



Prediction of intraoperative bleeding and blood transfusion in patients with recurrent retroperitoneal liposarcoma: a retrospective study

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Background: Surgery is the main treatment for recurrent retroperitoneal liposarcoma (RPLS). The aim of the present study was to explore the factors associated with blood loss during surgery for recurrent RPLS.

Methods: This retrospective study included patients with first recurrence of RPLS who were treated at our hospital between January 2015 and December 2019. Factors associated with intraoperative blood loss were identified by univariate and multivariate logistic regression analyses. Receiver-operating characteristic (ROC) curve analyses were conducted to evaluate whether tumor size and number of tumor-containing abdominal/pelvic zones were predictive of the need for blood transfusion.

Results: The study included 67 cases. The number of zones containing tumors was 1 in 4 cases (6%), 2 in 36 cases (53.7%), 3 in 14 cases (20.9%), and 4 in 13 cases (19.4%). Tumor size was associated with blood loss >500 mL [odds ratio (OR): 1.153, 95% confidence interval (CI): 1.051–1.266, P=0.003]. The number of tumor-containing zones was associated with blood loss >1,000 mL (OR: 3.161, 95% CI: 1.248–8.003, P=0.015) and >1,500 mL (OR: 2.674, 95% CI: 1.061–6.739, P=0.037). Multiple tumors were associated with blood loss >2,000 mL (OR: 3.161, 95% CI: 1.092–13.133, P=0.036) and >2,500 mL (OR: 2.674, 95% CI: 1.243–16.299, P=0.022). Tumor dedifferentiation was associated with blood loss >1,000 mL (OR: 4.802, 95% CI: 1.287–17.916, P=0.019) and >1,500 mL (OR: 9.249, 95% CI: 1.927–44.39, P=0.005). ROC curve analysis showed that tumor size >15.25 cm [area under the ROC curve (AUC): 0.772, P<0.001] and the number of tumor-containing zones >2.5 (AUC: 0.670; P=0.023) were predictive of the need for blood transfusion.

Conclusions: The main finding of the present study was that a larger tumor size, a larger number of tumor-containing zones, multiple tumors, and dedifferentiation were independently associated with a larger volume of intraoperative blood loss in patients with recurrent RPLS. The tumor size >15.25 cm and the tumor area >2.5 areas predicted the need for blood transfusion. Formulating the intraoperative blood transfusion plan for recurrent RPLS, it is necessary to pay attention to two spatial factors, tumor size and affected area, rather than one of them.

Keywords: Retroperitoneal liposarcoma (RPLS); recurrence; bleeding; intraoperative blood loss; risk factors

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Introduction

Retroperitoneal liposarcoma (RPLS) is a rare tumor with an incidence rate <1/100,000/year (1-5). RPLS includes many different histological tumor types and accounts for 50% of all retroperitoneal sarcomas (6). Because tumors in the retroperitoneal space can grow unnoticed for a long period of time, RPLS often presents at the time of diagnosis as a huge mass involving many surrounding organs and important blood vessels. As a result of this, the treatment for RPLS is often challenging.

Surgical resection is the mainstay of therapy for RPLS and is the only curative treatment available (2,3,7), and the roles of radiotherapy and chemotherapy in the management of RPLS remain controversial (8-13). Although RPLS metastasis is uncommon, local tumor recurrence occurs in >50% of patients after surgery (14,15). Moreover, 70% of RPLS-related deaths are due to local recurrence rather than distant metastasis or other reasons (8,16). The high recurrence rate of RPLS is thought to be due to various biological, anatomical, and surgical factors (17,18), and more extensive surgery is thought to reduce the risk of local recurrence (19-21). The main factors associated with an increased risk of postoperative local tumor recurrence are high tumor grade, dedifferentiated histological subtype, multifocality, and clear margins after surgical resection (19,22-25).

Reoperation remains the first treatment option for the local recurrence of RPLS (26), and surgery can be performed repeatedly if necessary. However, debate remains as to the indications for, and timing of, surgery after recurrence (18,27,28). The current consensus in China is that reoperation should be performed if the recurrent tumor is >10 cm in size or if organ dysfunction occurs due to compression (29). However, most patients with RPLS recurrence require emergency admission to hospital, with clinical symptoms, such as abdominal distension, intestinal obstruction, hydronephrosis, and/or lower limb edema. Although systematic resection of adjacent organs and structures is recommended to maximize the chances of an R₀ resection (19,21,30), extensive surgery can be particularly difficult in patients with tumor recurrence due to factors such as poor clinical status, gastrointestinal tract obstruction, infection, anemia, electrolyte disorders, hypoproteinemia, extensive adhesions of the abdominal organs, involvement of multiple major organs and blood vessels, and anatomical restrictions (31).

Intraoperative blood loss is an important complication of non-cardiac surgery, which may increase the postoperative incidence rate and mortality. For patients with obvious

surgical blood loss, hospitals with higher blood transfusion rate have lower 30-day mortality after adjustment for these patients (32). Although blood transfusion is an important treatment link to make up for intraoperative bleeding, in terms of surgical resection of soft tissue tumors, the selection of surgical margins, surgical methods, surgical sites, and the duration and difficulty of surgery vary widely. Therefore, it is difficult to perform preoperative evaluation for each case to assess the risk of surgery related complications, especially blood loss (33),

In addition, the experience and surgical skills of surgeons are particularly important. It is generally recommended that professional retroperitoneal tumor centers carry out multidisciplinary team (MDT), and make reliable surgical plans after fully assessing intraoperative risks before surgery (34,35). However, in spite of this, there are often unpredictable and uncontrollable bleeding during the operation. Professional retroperitoneal tumor surgeons usually face the situation that in order to preserve the safety of patients, the control of intraoperative bleeding risk is the first element, and the thoroughness of tumor resection may be affected by it. Although some of these factors would be expected to increase the risk of blood loss during reoperation, to the best of our knowledge, no previous clinical studies have investigated the factors associated with greater blood loss during surgery for recurrence of RPLS. Therefore, it is very important to predict the risk of the operation plan and make the operation plan before operation. This is the clinical focus of our research. In the past, the analysis of influencing factors on intraoperative bleeding of retroperitoneal tumors mainly focused on the initial patients, tumor size, pathological subtype, expanded resection scope and poor American Society of Anesthesiologists (ASA) physical status classification (36,37) diameter of specific large blood vessels involved, the vascular density in the tumor and the blood flow in the blood vessels (33).

The aim of the present study was to review the clinical data of patients with first recurrence of RPLS and to explore the factors associated with intraoperative blood loss. We present the following article in accordance with the STROBE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-4222/rc>).

Methods

Study design and participants

This retrospective study included patients with a first relapse of RPLS after surgery who were treated at our

Table 1 Clinical characteristics of the study participants

Characteristics	Value (n=67)
Sex, n (%)	
Male	42 (62.7)
Female	25 (37.3)
Age (years), mean \pm SD	53.46 \pm 10.47
Number of tumors, n (%)	
Single	32 (47.8)
Multiple	35 (52.2)
Tumor size (cm), median (range)	24.49 (9.0–88.0)
Number of tumor-containing zones, mean \pm SD	2.54 \pm 0.88
Number of tumor-containing zones, n (%)	
1 zone	4 (6.0)
2 zones	36 (53.7)
3 zones	14 (20.9)
4 zones	13 (19.4)
Intraoperative blood loss (mL), median [range]	1,150 [50–18,000]

SD, standard deviation.

hospital between January 2015 and December 2019. The inclusion criteria were pathological diagnosis of RPLS and first postoperative recurrence. The exclusion criteria were as follows: (I) administered radiotherapy, chemotherapy, or targeted therapy; (II) distant metastasis; and (III) previous surgical treatment for other tumor types. The study was conducted in accordance with the Declaration of Helsinki (revised in 2013). The study was approved by the ethics committee of Peking University International Hospital (No. 2018-027[BMR]). Because of the retrospective study design, the requirement of consent was waived.

Data collection and primary outcome

The following general, tumor, and treatment-related characteristics were extracted from medical records: age, sex, number of recurrent tumors (single or multiple), tumor size, number of tumor-containing zones, estimated intraoperative blood loss, amount of blood transfused, and results of enhanced computed tomography. The number of zones occupied by the outer edge of the tumor on imaging was determined according to the 4-zone method, in which the abdomen and pelvis were divided into the following 4 regions:

upper left abdomen, upper right abdomen, lower abdomen, and pelvic cavity (38). The area above the connecting line between the lowest points of the 10th ribs was divided into the left upper abdomen and the right upper abdomen based on the abdominal midline. The lower abdomen was defined as the lower area above the connecting line between the right and left anterior superior iliac spines. The area below the lower abdomen was defined as the pelvis. The primary outcome of the present study was intraoperative blood loss.

Statistical analysis

The analysis was performed using SPSS version 26.0 (IBM, Armonk, NY, USA). Shapiro-Wilk test was used to evaluate the normality of the measurement data. Normally distributed continuous data were presented as mean \pm standard deviation, non-normally distributed continuous data were described as median (range), and count data were expressed as n (%). Univariate (single factor, with outcome as a binary variable) logistic regression analysis was performed to screen for factors associated with intraoperative blood loss, and variables with $P < 0.10$ were included in a multivariate logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Receiver-operating characteristic (ROC) curve analysis was carried out to evaluate whether tumor size and number of tumor-containing zones could be predictive of the need for blood transfusion. $P < 0.05$ was taken to indicate a statistically significant difference. The area under the ROC curve (AUC) and the optimal cutoff values for tumor size and number of tumor-containing zones were calculated.

Results

Patient characteristics

Among the 84 patients screened, 3 were excluded due to treatment with radiotherapy, chemotherapy, or targeted therapy; 3 were excluded due to distant metastasis; 5 were excluded due to surgical treatment of other tumor types; 4 were excluded because surgery was refused; and 2 were excluded due to death during the perioperative period. The final analysis included 67 cases (42 males, 62.7%) aged 53.46 \pm 10.47 years. The recurrent RPLS tumors involved 1 zone in 4 cases (6%), 2 zones in 36 cases (53.7%), 3 zones in 14 cases (20.9%), and 4 zones in 13 cases (19.4%). The clinical characteristics of the study participants are summarized in *Table 1*.

Table 2 Univariate logistic regression analysis of factors associated with intraoperative blood loss volume

Factors	>500 vs. ≤500 mL		>1,000 vs. ≤1,000 mL		>1,500 vs. ≤1,500 mL		>2,000 vs. ≤2,000 mL		>2,500 vs. ≤2,500 mL	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.024 (0.973–1.077)	0.368	1.052 (1.001–1.106)	0.047	1.044 (0.993–1.098)	0.093	1.057 (1.001–1.117)	0.048	1.037 (0.983–1.094)	0.187
Tumor size	1.155 (1.061–1.258)	0.001	1.046 (0.999–1.096)	0.054	1.052 (1.004–1.101)	0.033	1.052 (1.004–1.101)	0.032	1.047 (1.001–1.095)	0.043
No. tumor-containing zones	2.064 (1.012–4.211)	0.046	2.003 (1.094–3.67)	0.024	1.813 (1.007–3.266)	0.048	1.684 (0.924–3.07)	0.089	1.928 (1.033–3.597)	0.039
Sex (female vs. male)	0.631 (0.217–1.835)	0.398	0.923 (0.343–2.486)	0.874	0.827 (0.297–2.301)	0.716	0.778 (0.263–2.298)	0.649	0.704 (0.228–2.174)	0.542
Tumor number (multiple vs. single)	1.136 (0.399–3.238)	0.811	1.949 (0.737–5.154)	0.179	2.414 (0.873–6.67)	0.089	3.25 (1.069–9.88)	0.038	3.6 (1.118–11.594)	0.032
Pathological type										
Dedifferentiated vs. highly differentiated	1.944 (0.654–5.784)	0.232	2.479 (0.879–6.995)	0.086	4.433 (1.377–14.271)	0.013	2.557 (0.785–8.321)	0.119	2.016 (0.611–6.652)	0.250
Mucinous vs. highly differentiated	0 (0–)	1.000	0 (0–)	1.000	0 (0–)	1.000	0 (0–)	1.000	0 (0–)	1.000
Polymorphism vs. highly differentiated	1,009,671,776.78 (0–)	0.999	3,051,452,480.94 (0–)	0.999	8.4 (0.63–112.085)	0.107	8.4 (0.63–112.085)	0.107	8.4 (0.63–112.085)	0.107

OR, odds ratio; 95% CI, 95% confidence interval.

Table 3 Multivariate logistic regression analysis of factors associated with intraoperative blood loss

Factors	>500 vs. ≤500 mL		>1,000 vs. ≤1,000 mL		>1,500 vs. ≤1,500 mL		>2,000 vs. ≤2,000 mL		>2,500 vs. ≤2,500 mL	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	–	–	1.052 (0.994–1.115)	0.08	1.044 (0.985–1.106)	0.148	1.052 (0.992–1.114)	0.089	–	–
Tumor size	1.153 (1.051–1.266)	0.003	1.006 (0.958–1.057)	0.809	1.031 (0.979–1.085)	0.252	1.04 (0.991–1.091)	0.108	1.038 (0.988–1.09)	0.136
No. tumor-containing zones	1.04 (0.445–2.429)	0.928	3.161 (1.248–8.003)	0.015	2.674 (1.061–6.739)	0.037	1.477 (0.689–3.162)	0.316	1.621 (0.766–3.428)	0.206
Tumor number (multiple vs. single)	–	–	–	–	2.221 (0.653–7.56)	0.202	3.788 (1.092–13.133)	0.036	4.500 (1.243–16.299)	0.022

OR, odds ratio; 95% CI, 95% confidence interval.

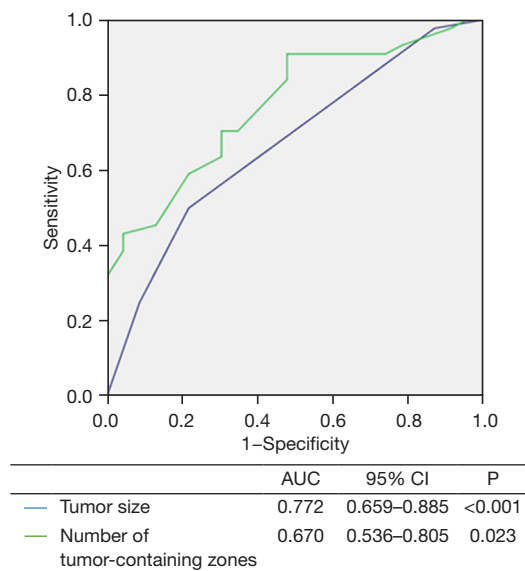


Figure 1 ROC curve analysis of the ability of tumor size and number of tumor-containing zones tumors to predict blood transfusion. AUC, area under the ROC curve; 95% CI, 95% confidence interval; ROC, receiver-operating characteristic.

Logistic regression analysis of factors associated with intraoperative blood loss

Logistic regression analysis was carried out using the following 5 different binary outcomes for intraoperative blood loss: >500 *vs.* ≤500 mL, >1,000 *vs.* ≤1,000 mL, >1,500 *vs.* ≤1,500 mL, >2,000 *vs.* ≤2,000 mL, and >2,500 *vs.* ≤2,500 mL. The univariate analysis revealed that older age was associated with intraoperative blood loss >1,000 mL ($P=0.047$) and >2,000 mL ($P=0.048$) (Table 2). Larger tumor size was associated with intraoperative blood loss >500 mL ($P=0.001$), >1,500 mL ($P=0.033$), >2,000 mL ($P=0.032$), and >2,500 mL ($P=0.043$). A larger number of tumor-containing zones was related to intraoperative blood loss >500 mL ($P=0.046$), >1,000 mL ($P=0.024$), >1,500 mL ($P=0.048$), and >2,500 mL ($P=0.039$). Multiple tumors were associated with intraoperative blood loss >2,000 mL ($P=0.038$), and >2,500 mL ($P=0.032$). Dedifferentiated tumors (*vs.* highly differentiated tumors) were related to intraoperative blood loss >1,500 mL ($P=0.013$). Sex had no significant association with intraoperative blood loss (Table 2).

Multivariate analysis revealed that tumor size was significantly associated with intraoperative blood loss >500 mL (OR: 1.153, 95% CI: 1.051–1.266, $P=0.003$). The number of tumor-containing zones was significantly

associated with intraoperative blood loss >1,000 mL (OR: 3.161, 95% CI: 1.248–8.003, $P=0.015$) and >1,500 mL (OR: 2.674, 95% CI: 1.061–6.739, $P=0.037$). Multiple tumors were significantly associated with intraoperative blood loss >2,000 mL (OR: 3.161, 95% CI: 1.092–13.133, $P=0.036$) and >2,500 mL (OR: 2.674, 95% CI: 1.243–16.299, $P=0.022$). Additionally, dedifferentiated tumors (*vs.* highly differentiated tumors) were related to intraoperative blood loss >1,000 mL (OR: 4.802, 95% CI: 1.287–17.916, $P=0.019$) and >1,500 mL (OR: 9.249, 95% CI: 1.927–44.39, $P=0.005$). However, age was not significantly associated with intraoperative blood loss in the multivariate analysis (Table 3).

ROC curve analysis

ROC curve analyses were carried out to evaluate if tumor size and number of tumor-containing zones could predict whether blood transfusion was required (analyzed as a binary variable). The AUC values were 0.772 (95% CI: 0.659–0.885, $P<0.001$) for tumor size and 0.670 (95% CI: 0.536–0.805, $P=0.023$) for the number of tumor-containing zones (Figure 1). The optimal cutoff values were 15.25 cm for tumor size and 2.5 for the number of tumor-containing zones.

Discussion

The main finding of the present study was that a larger tumor size, a larger number of tumor-containing zones, multiple tumors, and dedifferentiation were independently associated with a larger volume of intraoperative blood loss. Additionally, tumor size >15.25 cm and the involvement of >2.5 zones were predictive of the need for blood transfusion. Our findings indicated that larger size, multicentricity, involvement of more abdominal/pelvic zones and dedifferentiation are all tumor factors that increase the amount of intraoperative blood loss in patients treated for RPLS.

RPLS is a space-occupying mass that is usually challenging to resect because it presents as a large tumor involving many organs and large blood vessels in an anatomically complex region of the body. The risk of RPLS recurrence after surgery depends on various tumor-related factors, such as histological grade, size, location, metastasis, resectability, quality of the surgical margin, and rupture before or during the operation (5,19,22,24,25,39,40). Furthermore, repeat surgery for tumor recurrence is even more challenging due to the presence of abdominal

adhesions that develop in response to the resection and reconstruction of organs during the previous operation. Because it is difficult to evaluate the extent of RPLS invasiveness into adjacent organs/blood vessels and the degree of adhesions preoperatively, the accurate estimation of surgical risk can be highly challenging (41-44). Therefore, identifying parameters that are not only associated with surgical risk but also straightforward to measure preoperatively would improve the assessment of operative risk.

An important finding of the present study was that larger tumor size was independently associated with intraoperative blood loss >500 mL. Furthermore, a cutoff value of 15.25 cm for tumor size was predictive of the need for blood transfusion. Tumor size >15 cm has been reported to be associated with poorer outcomes in patients with RPLS (45-47). Furthermore, studies of other tumors have also demonstrated a positive association between tumor size and blood loss during surgery (48,49). Our findings are not unexpected, because a larger tumor would be more likely to involve a larger number of organs and large blood vessels, which would increase the risk of intraoperative blood loss. Because blood loss is independently associated with overall survival in patients with dedifferentiated RPLS (50,51), tumor size >15 cm could be a risk factor for surgical risk in patients with first recurrence of RPLS.

We also found that the number of tumor-containing zones was independently associated with intraoperative blood loss, and that the involvement of ≥ 3 regions (optimal cutoff of 2.5) was predictive of the need for blood transfusion. Although it would be expected that a larger tumor would occupy a larger number of zones, tumor size is not the only determinant of tumor regionalization. For example, we found that the involvement of 2 zones was most common for all tumor size subgroups (<10, 10–20, and >20 cm), and that involvement of all 4 zones occurred, even for tumors <10 cm. More invasive tumors that extend further and invade a larger number of organs and large blood vessels would be expected to occupy a larger number of zones, which might in part explain the higher blood loss during surgery (as resection of such masses is more challenging). Furthermore, centrally located tumors would be situated closer to midline structures, such as the abdominal aorta, vena cava, and their major branches, which would also increase the risk of significant blood loss during surgery. Therefore, tumor regionalization should be considered in addition to tumor size when evaluating the risks of bleeding during surgery for recurrent RPLS.

Other factors associated with intraoperative bleeding risk in the present study included multiple and dedifferentiated tumors. The presence of multiple tumors would increase the complexity of surgery and therefore increase the risk of significant blood loss. Furthermore, dedifferentiated RPLS is known to have more invasive and aggressive clinical behavior than well-differentiated RPLS (52).

The present study has some limitations. First, this was a retrospective analysis, so the findings might be prone to selection bias or information bias. Second, this was a single-center study, so the generalizability of the results is not known. Third, the sample size was quite small, so our analysis might have been underpowered to detect some real differences between groups. Fourth, only patients with first recurrence of RPLS were enrolled, so it remains to be established whether tumor size and number of tumor-containing zones are risk factors for intraoperative bleeding in patients undergoing their first operation or in patients undergoing repeat reoperation for recurrence. Additional studies are needed to confirm and extend our findings.

In conclusion, larger tumor size, a larger number of tumor-containing zones, multiple tumors, and dedifferentiation were independently associated with a larger volume of blood loss during surgery for RPLS recurrence. Furthermore, tumor size >15.25 cm and involvement of >2.5 zones were predictive of the need for blood transfusion. Larger size, multicentricity, involvement of more abdominal/pelvic zones, and dedifferentiation should be recognized as risk factors for bleeding during preoperative planning to facilitate the design of individualized treatment plans.

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Footnote

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Data Sharing Statement: Available at <https://atm.amegroups.com/article/view/10.21037/atm-22-4222/dss>

Conflicts of Interest: All authors have completed the

ICMJE uniform disclosure form (available at <https://atm.amegroupp.com/article/view/10.21037/atm-22-4222/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (revised in 2013). The study was approved by the ethics committee of Peking University International Hospital (No. 2018-027[BMR]). Because of the retrospective study design, the requirement of consent was waived.

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