Original Article

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Infiltration characteristics and influencing factors of retroperitoneal liposarcoma: Novel evidence for extended surgery and a tumor grading system

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Summary **This study sought to evaluate the infiltration tendency of retroperitoneal liposarcoma (RPLS) from a new pathological angle by exploring the infiltration characteristics, which could provide helpful information to facilitate surgical decision-making and prognosis prediction. Concurrently, we aim to identify significant indicators of infiltration. A total of 61 consecutive patients with RPLS at our institution were retrospectively analyzed. All patients received extended surgery. The tumor infiltration characteristics and influencing factors were studied based on the pathological diagnosis. Univariate and multivariate analyses of organ infiltration (OI) and surrounding fat infiltration (SFI) were performed. OI was found in 95 (28.5%) resected organs from 39 (60.7%) patients, and SFI was found in 119 (35.7%) resected organs from 47 (77%) patients. The tumor infiltrated the serosal layer of 13 organs (13/37, 35.1%), the muscularis layer of 18 organs (18/37, 48.6%) and the submucosa of 6 organs (6/37, 16.2%). The percentage of lipoblasts and the rates of necrosis and mitosis were all significantly higher in high-grade tumors (dedifferentiated, round cell, and pleomorphic). A high lipoblast percentage (≥ 20%) was the only independent risk factor for OI. A recurrent tumor and a high-grade tumor were independent risk factors for SFI. In conclusion, RPLS has a high infiltration tendency, such that it frequently infiltrates organs and surrounding fat tissue. Therefore, extended resection of the tumor and the adjacent organs is recommended. The percentage of lipoblasts was associated with the tumor grade and infiltration characteristics; thus, lipoblast percentage may become a new grading factor for RPLS.**

Keywords: Retroperitoneal sarcoma, liposarcoma, infiltration

1. Introduction

Liposarcoma is the most common histotype of retroperitoneal sarcoma (RPS) (*1*). Local recurrence of RPS was reported to be the leading cause of death in patients with this type of tumor (*1,2*). Pathological evaluation of the involved surgical margins is a major predictor of local tumor recurrence (*1,3,4*). To reduce the local recurrence, achieving negative surgical margins by extended resection of the tumor and the adjacent organs is recommended (*5-7*). The above recommendations were mostly based on analyses of clinical outcomes, such as local recurrence, metastasis and survival. The necessity of extended surgery can be directly evaluated by tumor infiltration based on the postoperative pathology. However, to the best of our knowledge, there are few studies offering details of retroperitoneal liposarcoma (RPLS) infiltration. RPS is reported to have a high rate of visceral infiltration (*8*); however, not all RPSs have similar infiltration characteristics (*8,9*).

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Therefore, we conducted a single-center study analyzing a large series of patients with RPLS who underwent extended surgery to explore the infiltration characteristics and influencing factors of RPLS, which could provide helpful information to facilitate surgical decision-making and prognosis prediction.

Despite the widespread application of some grading systems in the diagnosis and management of sarcomas, there is no accurate grading system for liposarcoma (*10*). Studying the clinico-pathological characteristics of RPLS, especially pathological details after extended resection, can help us establish a new grading rationale, which will provide more information for developing a more reliable grading system.

2. Materials and Methods

2.1. *Patients*

We retrospectively analyzed a total of 61 consecutive patients with RPLS from the Peking University Cancer Hospital Sarcoma Center between March 2015 and March 2017. The median follow-up time was 11 months (interquartile range [IQR], 7-20 months). All patients included in the study underwent surgery with curative intent. Pancreaticoduodenectomy was conducted when the tumor infiltrated the pancreatic head and greater part of the duodenum. If necessary, great vessels (such as the inferior vena cava, aorta and iliac vessels) were removed and replaced with polytetrafluoroethylene grafts. If the diaphragm and/or pericardium showed tumor invasion, partial diaphragm and/or pericardium resection and repair were performed. Our surgical policy was to remove the tumor with adjacent organs *en bloc*, which is more aggressive than most surgeries described in past studies (*5,7,8*).

2.2. *Pathological diagnosis*

All tumors were delivered to the pathology receiving room after the operation. Overall tumor size was defined as the sum of the perpendicular maximum diameters of the primary tumors as reported at the time of initial surgical resection, and tumors were grouped into three overall size categories: < 15 cm, 15-30 cm, and ≥ 30 cm. The specimen was orientated by the surgeon. All margins were perpendicularly sampled, with two or more sections taken from all margins. Additional sections were taken from the closest margin. Serial sampling of all resected organs and surrounding fat was performed, and the tissue between the tumor and organ were sampled every 2 cm.

Two sarcoma pathologists independently conducted the pathological diagnosis. The rate of necrosis, percentage of lipoblasts, and number of mitotic events per high-powered field were all recorded. The results of the serially sampled specimens are presented as their mean lipoblast percentage.

2.3. *Definitions*

The liposarcomas were subdivided into 5 pathological subtypes: well-differentiated, dedifferentiated, myxoid (< 5% round cell component), round cell (≥ 5% round cell), or pleomorphic. Additionally, the liposarcomas were divided into a high-grade group (dedifferentiated, round cell, and pleomorphic) and a low-grade group (well-differentiated and myxoid) (*11*).

Surrounding fat was defined as the fat tissue within 1 mm from the organ surface. The infiltration pattern was classified as organ infiltration (OI) and surrounding fat infiltration (SFI). OI was defined if infiltration of the bowel or parenchyma of the solid organ was observed. SFI was defined if only infiltration of the surrounding fat was observed, without OI.

Lipoblasts have hyperchromatic, indented or sharply scalloped nuclei and a lipid-rich mono- or multivacuolated cytoplasm (*10*). Intracytoplasmic vacuoles appear sharply marginated, which is distinct from the ill-defined vacuoles of pseudolipoblasts that contain mucin. The nucleus of a lipoblast may be pushed aside by a single large lipid vacuole, resulting in a signet-ring configuration, or it may remain centrally located with small indentations caused by multiple, small vacuoles, resulting in an appearance similar to that of sebaceous cells or adrenal spongiocytes. In addition to the above typical lipoblast characteristics, atypical or giant forms having large, irregular or multiple nuclei may be present (*12*).

Surgical resection was described as macroscopically complete (R0 or R1) or incomplete (R2) (*3*).

2.4. *Postoperative complications and follow-up*

Postoperative complications were graded according to the Clavien-Dindo classification (*13*). The patients were prospectively followed by clinical examination, chest X-ray, and abdominopelvic computed tomography (CT) or magnetic resonance imaging (MRI) every three months for the first two years, every six months for the subsequent three years, and yearly thereafter.

2.5. *Data analysis*

Data are presented as median and range, or number and percentage, where appropriate. Variables with a p-value ≤ 0.1 were considered in the multivariate models. Multivariable analysis of OI and SFI was carried out using logistic regression models. For patients who underwent macroscopically complete (R0 or R1) surgical resection, we analyzed the local disease-free survival (DFS) from the date of operation to the date of the last follow-up. Statistical analyses were performed using SPSS version 24.0 (Armonk, NY; IBM Corp) and

R version 3.4.0 (*http://www.r-project.org*). *P*-values less than 0.05 were considered statistically significant.

3. Results

3.1. *Patient characteristics*

Sixty-one patients were enrolled in our study. Thirty-two (52.5%) patients received primary treatment, and the remaining patients received operation after tumor recurrence. All the operations performed before recurrence were simple excisions of the tumor (along with adjacent organs only if visibly infiltrated). Complete macroscopic (R0 or R1) resection was achieved in 55 cases (90.2%). The most common histological type was dedifferentiated liposarcomas (28/61, 45.9%), and there were 17 (27.9%) well-differentiated liposarcomas, 3 (4.9%) myxoid liposarcomas, 4 (6.6%) round cell liposarcomas and 9 (14.8%) pleomorphic liposarcomas. The clinical-pathological characteristics of the entire series are displayed in Table 1.

3.2. *Overview of the operation and infiltration*

Three hundred and thirty-three organs were resected (5.5/patient). Colectomy was the most frequent procedure performed (50/61, 82.0%). Forty-nine (80.3%) patients had at least one organ and/or surrounding fat tissue infiltrated by the tumor. OI was found in 95 resected organs (95/333, 28.5%) of 39 (39/61, 60.7%) patients, and when the organ was infiltrated by the tumor, most of the fat surrounding the organ was also found to be infiltrated. SFI was found in 119 resected organs (119/333, 35.7%) of 47 (47/61, 77%) patients. Mesenteric fat was infiltrated in 13 patients (13/61, 21.3%) who underwent colectomy and/or resection of the small intestine. The details of OI and SFI of resected organs (> 10 patients) are displayed in Figure 1.

Table 1. Patients and characteristics

Characteristics	N (%)
Age [years; median (IQR)]	56 (48-63)
Sex	
Male	33 (54.1)
Female	28 (45.9)
Presentation	
Primary	32 (52.5)
Recurrent	29 (47.5)
Tumor site	
Left side	13 (21.3)
Right side	17 (27.9)
More than one area	31 (50.8)
Tumor number	
Single	46 (75.4)
Multiple	15 (24.6)
Tumor size	
< 15 cm	11 (18.0)
15-30 cm	31 (50.8)
≥ 30 cm	19 (31.1)
Number of organs resected [median (IQR)]	5 (2-8)
Histological subtype	
Well-differentiated	17 (27.9)
Dedifferentiated	28 (45.9)
Myxoid	3 (4.9)
Round cell	4 (6.6)
Pleomorphic	9 (14.8)
Resection margins	
Macroscopically complete	55 (90.2)
Macroscopically incomplete	6 (9.8)
Grade	
Low-grade	20 (32.8)
High-grade	41 (67.2)

IQR, interquartile range.

3.3. *Infiltration of the hollow viscera*

For the hollow viscera (including the colon, small intestine and stomach), 37 organs (37/95, 38.9%) were infiltrated by the tumor. Of these, the tumor infiltrated the serosal layer of 13 organs (13/37, 35.1%), the muscularis of 8 organs (18/37, 48.6%) and the submucosa of 6 organs (6/37, 16.2%) (Figure 2). The

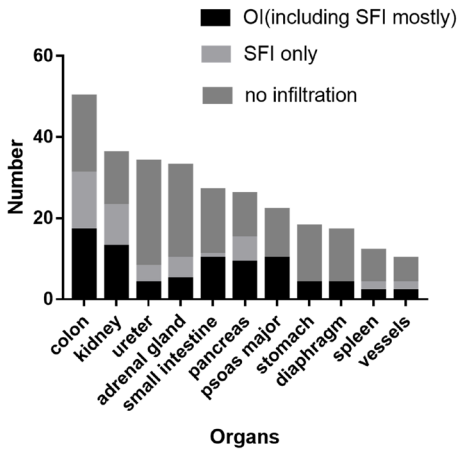

Figure 1. The details of OI and SFI of resected organs (> 10 patients). OI (including SFI in most cases): organ infiltration. When the organ is infiltrated by the tumor, most of the fat surrounding the organ is simultaneously infiltrated. SFI only: only surrounding fat infiltration was observed, without OI.

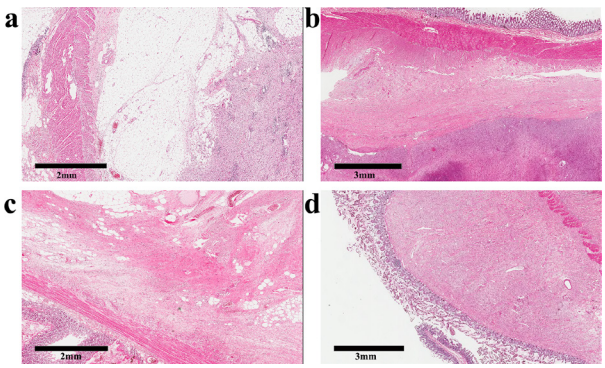

Figure 2. Infiltration of the hollow viscera. (a) Liposarcoma infiltration of the surrounding fat tissue of the colon; **(b)** Liposarcoma infiltration of the serosal layer of the colon; **(c)** Liposarcoma infiltration of the muscularis of the colon; **(d)** Liposarcoma infiltration of the submucosa of the duodenum.

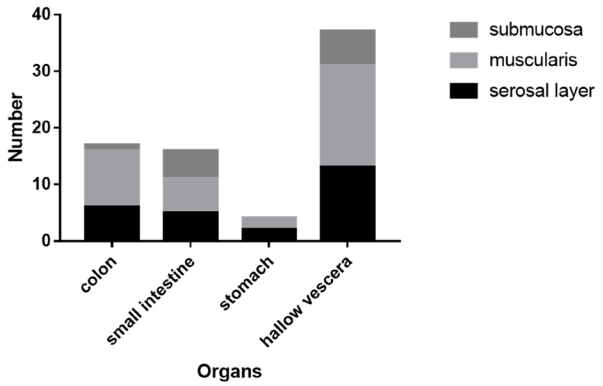

Figure 3. Infiltration details of the hollow viscera.

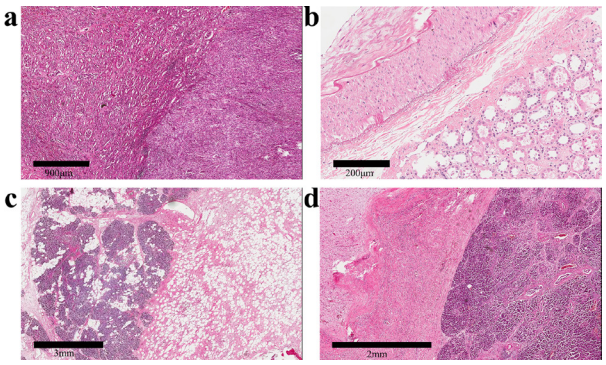

Figure 4. Infiltration of the kidney and pancreas. (a) Liposarcoma infiltration observed in the renal parenchyma; **(b)** Liposarcoma infiltration observed in only the perirenal fat sac, without the renal parenchyma being infiltrated; **(c)** Liposarcoma infiltration observed in the pancreatic parenchyma; **(d)** Liposarcoma infiltration observed in only the surrounding fat tissue of the pancreas, without the pancreatic parenchyma being infiltrated.

colon was the most frequently infiltrated organ (17/50, 34.0%). Of the colon samples, the tumor infiltrated the serosal layer in 6 patients (6/17, 35.3%), the muscularis in 10 patients (10/17, 58.8%) and the submucosa in 1 patient (1/17, 5.9%). Fourteen (14/50, 28.0%) patients showed infiltration of the surrounding fat tissue without colon infiltration (Figure 2a). Infiltration details of the hollow viscera are displayed in Figure 3.

3.4. *Infiltration of the kidney and pancreas*

Of the patients who underwent nephrectomy, 13 (13/36, 36.1%) were found to have tumor infiltration of the renal parenchyma and 10 (10/36, 27.8%) were found to have tumor infiltration in only the perirenal fat sac (Figure 4a and 4b). Of the patients who underwent a pancreas resection, 9 (9/26, 34.6%) were found to have tumor infiltration of the pancreatic parenchyma and 6 (6/26, 23.1%) showed tumor infiltration in only the surrounding fat tissue (Figure 4c and Figure 4d).

3.5. *Necrosis, lipoblast percentage, mitosis and grade*

Twenty-six (26/61, 42.6%) patients showed tumor

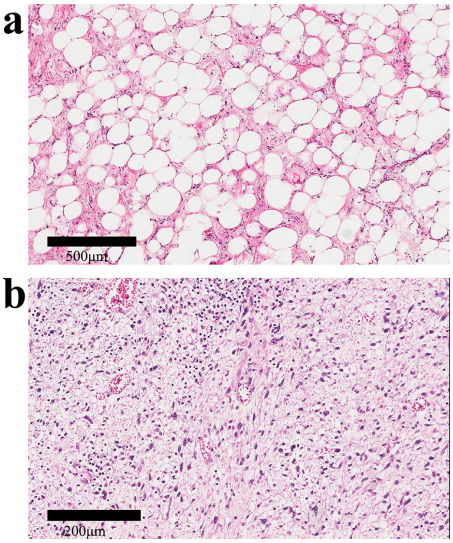

Figure 5. Lipoblast percentage. (a) Low lipoblast percentage (≤ 20%); **(b)** High lipoblast percentage (≥ 20%).

necrosis. Necrosis was found in 3 patients (3/20, 15%) with low-grade tumors and 23 patients (23/41, 56.1%) with high-grade tumors ($p = 0.002$). The median percentage of lipoblasts was 10% (IQR 5%-32.5%). In patients with low-grade tumors, the median percentage of lipoblasts was 5%, and 80.0% of patients had percentages no higher than 5% (Figure 5a). However, the median percentage of lipoblasts was 20% (IQR 5%-40%) in patients with high-grade tumors (Figure 5b). There was a statistically significant difference between the two groups ($p < 0.001$). Mitosis was observed in the tumors of 29 patients (29/61, 47.5%), and the median number of mitotic events per high-powered field was 3 (IQR 1.5-5.5) in these patients. Mitosis was found in the tumors of 3 patients (3/20, 15%) with low-grade tumors and 26 patients (26/41, 63.4%) with high-grade tumors ($p < 0.001$).

3.6. *Risk factors of OI and SFI*

The tumor site ($p = 0.037$), a high tumor grade ($p = 0.002$), necrosis ($p = 0.022$) and a high lipoblast percentage (≥ 20%) ($p = 0.002$) were all significantly associated with OI in the univariate analysis. In the multivariate analysis, these associations were confirmed for the high lipoblast percentage (≥ 20%) (OR: 11.67; 95% CI: 2.39-56.87; $p = 0.002$).

In the univariate analysis, recurrent tumor ($p = 0.034$), a high tumor grade ($p = 0.001$) and a high lipoblast percentage (≥ 20%) ($p = 0.024$) were all significantly associated with SFI. Multivariate analysis showed that recurrent tumors (OR: 6.18; 95% CI: 1.24-30.75; $p = 0.026$) and high-grade tumors (OR: 11.62; 95% CI: 2.61-51.64; $p = 0.001$) were independent risk factors for SFI. The univariate and multivariate analyses of risk factors of OI and SFI are shown in Table 2.

Table 2. Univariate and multivariate analyses of OI and SFI

Characteristics	OI			SFI		
	Univariate analysis *p*-value	Multivariate analysis OR (95% CI)	*p*-value	Univariate analysis *p*-value	Multivariate analysis OR (95% CI)	*p*-value
Age	0.143			0.232		
Sex	0.557			0.340		
Male						
Female						
Presentation	0.437			0.034		0.026
Primary					1	
Recurrent					6.18 (1.24-30.75)	
Tumor site						
Left side	0.042	1	0.371	0.358		
Right side	0.583	0.49 (0.06-4.18)	0.516	0.271		
More than one area	0.037	0.37 (0.06-2.43)	0.172	0.153		
Tumor number	0.115			0.276		
Single						
Multiple						
Tumor size						
< 15 cm	0.267			0.691		
15-30 cm	0.156			0.758		
≥ 30 cm	0.539			0.421		
Grade	0.002		0.155	0.001		0.001
Low-grade		1			1	
High-grade		2.89 (0.67-12.50)			11.62 (2.61-51.64)	
Necrosis	0.022		0.486	0.232		
No		1				
Yes		1.79 (0.35-9.10)				
Lipoblast percentage	0.002		0.002	0.024		0.089
< 20%		1			1	
≥ 20%		11.67 (2.39-56.87)			7.53 (0.74-76.87)	
Mitosis	0.069		0.735	0.114		
No		1				
Yes		0.76 (1.50-3.75)				

IQR, interquartile range; OI, organ infiltration; SFI, surrounding fat infiltration.

3.7. *Postoperative morbidity*

Grade 3-4 postoperative morbidity occurred in 13 (13/61, 21.3%) patients. Grade 3a, 3b and 4 occurred in 6 (6/61, 9.8%), 3 (3/61, 4.9%), and 4 patients (4/61, 6.6%), respectively. Four patients had abdominal infections. Three patients had grade B postoperative pancreatic fistulas (POPF). Four patients had postoperative hemorrhages: 2 patients were due to gastroduodenal artery bleeding; 1 patient was due to gastrointestinal anastomosis bleeding and 1 patient was due to rupture of the iliac artery and artificial vessel anastomosis. One patient had necrosis of the left lower extremity, and thrombosis of the inferior vena cava occurred in 1 patient. Surgical reintervention was necessary in 7 patients (7/61, 11.5%). Three patients underwent surgery for abdominal infection, 2 for gastroduodenal arterial bleeding, 1 for rupture of the iliac artery and artificial vessel anastomosis, and 1 for necrosis of the left lower extremity. Three patients (3/61, 4.9%) died of postoperative complications within 90 days of surgery. Of these, 1 patient underwent reoperation for abdominal infection. The 2 remaining deaths were due to myocardial infarction and renal failure, respectively.

3.8. *Follow-up*

Of the 55 patients who underwent macroscopically complete (R0 or R1) resection, 3 patients (3/55, 5.6%) experienced local recurrence, and 1 patient experienced death after recurrence. The 1-year DFS was 91.2% (95% CI: 83.2%-100.0%) in patients with macroscopically complete resection. Of the 6 patients who underwent R2 resection during the operation, 3 patients died of tumor progression. The 1-year overall survival (OS) was 91.2% (95% CI: 84.1%-99.9%) in all the patients who received extended surgery.

The patient's ability to perform general daily activities was scored according to a modified Barthel Index (mBI) (*14*). Fifty-seven patients (93.4%) scored 100, and the remaining patients scored higher than 70.

4. Discussion

In this study, 61 consecutive patients with RPLS were surgically treated at our center. Reviewing the pathological results, we found that the infiltration of RPLS had several characteristics. As RPLS tends to infiltrate adjacent organs, the tumor infiltrated at least one organ and/or the surrounding fat tissue in

most patients (49/61, 80.3%) evaluated in our study. In addition, the RPLS infiltrated the deep layer of the cavity organs. The above results indicate that RPLS has a strong ability to infiltrate surrounding areas. This conclusion is of great importance because surgeons too often believe that RPLS is a mass that only presses against but does not infiltrate the adjacent organs; consequently, patients undergo simple resection of the tumor itself and may be at increased risk of more frequent tumor recurrence. Our notion supports a policy of extended surgery beyond visible infiltrations.

In our study, extended resection of the tumor and adjacent kidney was performed based on the preoperative imaging features and intra-operative exploration. However, the postoperative pathological diagnosis showed only 36.1% of the patients who underwent nephrectomy had renal parenchyma infiltration, and 27.8% were found to have tumor infiltration in only the perirenal fat sac. The above infiltration characteristics may suggest the reasonability to preserve these uninvaded organs. However, there are no current techniques to evaluate RPLS infiltration accurately before or during the operation. Preserving kidneys without reliable evaluation of parenchymal infiltration may result to the increase probability of recurrence. Moreover, previous studies have indicated that renal resection during the primary surgery provided better DFS (*15,16*). Furthermore, a published study with more than four years of follow-up revealed that patients who underwent renal resection did not require treatment for renal insufficiency, even among patients who received postoperative chemotherapy (*17*). Additionally, during kidney-preserving surgery, exploration is necessary to determine whether the tumor has invaded the renal parenchyma, which may lead to rupture of the RPLS and increase the probability of recurrence and peritoneal metastasis (*18*). Therefore, nephrectomy is recommended for RPLS that occurs adjacent to the kidney. The detailed imaging features of patients with renal parenchymal infiltration needs to be studied in the future, which can help with determination of renal parenchymal infiltration before operation.

In this study, we showed for the first time that a considerable proportion of resected pancreases had only SFI and were free of parenchymal infiltration, even though extended resection of the tumor and adjacent pancreas was performed based on the preoperative imaging features and intra-operative exploration. Currently, no technique can accurately assess parenchymal infiltration before or during surgery. Preserving pancreas without reliable evaluation of parenchymal infiltration results to the increase probability of positive surgical margin and local recurrence. Furthermore, it was reported that the clinical outcomes of individuals with recurrent tumors were worse than primary tumors (*19-21*). In addition, although POPF accounted for 23.1% of all Grade 3 and 4 complications in the present study, drainage was effective in those cases. Furthermore, no long-term morbidity related to pancreas resection occurred during the follow-up. Therefore, organ preservation will be possible only if preoperative or intra-operative techniques are developed to accurately assess adjacent organ involvement.

Grade 3-4 postoperative complications occurred in 13 patients (21.3%), and surgical reintervention was necessary in 7 patients (11.5%). These results are comparable to those of previous studies of extended resection for RPS, which revealed severe postoperative complication rates of 16.4-30% and surgical reintervention rates of 12-14% (*5,22,23*). Bonvalot *et al*. (*5*) and MacNeill *et al*. (*23*) reported that removing organs can increase postoperative complications. However, these previous studies also showed that postsurgical morbidity did not affect the oncological outcome (*5,23*). Considering the strong infiltrative ability of RPLS mentioned above, preserving the organs and removing the invaded surrounding fat necessitates only the surgeon's careful consideration on the recurrent risks and benefits. Our data also showed that the perioperative mortality, rate of postoperative morbidity and rate of reoperation after extended surgery were acceptable. Currently, extended resection including the tumor and adjacent organs should be suggested to achieve radical treatment.

Furthermore, our study found that recurrent and high-grade tumors can significantly increase the incidence of SFI. This association may be the cause of the high local DFS of patients with recurrent and high-grade tumors observed in previous studies (*1,24,25*). Previous studies have shown that patients with high-grade sarcomas do not significantly benefit from extended resection (*7,26*) and that distant metastasis was a limiting factor. Lehnert T *et al*. (*21*) reported that consequent reoperation led to satisfactory long-term survival rates after resection of recurrent tumors. However, Gronchi *et al*. (*19*) reported that a second surgery is of limited benefit for individuals with recurrent tumors. Park JO *et al*. (*20*) reported that only patients with local recurrence growth rates slower than 0.9 cm per month were associated with improved survival after aggressive resection of the local recurrence. There is no consensus on the treatment of recurrent tumors. If an operation is conducted for recurrent and high-grade tumors, a more extended resection including retroperitoneal fat and tumor adjacent organs is the recommended approach to reduce local DFS because of their higher rate of SFI.

Lipoblasts are conceptually an immature or precursor form of adipocytes and are essentially identified in neoplastic conditions (*12*). Traditionally, great emphasis has been placed on the identification of lipoblasts as a diagnostic marker for liposarcoma (*10*). However, as far as we know, the relation between the lipoblast count and the tumor grade or degree of

infiltration has not been explored in previous studies. In our study, quantitative analysis of lipoblasts was carried out, and interestingly, we found that an increase in lipoblast percentage can significantly increase the incidence of OI (OR: 11.67; 95% CI: 2.39-56.87; p = 0.002). Moreover, there was also a tendency to increase the occurrence of SFI (OR: 7.53; 95% CI: 0.74-76.87; p = 0.089). Therefore, lipoblast percentage can be considered a new indicator to predict the ability of infiltration.

Our results show that the rate of necrosis was significantly increased in high-grade tumors. The grading system published by the National Cancer Institute (NCI) (*27*) and the French Federation of Cancer Centers Sarcoma Group (FNCLCC) (*28*) both consider necrosis and mitosis as indicators of oncological outcomes. However, the percentage of lipoblasts has never been considered in previous studies (*27,29-31*). Some studies have shown that RPLS infiltration of adjacent organs is associated with a poor prognosis (*25*), and an increase in the percentage of lipoblasts can significantly increase the infiltration of RPLS. Thus, the lipoblast percentage can also be considered a grading factor for RPLS. As this study was limited by its short follow-up time, the relationship between lipoblast percentage and oncological outcome cannot be verified for the time being.

To improve the prognosis of patients with RPLS, extended resection of the tumor and the adjacent organs is recommended (*5-7*). In the present study, the 1-year DFS rate was 91.2% in patients with macroscopically complete resection. Of the 6 patients who underwent R2 resection during the operation, 3 patients died of tumor progression. Although the follow-up period is short, the follow-up results to date are encouraging. Furthermore, during the follow-up period, all living patients had a high quality of life. However, a larger sample size and longer follow-up time will help further validate the efficacy of extended surgery in our center.

In conclusion, RPLS has a high infiltrative tendency, such that it frequently infiltrates organs and surrounding fat. Meanwhile, the perioperative mortality, rate of postoperative morbidity and rate of reoperation after extended surgery were deemed acceptable. Therefore, extended resection of the tumor and the adjacent organs should be recommended. Moreover, the percentage of lipoblasts was found to be associated with the tumor grade and infiltration characteristics. Thus, the lipoblast percentage may become a new grading factor for RPLS.

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