

# Predictive factors and a novel nomogram for recurrence of primary retroperitoneal liposarcoma: Comprehensive analysis of 128 cases

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Received January 19, 2023; Accepted April 17, 2023

DOI: 10.3892/ol.2023.13843

**Abstract.** Since primary retroperitoneal liposarcoma (PRPLS) is rare in the clinic, related clinical studies are lacking. The present study was designed to investigate the predictive factors of short-term ( $\leq 1$  year) recurrence (STR) and construct a novel nomogram of local recurrence-free survival (LRFS) for surgically resected PRPLS. A total of 128 PRPLS cases who underwent radical surgery were retrospectively analyzed. Based on the interval from the operation to tumor recurrence, the predictors of STR were screened using univariate and multivariate logistic regression analyses. Cox proportional hazard regression models were applied to identify the predictors of LRFS. Furthermore, the independent predictors acquired from multivariate analyses were used to construct a nomogram. Multivariate logistic regression analysis revealed that age  $\geq 55$  years [odds ratio (OR)=5.607,  $P=0.010$ ], operative time  $\geq 260$  min (OR=9.716,  $P=0.005$ ) and tumor necrosis (OR=3.781,  $P=0.037$ ) were independent risk factors of STR for PRPLS. In the Cox regression analysis, clinical symptoms [hazard ratio (HR)=1.746,  $P=0.017$ ], resection method (OR=0.370,  $P=0.021$ ) and de-differentiated histological subtype (HR=1.975,  $P=0.048$ ) were identified as independent predictors of LRFS. Subsequently, the independent predictors acquired from multivariate analyses were used to construct a nomogram for LRFS. Age, operative time, tumor necrosis, clinical symptoms, resection method and histological subtype were related to recurrence for surgically resected PRPLS and a novel nomogram was constructed based on the above predictors.

## Introduction

As the most common primary retroperitoneal malignancy, primary retroperitoneal liposarcoma (PRPLS) originates from the adipose tissue in the retroperitoneal space. Although PRPLS accounts for  $<0.1\%$  of all malignant tumors, it has hidden clinical symptoms and rapid progress (1-3). Therefore, most PRPLS tumors are huge and have a complex relationship with adjacent organs, making the operation difficult and frequently requiring combined organ resection. The features of multicentric origin lead to a high local recurrence rate of PRPLS and most patients with PRPLS have a history of repeated surgery during the disease course. Although the tumor resection rate is gradually increased due to the continuous improvement of surgical technology and methods, the 5-year local recurrence rate of PRPLS is still up to 20-75% and this is also the main cause of death for PRPLS cases (3-5). Identifying the risk factors for neoplasm recurrence and carrying out targeted prevention and treatment are the focus and difficulties of current clinical research.

To date, the mechanisms of PRPLS recurrence have remained largely elusive and the following factors are considered to have a role (6-8). First, the huge tumor volume and dense adhesion lead to the disappearance of the anatomical space between the surrounding structures with the tumor capsule and this change may increase the operative difficulty and result in an increased probability of residual tumor tissue or capsule. Furthermore, the tumor's invasion of internal organs, blood vessels or nerves may make the complete resection of PRPLS difficult. In addition, PRPLS is similar to normal adipose tissue and lobulated retroperitoneal liposarcoma (RPLS) is easy to be considered as multiple tumors and resected in pieces, which may lead to residual tumor tissue.

Since PRPLS is rare in the clinic, related clinical studies are lacking (9-12). Wu *et al* (9) revealed that pathological subtype and histological grade were associated with local recurrence, and histological grade could be used as an independent marker. In the study by Yan *et al* (10), increased intraoperative bleeding and poor tumor classification were proved to be associated with a poor prognosis of PRPLS. Furthermore, Sun *et al* (11) found that age, recurrence, tumor site and tumor necrosis were useful

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**Key words:** primary retroperitoneal liposarcoma, short-term recurrence, local recurrence-free survival, predictive factor

markers of RPLS prognosis. However, published studies were designed for both primary and local recurrent RPLS, and the short- and long-term recurrence of tumors were not carefully distinguished (12,13). Prognostic factor analysis of short-term ( $\leq 1$  year) recurrence (STR) and nomogram construction for PRPLS were both lacking. Therefore, the present study was performed to explore the predictors of STR and construct a novel nomogram of local recurrence-free survival (LRFS) for surgically resected PRPLS.

## Materials and methods

**Study participants.** Patients with PRPLS who underwent radical operation at the First Medical Center of Chinese People's Liberation Army (PLA) General Hospital (Beijing, China) were included in this retrospective observational study. Relevant clinical data were collected using an electronic medical record (EMR) system. The inclusion criteria were as follows: i) Primary tumor with radical surgery (R0 resection) at our unit; ii) tumor originated from the retroperitoneal soft tissue and postoperative pathology confirmed liposarcoma; and iii) hospitalization period from January 2008 to December 2021. The exclusion criteria were as follows: i) Recurrent cases; ii) patients who did not undergo surgery, underwent palliative surgery (R2 resection) or with positive postoperative margin (R1 resection); iii) patients who died from surgical complications or other causes; and iv) cases lost to follow-up or refused to participate. This study was approved by the Medical Ethics Committee of the First Medical Center of the Chinese PLA General Hospital.

**Data collection and outcome evaluation.** The following case data were collected from the EMR system: Sex, age, body mass index (BMI), preoperative neutrophil/lymphocyte ratio (NLR), abdominal operation history, clinical symptoms, tumor resection method, combined organ excision, operative time, intraoperative bleeding, application of intraperitoneal chemotherapy drug, transfer to intensive care unit (ICU), tumor diameter, multiple primary tumors, tumor shape, tumor capsule, histological subtype and tumor necrosis. The case data were acquired in three categories: Demographic characteristics, surgical characteristics and pathological characteristics. The preoperative clinical symptoms observed in the present study included abdominal pain and distension, gastrointestinal obstruction, back pain and lower limb paresthesia, which were caused by tumor compression or invasion. The sampling time to determine the preoperative NLR was 2-3 days prior to the surgery. Combined organ resection was selected if the tumor had invaded surrounding organs and piecemeal resection was considered only when complete resection was not feasible. A negative resection margin was defined as R0 resection and procedures with a positive postoperative margin were considered an R1 resection. R2 resection (palliative) was considered if there was any residual tumor observed during an operation. The intraperitoneal chemotherapy drug used in this study was mainly implantable sustained-release fluorouracil, which was placed in the abdominal cavity prior to closure. The tumor diameter was expressed as the largest tumor diameter after the postoperative assessment.

**Postoperative follow-up.** In the present study, patients had a follow-up every 3-4 months in the first 2 years after the surgery and every 6 months thereafter. During the follow-up period, routine physical examination and abdominopelvic magnetic resonance imaging or computerized tomography were performed to evaluate the recurrence of RPLS. Based on the interval from operation to neoplasm recurrence, the included PRPLS cases were divided into an STR ( $\leq 1$  year) group and non-STR ( $> 1$  year) group. LRFS was defined as the period from radical operation to local recurrence.

**Statistical analysis.** SPSS software (version 26.0; IBM Corporation) and R software (version 4.2.2) were used for the statistical analyses. Categorical data were expressed as n (%) and compared using the two-sided  $\chi^2$  test. The median (interquartile range, IQR) was used to illustrate continuous variables and comparison among groups was performed using the Mann-Whitney U-test. In addition, receiver operating characteristic (ROC) curves of continuous outcomes were drawn and dichotomous outcomes were obtained based on cut-off values. Subsequently, binary logistic regression analysis and Cox proportional hazard regression analysis were conducted to determine the predictors of STR and LRFS, respectively. Variables with  $P < 0.15$  in the univariate analysis were included in the multivariate analysis and variables with  $P < 0.05$  in the multivariate analysis were considered independent predictors. LRFS rates were estimated based on the Kaplan-Meier method and were compared between groups by the log-rank test. A nomogram was constructed using the independent predictors, aiming to predict 1-, 3- and 5-year LRFS of surgically resected PRPLS.

## Results

**Patient selection.** Initially, 396 patients with pathologically confirmed RPLS were retrieved using the EMR system. Of these, 64 did not undergo radical surgery, 196 were recurrent cases, three died from surgical complications or other causes and five were lost to follow-up. After excluding these patients, the data from the remaining 128 patients were finally included in the present analysis. At a median follow-up time of 30.0 (IQR, 14.3-67.5) months, 94 patients (73.4%) had tumor recurrence and 28 (21.9%) experienced STR (Fig. 1). The 1-, 3- and 5-year LRFS rates were 78.1, 47.3 and 35.5%, respectively.

**Logistic regression analysis for STR.** According to the interval from surgery to neoplasm recurrence, the 128 PRPLS cases were divided into the STR (n=28) and non-STR (n=100) group. The demographic, surgical and pathological characteristics of the two groups were compared and statistically significant differences were found in preoperative NLR ( $P=0.040$ ), clinical symptoms ( $P=0.012$ ), resection method ( $P=0.034$ ), operative time ( $P=0.015$ ), intraoperative blood loss ( $P=0.002$ ), transfer to ICU ( $P=0.003$ ), tumor capsule ( $P=0.001$ ), histological subtype ( $P=0.006$ ) and tumor necrosis ( $P<0.001$ ) (Table I). In addition, ROC curves of continuous outcomes were drawn and dichotomous outcomes were obtained based on cut-off values, including age ( $\geq 55$  or  $< 55$  years), BMI ( $\geq 23$  or  $< 23$  kg/m<sup>2</sup>), preoperative NLR ( $\geq 2.38$ , or  $< 2.38$ ), operative time ( $\geq 260$  or  $< 260$  min), intraoperative blood loss ( $\geq 1,200$  or

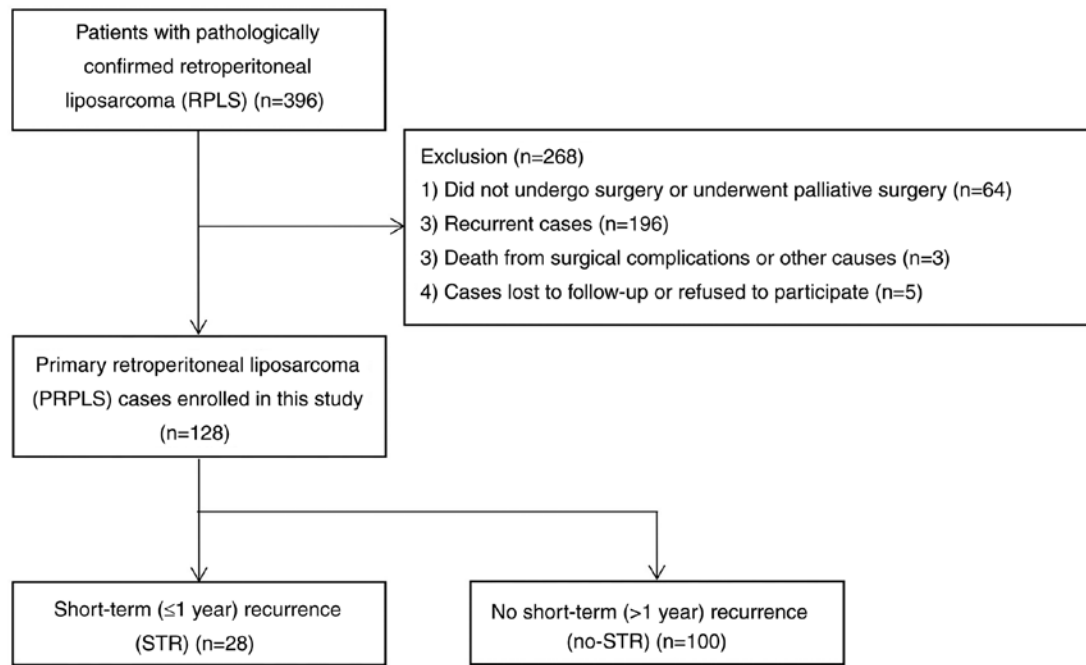


Figure 1. Flowchart of patient selection.

<1,200 ml) and tumor diameter ( $\geq 20$  or  $<20$  cm) (Fig. S1). Of these converted variables, age ( $\geq 55$  vs.  $<55$  years;  $P=0.015$ ), preoperative NLR ( $\geq 2.38$  vs.  $<2.38$ ;  $P=0.005$ ), operative time ( $\geq 260$  vs.  $<260$  min;  $P<0.001$ ) and intraoperative blood loss ( $\geq 1,200$  vs.  $<1,200$  ml;  $P=0.001$ ) were associated with STR. Subsequently, the variables of age ( $\geq 55$  vs.  $<55$  years), preoperative NLR ( $\geq 2.38$  vs.  $<2.38$ ), clinical symptoms, resection method, operative time ( $\geq 260$  vs.  $<260$  min), intraoperative blood loss ( $\geq 1,200$  vs.  $<1,200$  ml), transfer to ICU, intact tumor capsule, histological subtype and tumor necrosis were further included in a multivariate logistic regression analysis. The multivariate analysis revealed that age  $\geq 55$  years [odds ratio (OR)=5.607,  $P=0.010$ ], operative time  $\geq 260$  min (OR=9.716,  $P=0.005$ ) and tumor necrosis (OR=3.781,  $P=0.037$ ) were independent risk factors of STR (Table II). In addition, the above three variables were included in a multivariate logistic regression model for further analysis and the re-analysis also indicated that age  $\geq 55$  years (OR=5.421,  $P=0.003$ ), operative time  $\geq 260$  min (OR=10.524,  $P<0.001$ ) and tumor necrosis (OR=7.231,  $P<0.001$ ) were independent risk factors (Table III).

**Cox regression analysis and nomogram construction for LRFS.** Univariate and multivariate Cox proportional hazard regression models were constructed to identify the predictors of LRFS. Univariate analysis indicated that clinical symptoms [hazard ratio (HR)=1.947,  $P=0.002$ ], complete resection (HR=0.239,  $P<0.001$ ), operative time (HR=1.006,  $P<0.001$ ), intraoperative blood loss (HR=1.001,  $P<0.001$ ), transfer to ICU (HR=1.947,  $P=0.009$ ), tumor capsule (HR=0.594,  $P=0.029$ ), histological subtype ( $P=0.003$ ) and tumor necrosis (HR=1.647,  $P=0.028$ ) were associated with LRFS. Variables with  $P<0.15$  in the univariate analysis were included in the multivariate analysis. Multivariate Cox regression analysis revealed that clinical symptoms (HR=1.746,  $P=0.017$ ), complete resection (HR=0.370,  $P=0.021$ ) and de-differentiated vs.

well-differentiated histological subtype (HR=1.975,  $P=0.048$ ) were independent predictors of LRFS (Table IV). In addition, Kaplan-Meier curves of LRFS for clinical symptoms, resection method and histological subtype were drawn, and the curves also showed that clinical symptoms ( $P=0.002$ ), resection method ( $P<0.001$ ) and histological subtype ( $P=0.002$ ) were important factors affecting LRFS (Fig. 2). Subsequently, a nomogram was constructed using age, clinical symptoms, resection method, operative time, histological subtype and tumor necrosis to predict the 1-, 3- and 5-year LRFS of surgical resected PRPLS (Fig. 3). The prediction model's concordance index (C-index) was 0.701, suggesting a good discriminative capability of the nomogram. The calibration plots for the LRFS probability at 1, 3 and 5 years also indicated that the nomogram had a good calibration (Fig. 4).

## Discussion

As a rare soft tissue sarcoma, PRPLS has a poor prognosis and poses a serious threat to human health. Owing to the unclear effects of radiotherapy and chemotherapy on RPLS, the application of adjuvant therapy is still controversial. Therefore, none of the cases included in the present study received radiotherapy or chemotherapy prior to or after surgery. The therapeutic effect and application time of radiotherapy and chemotherapy on RPLS still require to be further explored. At present, surgical resection remains the method of choice for PRPLS cases with indications to obtain potential cure opportunities (5-7,14,15). In the present study, the tumor was completely resected under the condition of conforming to the standard of safe resection margin (8). However, the 1-, 3- and 5-year LRFS rates of PRPLS cases were still as low as 78.1, 47.3 and 35.5%, respectively. For PRPLS cases who experienced recurrence after surgery and had surgical indications, a second operation should be conducted (7). Owing to

Table I. Characteristics of included primary retroperitoneal liposarcoma cases in STR group and non-STR group.

Variable	Total (n=128)	STR group (n=28)	Non-STR group (n=100)	P-value
Sex				0.840
Male	71 (55.5)	16 (57.1)	55 (55.0)	
Female	57 (44.5)	12 (42.9)	45 (45.0)	
Age, years	54 (48, 64)	59 (51, 65)	53 (47, 62)	0.076
BMI, kg/m <sup>2</sup>	23.55 (21.49, 25.24)	23.55 (21.08, 24.66)	23.55 (21.57, 25.44)	0.614
Preoperative NLR	2.99 (1.95, 3.58)	3.57 (2.56, 3.74)	2.72 (1.74, 3.58)	0.040
Previous abdominal surgery				0.697
Yes	31 (24.2)	6 (21.4)	25 (25.0)	
No	97 (75.8)	22 (78.6)	75 (75.0)	
Clinical symptoms				0.012
Yes	74 (57.8)	22 (78.6)	52 (52.0)	
No	54 (42.2)	6 (21.4)	48 (48.0)	
Resection method				0.034
Piecemeal	9 (7.0)	5 (17.9)	4 (4.0)	
Complete	119 (93.0)	23 (82.1)	96 (96.0)	
Combined organ excision				0.082
Yes	73 (57.0)	20 (71.4)	53 (53.0)	
No	55 (43.0)	8 (28.6)	47 (47.0)	
Operative time, min	184 (140, 240)	209 (163, 280)	178 (136, 235)	0.015
Intraoperative blood loss, ml	475 (200, 1000)	900 (313, 1800)	400 (200, 875)	0.002
Intraperitoneal chemotherapy drug application				0.810
Yes	62 (48.4)	13 (46.4)	49 (49.0)	
No	66 (51.6)	15 (53.6)	51 (51.0)	
Transfer to ICU				0.003
Yes	25 (19.5)	11 (39.3)	14 (14.0)	
No	103 (80.5)	17 (60.7)	86 (86.0)	
Pathological characteristics				
Tumor diameter, cm	25.0 (18.6, 32.0)	25.8 (19.0, 32.8)	25 (18.6, 32)	0.723
Multiple primary tumors				0.338
Yes	24 (18.8)	7 (25.0)	17 (17.0)	
No	104 (81.2)	21 (75.0)	83 (83.0)	
Tumor shape				0.908
Irregular	40 (31.3)	9 (32.1)	31 (31.0)	
Regular	88 (68.7)	19 (67.9)	69 (69.0)	
Tumor capsule				0.001
Intact	98 (76.6)	15 (53.6)	83 (83.0)	
Broken	30 (23.4)	13 (46.4)	17 (17.0)	
Histological subtype				0.006
Well-differentiated	45 (35.2)	5 (17.9)	40 (40.0)	
De-differentiated	18 (14.1)	9 (32.1)	9 (9.0)	
Other subtypes	65 (50.7)	14 (50.0)	51 (51.0)	
Tumor necrosis				<0.001
Yes	36 (28.1)	16 (57.1)	20 (20.0)	
No	92 (71.9)	12 (42.9)	80 (80.0)	

Values are expressed as the median (lower quartile, upper quartile) for continuous variables and n (%) for categorical variables. STR, short-term recurrence; BMI, body mass index; NLR, neutrophil/lymphocyte ratio; ICU, intensive care unit.

Table II. Multivariate analysis of predictors for short-term ( $\leq 1$  year) recurrence.

Variable	$\beta$ coefficient	OR (95% CI)	P-value
Age $\geq 55$ years	1.724	5.607 (1.517-20.726)	0.010
Preoperative NLR $\geq 2.38$	1.416	4.121 (0.889-19.096)	0.070
Clinical symptoms	1.000	2.717 (0.760-9.714)	0.124
Complete resection	-0.812	0.444 (0.066-3.007)	0.406
Combined organ excision	-0.308	0.735 (0.214-2.528)	0.625
Operative time $\geq 260$ min	2.274	9.716 (1.975-47.791)	0.005
Intraoperative blood loss $\geq 1,200$ ml	-0.284	0.753 (0.162-3.492)	0.717
Transfer to ICU	0.577	1.781 (0.349-9.095)	0.488
Intact tumor capsule	-0.761	0.467 (0.124-1.764)	0.262
Histological subtype			0.088
De-differentiated vs. well-differentiated	1.706	5.506 (0.833-36.376)	0.077
Other subtypes vs. well-differentiated	0.054	1.055 (0.229-4.871)	0.945
Tumor necrosis	1.330	3.781 (1.087-13.156)	0.037

NLR, neutrophil/lymphocyte ratio; ICU, intensive care unit; OR, odds ratio; CI, confidence interval.

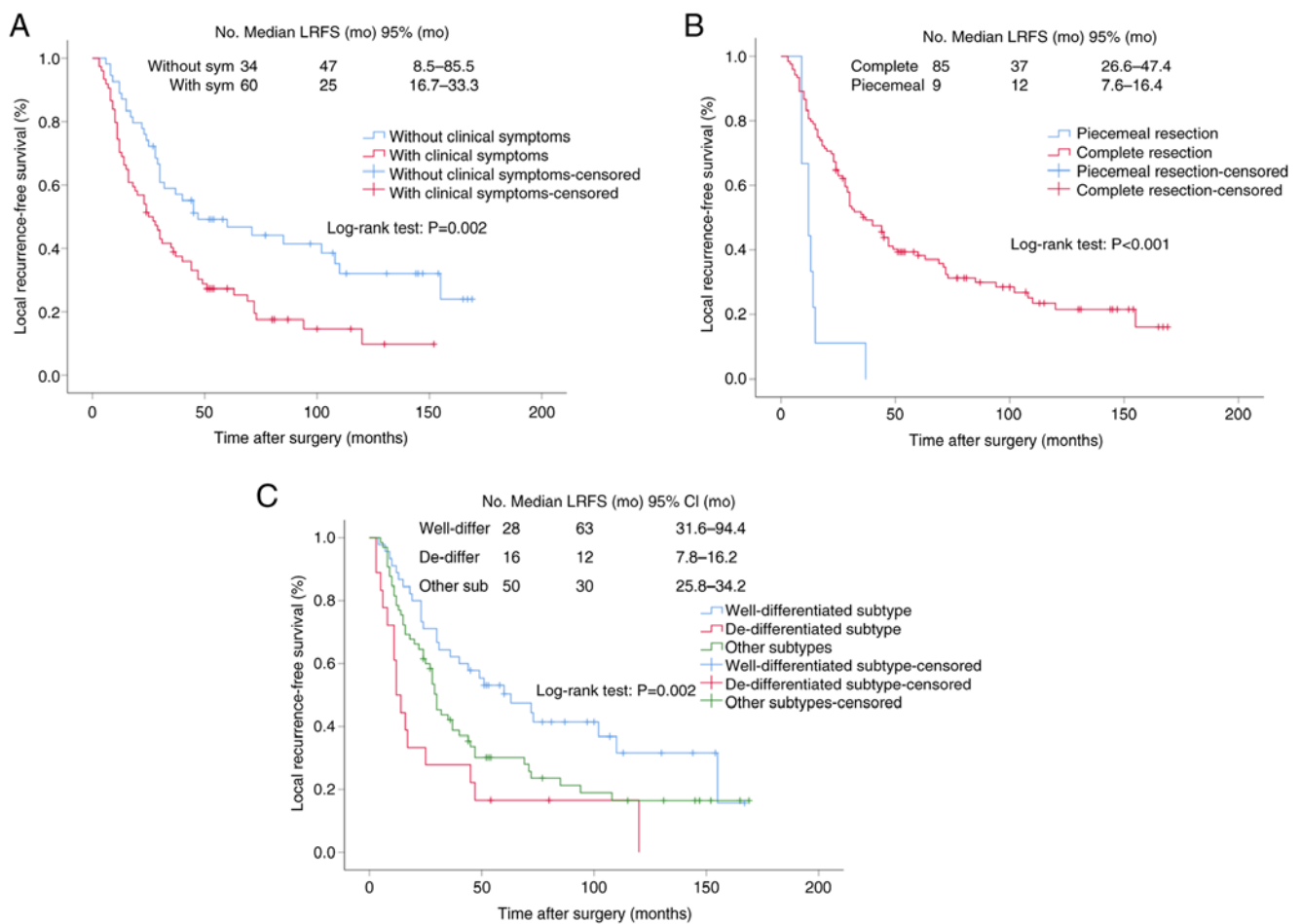


Figure 2. Kaplan-Meier curves of LRFS for (A) clinical symptoms, (B) resection method and (C) histological subtype. LRFS, local recurrence-free survival; sym, symptoms; differ, differentiation.

the previous lack of risk factor analysis and a nomogram for PRPLS recurrence, the present study was performed to identify the predictors and construct the nomogram to facilitate

targeted prevention of recurrence. After excluding the interaction between variables, multivariate analyses indicated that operative time was an important predictor for both STR and

Table III. Further multivariate analysis for short-term ( $\leq 1$  year) recurrence.

Variable	$\beta$ coefficient	OR (95% CI)	P-value
Age $\geq 55$ years	1.690	5.421 (1.768-16.616)	0.003
Operative time $\geq 260$ min	2.354	10.524 (3.131-35.374)	<0.001
Tumor necrosis	1.978	7.231 (2.526-20.696)	<0.001

OR, odds ratio; CI, confidence interval.

Table IV. Univariate and multivariate analyses of predictors for local recurrence-free survival.

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Sex (male)	1.138	0.754-1.719	0.538			
Age	1.009	0.990-1.028	0.356			
Preoperative NLR	1.030	0.986-1.076	0.184			
BMI (kg/m <sup>2</sup> )	0.954	0.896-1.017	0.147	0.955	0.891-1.024	0.196
Previous abdominal surgery	1.007	0.628-1.614	0.979			
Clinical symptoms	1.947	1.267-2.994	0.002	1.746	1.105-2.760	0.017
Complete resection	0.239	0.116-0.492	<0.001	0.370	0.159-0.861	0.021
Combined organ excision	1.402	0.924-2.127	0.112	0.703	0.431-1.148	0.159
Operative time	1.006	1.003-1.009	<0.001	1.004	1.000-1.007	0.059
Intraoperative blood loss	1.001	1.000-1.001	<0.001	1.000	1.000-1.001	0.095
Intraperitoneal chemotherapy drug application	0.936	0.624-1.405	0.749			
Transfer to ICU	1.947	1.178-3.220	0.009	1.026	0.567-1.856	0.933
Tumor diameter	1.013	0.994-1.033	0.171			
Multiple primary tumors	1.589	0.966-2.614	0.068	1.379	0.796-2.390	0.252
Tumor shape	1.458	0.949-2.240	0.085	0.998	0.594-1.677	0.993
Tumor capsule	0.594	0.372-0.949	0.029	0.865	0.476-1.572	0.635
Histological subtype			0.003			0.126
De-differentiated vs. well-differentiated	2.888	1.555-5.363	0.001	1.975	1.006-3.875	0.048
Other subtypes vs. well-differentiated	1.638	1.029-2.608	0.037	1.423	0.875-2.314	0.155
Tumor necrosis	1.647	1.055-2.573	0.028	1.253	0.761-2.064	0.375

BMI, body mass index; NLR, neutrophil/lymphocyte ratio; ICU, intensive care unit; HR, hazard ratio; CI, confidence interval.

LRFS. In the present study, therefore, operative time was used to construct the nomogram. As retroperitoneal malignancies are clinically rare, a limited number of PRPLS cases were included in the present study. Dividing the included cases into modeling and validation sets may have reduced the accuracy of the predictive model. Thus, the nomogram was not validated by an external patient series, limiting its value. The prediction model's C-index and calibration plots indicated that the nomogram established in the present study had a good calibration.

Previous research has found a correlation between age and survival time for patients with PRPLS who underwent radical surgery, but a correlation between age and postoperative recurrence has not been reported (2,11,16). In this analysis, age  $\geq 55$  years was proved to be an independent risk factor for STR. Decreased immune function, aging organs and disordered anatomy accompanied by increased age may contribute to

this phenomenon. Tumor necrosis may be caused by the rapid growth and chronic ischemic injury of solid tumors, which may reflect the degree of tumor malignancy and hypoxia in the tumor. Therefore, tumor necrosis is significantly correlated with the prognosis for numerous common tumor types. In general, a large extent of tumor necrosis and a low degree of differentiation indicate a high degree of malignancy, which may lead to a higher recurrence rate and unfavorable prognosis (10,11,17).

Prolonged surgical duration was another important predictor for 1-year recurrence. Huge tumor volume, dense adhesion and tumor invasion of surrounding tissues and organs bring great difficulties to the radical operation, thus further prolonging the operation time, increasing the chance of residual tumor and tumor cells disseminating and spreading (18,19). In addition, the huge tumor may compress and invade the internal

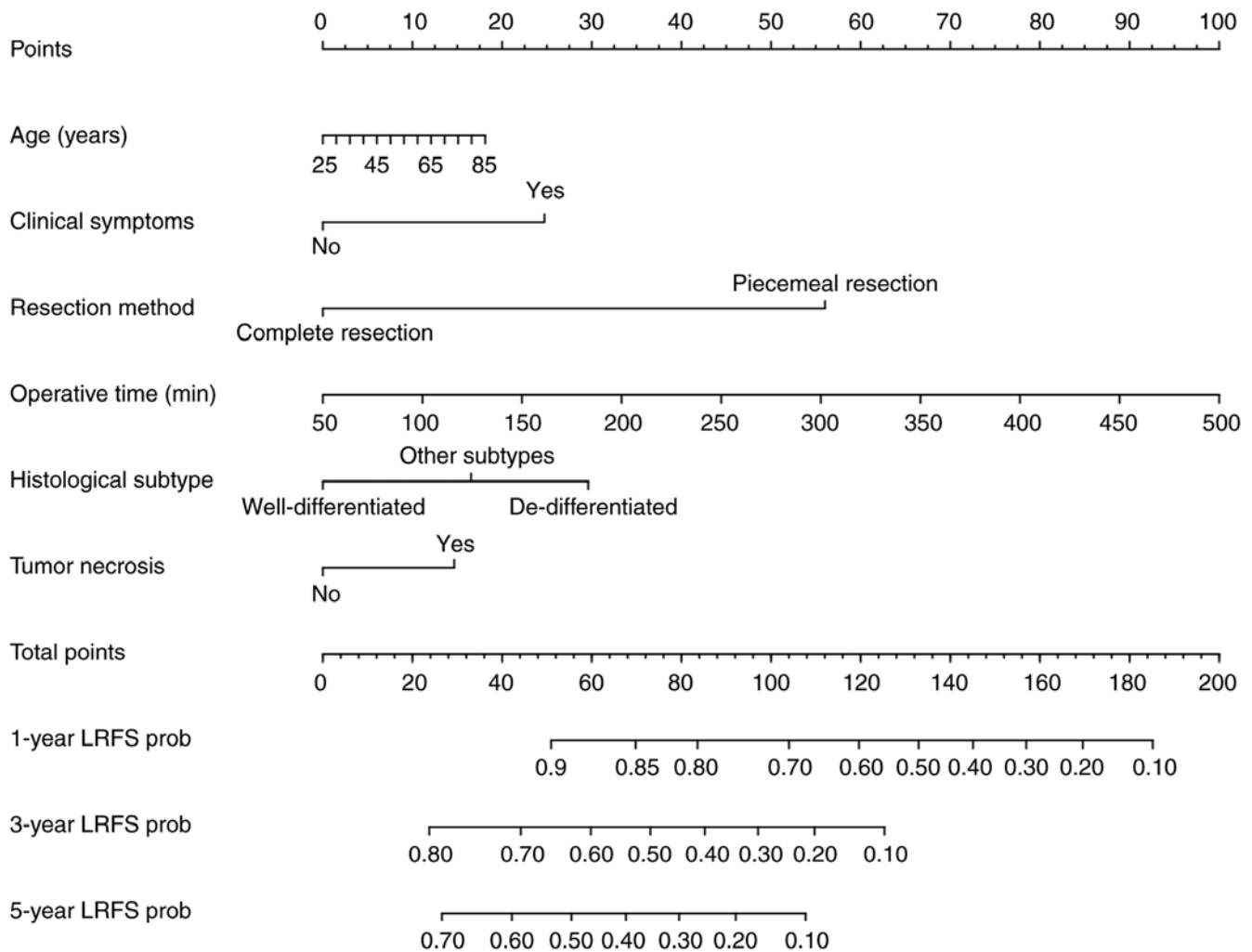


Figure 3. Nomogram for 1-, 3- and 5-year LRFS in patients with primary retroperitoneal liposarcoma. LRFS, local recurrence-free survival.

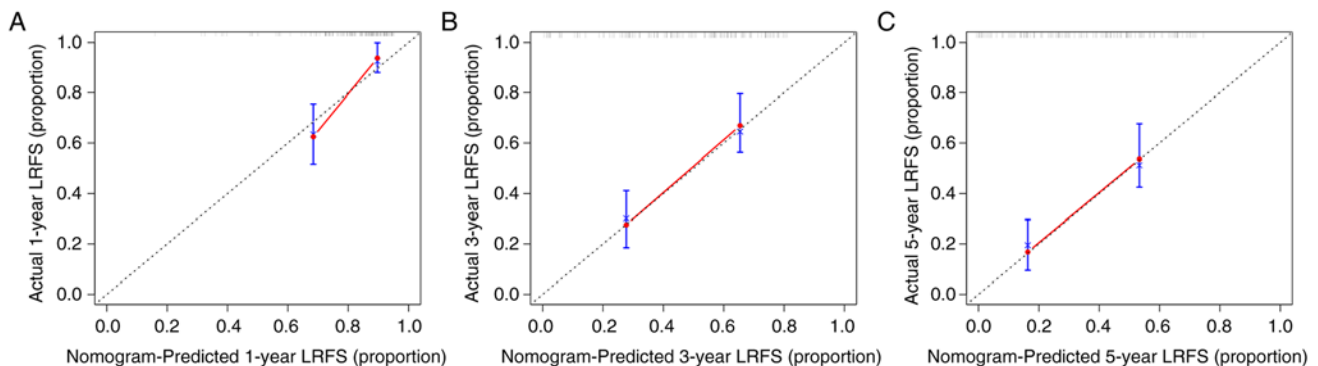


Figure 4. Calibration plots for internal validation of (A) 1-, (B) 3- and (C) 5-year LRFS nomogram. LRFS, local recurrence-free survival.

organs, resulting in non-specific clinical symptoms, such as abdominal pain and distension, gastrointestinal obstruction, back pain and lower limb paresthesia (17). Piecemeal resection was considered only when complete resection was impossible to complete and piecemeal resection also increased the risk of intraoperative bleeding and tumor cell dissemination (12,20). Furthermore, prolonged operative time increases the exposure time, possibility of injury and degree of edema in tissues, leading to an increased risk of intraoperative bleeding and

transfer to ICU. As a consequence, the clinical symptoms, resection method, intraoperative blood loss and transfer to the ICU were related to the operative duration and may affect PRPLS recurrence. Tumor-related inflammation may induce the tumor itself or surrounding cells to express various molecules, thus forming a micro-environment that may promote tumor progression (21,22). As a common marker of the serologic inflammatory response, elevated preoperative NLR was also found to be associated with STR in this study.



Histological subtypes, including well-differentiated, de-differentiated, mixed, mucinous and pleomorphic subtype, was also an important predictor for PRPLS recurrence (10,23). According to previous literature evidence, the prognosis of different histological subtypes exhibited marked variation and well-differentiated PRPLS had a lower local recurrence rate and a significantly prolonged the recurrence interval as compared to other subtypes (8,12). The present study also indicated that the incidence of tumor recurrence was significantly lower in the well-differentiated group and the de-differentiated histological subtype was able to be used as an independent risk factor of LRFS for PRPLS cases. De-differentiated PRPLS frequently has an incomplete tumor capsule and irregular tumor shape, which makes the boundary between the tumor and normal tissue difficult to identify, thus prolonging the operation time, increasing intra-operative bleeding and hampering the completion of radical resection (10,19,23,24).

Therefore, ensuring the integrity of the tumor resected by the first operation was particularly important and the tumor with its surrounding tissue should be excised as whole as possible to ensure a negative margin (25). Furthermore, intraoperative pathological examination is recommended to confirm the histological subtypes and the condition of tumor necrosis. For de-differentiated PRPLS cases with tumor necrosis, careful operation and examination, and appropriate expansion of tumor resection are requisite to avoid residual tumor tissue. Furthermore, a shortened review interval and increased review number after the operation are also required, so as to detect the STR of tumors.

Although the present study was the first to explore prognostic factors of STR and construct a novel nomogram of LRFS for surgically resected PRPLS, it had certain limitations. First, the analysis was performed utilizing a retrospective database from a single center, affecting the quality of evidence. Furthermore, case data with a large time span may have been one of the sources of information bias. In addition, the small sample size caused by the low incidence also affected the reliability of the analysis results to a certain extent. In the future, multicenter prospective studies with large samples and long-term follow-up are required to further validate and complement the results of the present analysis.

In conclusion, age  $\geq 55$  years, operative time  $\geq 260$  min and tumor necrosis were identified as independent risk factors of STR for surgically resected PRPLS. Clinical symptoms, piecemeal resection and de-differentiated histological subtype may be used as independent predictors of LRFS. Based on the above variables, a nomogram with good calibration was constructed to predict the 1-, 3- and 5-year LRFS for surgically resected PRPLS.

## Acknowledgements

Not applicable.

## Funding

No funding was received.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Authors' contributions

ZY and PL conceived and designed the study and drafted the manuscript. ZY, XZ and SZ participated in writing the manuscript, as well as analyzing and interpreting the data. JG and NL collected and analyzed the data and produced the tables and figures. ZY and PL confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

## Ethics approval and consent to participate

The present study was approved by the ethics committee of the Chinese PLA General Hospital (Beijing, China). This study was undertaken according to the provisions of the Declaration of Helsinki. The requirement for written informed consent was waived due to the retrospective nature of the study.

## Patient consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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