8±15.3), the SUV was variable according to cell types, as follows: diffuse large B cell (SUV_{max}=41.4), high grade B cell (SUV_{max}=14), follicular (SUV_{max}=11.3), and low-grade B-cell lymphoma (SUV_{max}=8.4). In two prostate cancer cases detected initially as RPMs, metastatic lesions had a high FDG uptake (SUV_{max}=7.9±2.1), whereas the primary prostate tumour showed faint or weak FDG uptake. Despite being benign

RPMs, schwannomas demonstrated moderate FDG uptake (n=3; SUV_{max}=3.5±0.8), and partly included calcifications.

Discussion

In the present study, 70.3% (52/74) of retroperitoneal lesions were malignant, which is similar to data from previous reports.[18] Despite a relatively high proportion of malignancy in these cases, the clinical differential diagnosis of benign and malignant tumours is essential for deciding on a therapeutic strategy. Although CT and MRI have been widely used for such differential diagnoses, it remains difficult to differentiate between malignant and benign RPMs given their heterogeneity and the substantial overlap of imaging findings. Although certain metabolic features of RPMs in FDG PET/CT might help this, to the authors' knowledge, there are few studies on the utility of FDG PET/CT for the differential diagnosis of RPM. The best diagnostic decision tree for these masses was developed in the present study based on PET/CT features that could precisely distinguish benign and malignant RPMs.

The metabolic information from FDG PET/CT is often more sensitive than conventional imaging for the detection of metastases in several malignant lesions.[19] Although primary RPMs, such as leiomyosarcomas, are known to metastasise to other sites,[20] hypermetabolic lesions related to metastasis of primary RPMs were not detected in the present cohort. Four patients had hypermetabolic lesions separate from RPMs, two of which were primary

Table 4
Comparisons of diagnostic performance according to the different PET/CT criteria.

Diagnostic flow models	Sensitivity	Specificity	Accuracy
Tumour SUV_{max} in all RPMs	50%[*] (26/52)	100% (22/22)	64.9%[‡] (48/74)
Tumour size in all RPMs	61.5%[†] (32/52)	86.4% (19/22)	68.9%[¶] (51/74)
Combined tumour SUV_{max}/size in RPM according to the presence of fat	90.4%[*†] (47/52)	95.5% (21/22)	91.9%[‡¶] (68/74)

SUV_{max}, maximum standard uptake value; RPMs, retroperitoneal masses; *, †, ‡, ¶, all p< 0.001.

Table 5
Differential PET/CT findings according to RPM histological tumour type.

Histopathological diagnosis	SUV$_{max}$ (range)	Size (cm, range)	Presence of fat	Presence of calcifications
De-differentiated liposarcoma (21)	6.6±3.7 (1.2—41.3)	19.3±3.5 (4—33)	17/21 (81%)	8/21 (38.1%)
Differentiated liposarcoma (9)	2.6±0.7 (0.9—4.2)	19.4±5.7 (5.3—30)	9/9 (100%)	0/9 (0%)
Leiomyosarcoma (6)	17.1±6.4 (7.1—27.6)	10.4±1.8 (8.2—13.8)	0/6 (0%)	3/6 (50%)
Undifferentiated sarcoma (4)	7.5±3.4 (2.8—11.1)	20.7±10.3 (9.7—35)	0/4 (0%)	2/4 (50%)
Lymphoma (4)	18.8±15.3 (8.4—41.4)	10±3.9 (6—15)	0/4 (0%)	0/4 (0%)
Prostate cancer (2)	7.9±2.1 (6.8—8.9)	5.1±2.4 (3.9—6.3)	0/2 (0%)	1/2 (50%)
Fat necrosis (4)	1.7±2.1 (0.5—4.8)	8.2±3.4 (5.2—13)	2/4 (50%)	2/4 (50%)
Leiomyoma (3)	2.5±0.8 (2—3.3)	7.4±2.2 (5.6—9.5)	0/3 (0%)	0/3 (0%)
Schwannoma (3)	3.5±0.8 (2.9—4.4)	7.2±3.9 (4.5—11)	0/3 (0%)	2/3 (75%)
Angiomyolipoma (3)	1.1±0.7 (0.7—1.9)	12.4±7.6 (5.7—19)	3/3 (100%)	0/3 (0%)
Lipoma (1)	0.4	9.6	1/1 (100%)	0/1 (0%)

SUV$_{max}$, maximum standard uptake value.

lymphomas and two were prostate cancer metastases. Previous studies have reported that lymphomas and cases of prostate cancer often present initially as RPMs.[21,22] In addition, these diseases should be discerned from primary retroperitoneal malignant tumours because their primary treatment should be medical not surgical resection. In fact, these RPMs from four patients in which FDG PET/CT was performed for pretreatment evaluation were histopathologically confirmed at biopsy to avoid unnecessary surgical resection. Although the presence of separable hypermetabolic foci suggesting metastatic lesions could be a feature to suggest malignancy, this finding did not support further information in addition to SUV$_{max}$ for distinguishing benign and malignant RPMs in the present study. Therefore, this finding was not included in the decision tree (Fig 2).

Previous articles have demonstrated that the SUV$_{max}$ was the most important contribution for distinguishing benign from malignant soft-tissue lesions.[10–13] The present study of retroperitoneal soft-tissue lesions also indicated that the SUV$_{max}$ had good diagnostic performance for differentiating benign from malignant RPMs compared with various other PET/CT parameters; however, low sensitivity (50%) and NPV (45.8%) did not yield high accuracy for discerning benign and malignant RPMs. Furthermore, a recent article including retroperitoneal/intra-abdominal lesions reported that SUV$_{max}$ could not distinguish malignant and benign tumours.[23] This result was explained by malignant fatty mass with lower SUV$_{max}$, such as well-differentiated liposarcoma, Similarly, the fat-containing RPMs also demonstrated relatively low FDG uptake, compared with RPMs without a fat component. Thus, due to this different degree of FDG uptake, the optimal cut-off SUV$_{max}$ for distinguishing benign from malignant RPMs should be different according to the presence of a fat component, which improved the diagnostic performance and accuracy in the present study.

Historically, the size of the mass has been used as a traditional diagnostic index for differentiating between malignant and benign tumours. Tumour size was measured as the longest tumour diameter on CT. Retroperitoneal tumours are usually large at the time of diagnosis because the retroperitoneal space consists of loose connective tissue, and unrestricted tumour growth can arise without symptoms.[24] Although the present patients also demonstrated a large average tumour size (mean, 14±1.9 cm), malignant RPMs were significantly larger than benign RPMs, which was consistent with in previous studies.[6,25] Interestingly, malignant RPMs with a fat component were larger than benign RPMs with a fat component, whereas there was no significant difference in size between malignant and benign RPMs without fat. This result may be reflected by the high incidence of liposarcomas with a fat component in the retroperitoneal cavity, for which an extremely large size is one of the inherent characteristics.[26–28] Thus, tumour size could be applied as the useful indicator distinguishing malignant and benign only in RPMs with a fat component.

In previous articles using CT and MRI for differentiating RPMs, dividing RPMs according to the presence of a fat component helped to narrow the wide spectrum of these possible lesions to include in the differential diagnosis.[7,8] In the present study, fat-containing RPMs revealed distinguishable PET/CT findings, which had lower FDG uptake and larger size, compared with their counterparts. Because tumour SUV$_{max}$ and size demonstrated a high PPV and specificity, it may be reasonable to consider all cases with tumour SUV$_{max}$ or size exceeding cut-offs as malignant. In fat-containing RPMs, the combination of SUV$_{max}$ and tumour size significantly improved the diagnostic performance of PET/CT compared with the use of a single diagnostic criterion in the present study. Among a total of 33 RPMs with a fat component, e.g., 26 cases had two criteria, SUVmax >13 cm, which proved to be malignant RPMs except one case. Conversely, seven RPMs with low SUVmax (≤1.9) and small size (≤13 cm) proved to be benign lesions except one case. In other words, the combination of these two criteria could improve the accuracy of PET/CT by decreasing false-positive or -negative cases. In RPMs without fat, only tumour SUV$_{max}$, with a different cut-off from that of RPMs without fat, was useful for the differential diagnosis. Therefore, to draw optimal diagnostic results, information regarding tumour SUV$_{max}$, size, and the presence of fat, was required, as shown in Fig 2. Furthermore, these new combined diagnostic criteria showed the best sensitivity and accuracy for detecting malignant RPMs when compared to the use of single criteria.

There have been few previous studies showing the degree of FDG uptake according to the RPM histological tumour type. In RPMs originating from retroperitoneal fat tissue, FDG uptake in liposarcoma was correlated with the tumour grade. Dedifferentiated liposarcomas, with a high-grade tumour, had high FDG uptake, whereas well-differentiated liposarcomas, with a low-grade tumour, showed low FDG uptake. It has been reported that well-differentiated liposarcomas are often misclassified as benign lipomas, due to their heterogeneity and biopsy sampling error.[29] Although the present study included only one retroperitoneal lipoma case due to its relative rarity, it had a lower FDG uptake and smaller size than well-differentiated liposarcomas. In RPMs originating from retroperitoneal muscular tissue, leiomyosarcomas ($n=6$; SUV, 17.1 ± 6.4) and leiomyomas ($n=3$; SUV, 2.5 ± 0.8) showed significant differences in FDG uptake, which may contribute to the differential diagnosis of these two tumours with similar radiological features. In the present study, the presence of calcification was not effective to distinguish between benign and malignant RPMs; however, it may help to predict specific diagnosis due to showing different frequency according to the RPM histological tumour type.

The present study has several limitations. First was its retrospective design, and only RPMs with histological confirmation were included. A second limitation was the relatively small cohort given the low incidence of RPMs, which weakened the statistical power. A validation analysis of the newly devised diagnostic criteria could not be performed. Therefore, further study with a larger population is needed. Finally, contrast-enhanced CT or MRI features, such as tumour border, enhancement, and complications, were not included in the present analysis, because those were performed at outside hospitals in many cases. Uncertainty and heterogeneity of the imaging protocols used and usage of different systems meant that these data were excluded from the study. Nonetheless, this study provides valuable information on a poorly investigated topic.

In conclusion, FDG PET/CT is useful to differentiate newly detected benign and malignant RPMs. The suggested new PET/CT diagnostic criteria, combining SUV_{max} and tumour size according to the presence of a fat component, may be optimal to distinguish benign and malignant RPMs. PET/CT features according to RPM histological tumour type may also provide additional information for the specific differential diagnosis of RPM. Regardless, larger prospective studies are needed to confirm the present results.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

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