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Original Article

Prognostic factors in retroperitoneal liposarcoma after R0 resection: a study of age, histologic type, tumor stage, and differentiation grade

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Abstract: Objective: This study aimed to identify prognostic factors affecting progression-free survival (PFS) in patients with retroperitoneal liposarcoma (RPLS) after R0 resection. Methods: A retrospective analysis was conducted on 183 RPLS patients who underwent R0 resection, evaluating general information, clinicopathological data, laboratory parameters, and follow-up outcomes. Based on follow-up outcomes, patients were categorized into progression-free survival (PFS) group (PFS, n=121) and disease progression group (DP, n=62). The general information, clinicopathological data, and laboratory parameters of the two groups were systematically compared, with statistically significant factors subsequently incorporated into the Cox multivariate regression analysis. Significant prognostic factors identified through Cox analysis were further evaluated using Kaplan-Meier (K-M) survival analysis, serving as the foundation for constructing the predictive model. The model's performance was rigorously assessed for 1-year, 3-year, and overall PFS prediction. Results: Multivariate analysis identified age (*HR*=1.034, 95% CI=1.011-1.057, *P*=0.003), histologic subtype (Well-differentiated liposarcoma as reference. Dedifferentiated liposarcoma: *HR*=0.130, 95% CI=0.029-0.578, *P*=0.007. Myxoid/round cell liposarcoma: *HR*=0.190, 95% CI=0.084-1.635, *P*=0.190. Pleomorphic liposarcoma: *HR*=0.176, 95% CI=0.036-0.865, *P*=0.032. Mixed-type liposarcoma: *HR*=0.793, 95% CI=0.157-4.008, *P*=0.799), tumor stage (*HR*=0.440, 95% CI=0.257-0.755, *P*=0.003), and tumor differentiation grade (*HR*=0.395, 95% CI=0.236-0.661, *P*<0.001) as independent risk factors. The predictive models demonstrated excellent discriminative ability: 1-year model (AUC=0.944, NB=0.05-0.80), 3-year model (AUC=0.861, NB=0.05-0.73), the overall mode (AUC=0.903, NB=0.03-0.90). Conclusion: Advanced age, DDLPS, PLS, stage III-IV disease, and poor tumor differentiation were identified as independent predictors of shorter PFS in RPLS patients following R0 resection.

Keywords: Retroperitoneal liposarcoma, R0 resection, prognostic model, independent predictors

Introduction

Only 10%-15% of all soft tissue sarcomas are retroperitoneal sarcomas, a rare and aggressive cancer with an estimated annual incidence of 0.5 cases per 100,000 individuals [1]. Among RPS, retroperitoneal liposarcoma (RPLS) is the most common histological subtype, accounting for approximately 45% of cases [2]. Due to its propensity for local recurrence and resistance to standard treatments, RPLS is associated with a generally poor prognosis and exhibits significant biological variability [3]. Unlike extremity sarcomas, which often present with obvious symptoms like pain or impaired function, RPLS typically develops insidiously within the expansive retroperitoneal space. This results in the formation of large, painless masses that remain asymptomatic until they compress adjacent organs or vital structures [4]. Consequently, RPLS is frequently diagnosed at advanced stages, complicating surgical resection and resulting in poorer clinical outcomes compared to sarcomas in the extremities [5].

Surgical resection remains the only effective treatment for RPLS. The current guideline-recommended approach is aggressive tumor removal with microscopically negative margins

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(R0 resection) [6]. Available data suggest that R0 resection is the most effective strategy for lowering local recurrence rates and improving overall survival in RPLS patients [7]. However, even with rigorous surgical intervention, recurrence rates remain substantial, with 30% to 50% of patients experiencing relapse within three years of resection [8]. This significant recurrence risk underscores the limitations of current treatment strategies and highlights the urgent need for improved prognostic tools [9]. To address this, the present study retrospectively analyzed laboratory indicators, surgical data, and follow-up outcomes from RPLS patients who underwent R0 resection. The goal is to develop a comprehensive prognostic model that can guide early intervention for high-risk patients and inform personalized treatment plans, ultimately improving clinical outcomes and quality of life for the RPLS patient population.

Materials and methods

Case selection

This retrospective study included 220 patients who were initially diagnosed with RPLS and underwent R0 resection at Peking University People's Hospital between February 2019 and February 2022. After excluding 18 cases with insufficient clinical data, 7 patients with significant organ dysfunction, 9 patients who received preoperative treatments, and 3 patients lost to follow-up, a final cohort of 183 RPLS patients was included. Each case was independently reviewed by two experienced pathologists to confirm the diagnosis of RPLS. All patients were followed up postoperatively for a period of 10 to 57 months (median: 43.4 months), during which comprehensive clinicopathological data were collected. Outcomes, including recurrence, metastasis, and mortality, were documented. Progression-free survival (PFS) was defined as the duration from surgery to either re currence or death. Based on follow-up results, patients were divided into two groups: the PFS group (n=121) and the disease progression group (DP, n=62). The study protocol was approved by the Biomedical Ethics Review Committee of Peking University International Hospital (Ethics No: 2023-KY-0072-02).

Inclusion criteria: (1) Patients who met the diagnostic criteria for RPLS as outlined in the UK Guidelines for the Management of Soft Tissue Sarcomas, characterized by heterogeneous fatty density masses, with pathological confirmation through immunohistochemical staining [10]. (2) Patients who underwent primary R0 resection at our institution. (3) Patients with complete clinical records.

Exclusion criteria: (1) Patients with severe dysfunction of major organs. (2) Patients with concurrent malignancies. (3) Patients with immunocompromised conditions. (4) Patients who experienced perioperative mortality (including intraoperative or in-hospital deaths).

Data collection

The primary endpoints of this study were DP and PFS. DP was defined as the emergence of new lesions or significant enlargement of existing lesions, confirmed by radiographic examination. PFS refers to the time from surgery to either tumor progression or death from any cause. Clinical and imaging evaluations were conducted at each follow-up visit. Postoperative monitoring was performed every three months during the first two years, every six months from the third to the fifth year, and annually thereafter. The follow-up duration was measured in months, with the final follow-up scheduled for February 2025.

Clinical data were collected for all patients, including general information such as age, gender, body mass index, and medical history (diabetes mellitus, hypertension, cardiovascular disease, alcohol consumption, and smoking habits). Additional clinicopathological data were gathered, including histological subtype, in situ invasion, number of tumors, maximum tumor diameter, presence of symptoms, tumor stage, tumor differentiation grade, involvement of other organs, and features such as necrosis, hemorrhage, and ossification. Surgical data collected included operative time, intraoperative blood loss, and blood transfusion requirements. The most recent preoperative laboratory parameters were also recorded, including creatinine, platelet, neutrophil, lymphocyte, fibrinogen, globulin, albumin, albumin-to-globulin ratio (A/G ratio), systemic immune-inflammation index, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio.

According to the World Health Organization classification, RPLS is divided into five histological types: (a) well-differentiated liposarcoma, (b) dedifferentiated liposarcoma, (c) myxoid/round cell liposarcoma, (d) pleomorphic

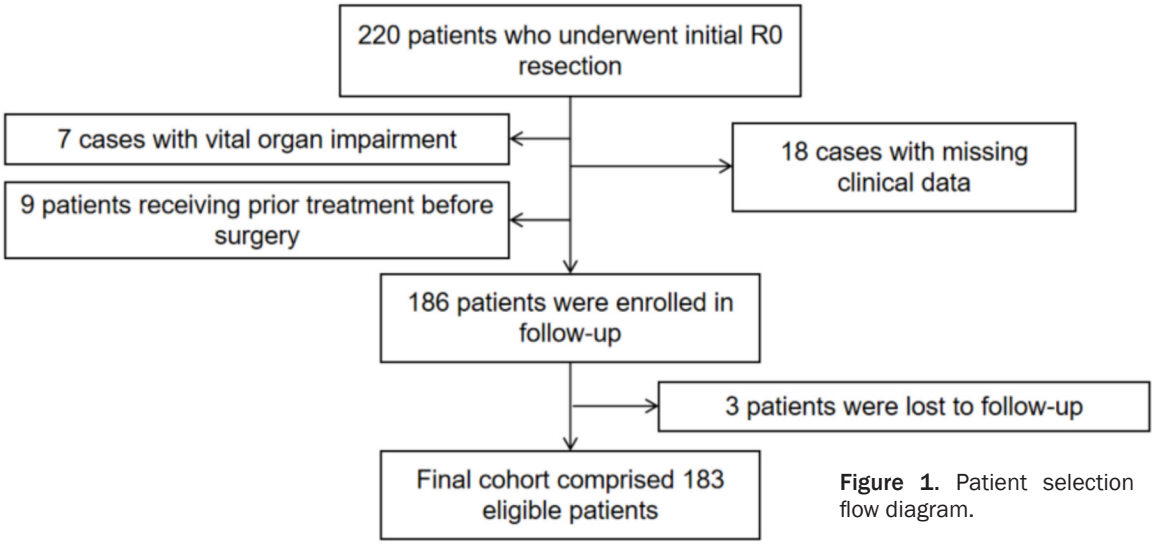

Figure 1. Patient selection flow diagram.

liposarcoma, and (e) mixed-type liposarcoma [11]. While the role of radiation and chemotherapy in the treatment of RPLS is still controversial, all patients in this study underwent R0 resection only, with no adjuvant therapy administered.

Statistical analysis

Data processing and analysis were performed using SPSS 27.0 statistical software. The Shapiro-Wilk test was used to assess the normality of the data. Normally distributed continuous variables were expressed as mean ± standard deviation ($\overline{x} \pm s$) and compared using the independent samples t-test. Non-normally distributed data were presented as median (Q_{25}, Q_{75}) and analyzed using the Mann-Whitney U test. Categorical variables were described as n (%) and compared using the χ^2 test. PFS was evaluated using the Kaplan-Meier (K-M) method, and independent risk factors were identified through Cox proportional hazards regression analysis. Based on these factors, prediction models for 1-year, 3-year, and overall PFS were developed. Model performance was assessed using the area under the receiver operating characteristic (ROC) curve (AUC), calibration curves, and decision curve analysis (DCA). $P<0.05$ was considered statistically significant.

Results

Patient selection flow diagram

The patient selection process for RPLS is illustrated in **Figure 1**. A total of 183 patients with complete follow-up data were included in the final analysis.

Comparison of general information between PFS and DP groups

General characteristics of the PFS and DP groups are summarized in **Table 1**, including age, gender, and medical history (diabetes mellitus, hypertension, cardiovascular disease, alcohol consumption, and smoking habits). A statistically significant difference in age was observed between the two groups ($P<0.05$).

Comparison of clinicopathological data between PFS and DP groups

Clinicopathological data for both groups are presented in **Table 2**. Significant differences were found in histological subtype, maximum tumor diameter, tumor stage, and tumor differentiation grade (all $P<0.05$).

Comparison of laboratory parameters between PFS and DP groups

Laboratory parameters for the two groups are detailed in **Table 3**. A statistically significant difference was observed in the A/G ratio ($P<0.05$).

Identification of independent risk factors by Cox multivariate regression analysis

The results of the Cox multivariate regression analysis are shown in **Table 4**. Independent risk factors identified included: age (*HR*=1.034,

Table 1. Comparison of general information between PFS and DP groups

Characteristics	PFS (n=121)	DP (n=62)	t/χ^2	*P*
Age (years)	51.76±11.58	56.52±12.21	-2.582	0.011
Gender			2.593	0.107
Male	57 (47.11)	37 (59.68)		
Female	64 (52.89)	25 (40.32)		
Body mass index, kg/m^2	20.22±1.79	20.44±1.59	-0.831	0.407
Diabetes mellitus			0.686	0.408
Yes	30 (24.79)	12 (19.35)		
No	91 (75.21)	50 (80.65)		
Hypertension			0.151	0.698
Yes	14 (11.57)	6 (9.68)		
No	107 (88.43)	56 (90.32)		
Cardiovascular disease			0.262	0.609
Yes	4 (3.31)	3 (4.84)		
No	117 (96.69)	59 (95.16)		
Alcohol consumption			0.131	0.717
Yes	8 (6.61)	5 (8.06)		
No	113 (93.39)	57 (91.94)		
Smoking habits			2.804	0.094
Yes	34 (28.10)	25 (40.32)		
No	87 (71.90)	37 (59.68)		

Note: PFS, progression-free survival; DP, disease progression.

95% CI=1.011-1.057, *P*=0.003), histologic subtype (using WDLPS as reference: DDLPS: *HR*=0.130, 95% CI=0.029-0.578, *P*=0.007; MLPS: *HR*=0.190, 95% CI=0.084-1.635, *P*=0.190; PLS: *HR*=0.176, 95% CI=0.036-0.865, *P*=0.032; MixLPS: *HR*=0.793, 95% CI=0.157-4.008, *P*=0.799), tumor stage (*HR*=0.440, 95% CI=0.257-0.755, *P*=0.003), and tumor differentiation grade (*HR*=0.395, 95% CI=0.236-0.661, *P*<0.001). These independent risk factors were subsequently incorporated into the nomogram-based predictive model (**Figure 2**).

Survival analysis based on predictive variables

Kaplan-Meier survival analyses based on predictive variables are presented in **Figure 3**. Patients aged <60 years had significantly better PFS compared to those aged ≥60 years (*P*=0.005) (**Figure 3A**). Significant differences in survival were observed among different histological subtypes (*P*<0.001) (**Figure 3B**), different tumor stages (*P*<0.001) (**Figure 3C**), and different tumor differentiation grades (*P*<0.001) (**Figure 3D**).

Evaluation and validation of prognostic prediction models

Figure 4 demonstrates the evaluation results of the 1-year prognostic prediction model for RPLS patients. **Figure 4A** presents the 1-year Kaplan-Meier survival curves for all patients. The ROC curve (**Figure 4B**) reveals an AUC value of 0.944 for the 1-year prediction. The calibration curve (**Figure 4C**) shows a close alignment between the black and gray lines, indicating the high overall accuracy of the model. The DCA results (**Figure 4D**) demonstrate that the model provides a favorable net benefit (NB) across the 0.05-0.80 threshold range at the 1-year time point.

Figure 5 presents the evaluation of the 3-year prognostic prediction model for RPLS patients. **Figure 5A** demonstrates favorable 3-year overall survival outcomes for the entire cohort. The ROC curve (**Figure 5B**) achieved an AUC value of 0.861 for the 3-year prediction model. The calibration curve (**Figure 5C**) shows suboptimal alignment between the solid and dashed lines, indicating reduced accuracy of the 3-year prediction model. The DCA results (**Figure 5D**) confirm that the model maintains a clinically useful NB across probability thresholds ranging from 0.05 to 0.73 at the 3-year timepoint.

Figure 6 presents a comprehensive evaluation of the prognostic prediction model for RPLS patients. **Figure 6A** demonstrates favorable overall survival outcomes. The ROC curve (**Figure 6B**) achieved an excellent AUC value of 0.903. The calibration curve (**Figure 6C**) shows strong agreement between predicted and observed outcomes. The DCA results (**Figure 6D**) indicate clinically meaningful NB across a wide range of probability thresholds (0.05-0.90).

Discussion

RPLS is a rare malignant tumor whose incidence has been steadily increasing in recent

Table 2. Comparison of clinicopathological data between PFS and DP groups

Characteristics	PFS (n=121)	DP (n=62)	t/χ^2	*P*
Histological subtype			38.619	<0.001
Well-differentiated liposarcoma	88 (72.73)	19 (30.65)		
Dedifferentiated liposarcoma	14 (11.57)	26 (41.94)		
Myxoid/round cell liposarcoma	16 (13.22)	9 (14.52)		
Pleomorphic liposarcoma	1 (0.83)	6 (9.68)		
Mixed-type liposarcoma	2 (1.65)	2 (3.23)		
In situ invasion			2.903	0.088
Yes	32 (26.45)	24 (38.71)		
No	89 (73.55)	38 (61.29)		
Number of tumors			1.686	0.194
Solitary	82 (67.77)	36 (58.06)		
Multiple	39 (32.23)	26 (41.94)		
Maximum tumor diameter, cm	8.34±3.87	9.42±3.76	-1.810	0.072
≤5 cm	24 (19.83)	7 (11.29)		
5-10 cm	58 (47.93)	29 (46.77)		
>10 cm	39 (32.23)	36 (58.06)		
Presence of symptoms			3.305	0.069
Yes	58 (47.93)	21 (33.87)		
No	63 (52.07)	41 (66.13)		
Tumor stage			36.437	<0.001
I-II	115 (95.04)	37 (59.68)		
III-IV	6 (4.96)	25 (40.32)		
Tumor differentiation grade			29.583	<0.001
Well to moderately differentiated	110 (90.91)	35 (56.45)		
Poorly to undifferentiated	11 (9.09)	27 (43.55)		
Tumor involvement of other organs			0.865	0.352
Yes	17 (14.05)	12 (19.35)		
No	104 (85.95)	50 (80.65)		
Necrosis			0.162	0.688
Yes	15 (12.40)	9 (14.52)		
No	106 (87.60)	53 (85.48)		
Hemorrhage			1.854	0.173
Yes	26 (21.49)	19 (30.65)		
No	95 (78.51)	43 (69.35)		
Ossification			1.388	0.239
Yes	17 (14.05)	5 (8.06)		
No	104 (85.95)	57 (91.94)		
Operative time			0.833	0.361
<3 h	99 (81.82)	54 (87.10)		
≥3 h	22 (18.18)	8 (12.90)		
Intraoperative blood loss, mL	138.14±33.68	146.95±38.49	-1.594	0.113
Blood transfusion requirement			2.408	0.121
Yes	18 (14.88)	15 (24.19)		
No	103 (85.12)	47 (75.81)		

Note: PFS, progression-free survival; DP, disease progression.

years, with a distinct trend toward younger patient demographics [12]. R0 resection currently remains the most effective surgical treatment. While most patients achieve short-term dis-

Table 3. Comparison of laboratory parameters between PFS and DP groups

Characteristics	PFS (n=121)	DP (n=62)	*t/Z*	*P*
Creatinine, μmol/L	75.25±6.82	76.98±8.07	-1.526	0.129
Platelet, 10^9/L	239.95±67.80	247.16±74.84	-0.657	0.512
Neutrophil, 10^9/L	5.89 (4.67, 7.20)	6.11 (4.24, 7.84)	-0.277	0.782
Lymphocyte, 10^9/L	3.03 (2.28, 3.60)	2.74 (2.21, 3.33)	-1.449	0.147
Fibrinogen, g/L	3.62 (2.71, 4.88)	3.63 (2.72, 4.71)	-0.193	0.847
Globulin, g/L	29.18 (26.93, 31.34)	30.12 (27.07, 32.88)	-1.577	0.115
Albumin, g/L	38.79±3.92	37.57±4.66	1.867	0.064
Albumin-to-globulin ratio	1.35±0.20	1.27±0.25	2.197	0.029
Systemic immune-inflammation index	541.14 (314.75, 695.99)	560.84 (373.16, 710.94)	-1.053	0.293
Neutrophil-to-lymphocyte ratio	2.09 (1.44, 2.75)	2.29 (1.66, 2.97)	-1.218	0.223
Platelet-to-lymphocyte ratio	84.09 (59.07, 104.67)	90.54 (65.35, 129.23)	-1.321	0.187

Note: PFS, progression-free survival; DP, disease progression.

Table 4. Identification of independent risk factors by Cox multivariate regression analysis

Independent risk factors	B	SE	Wald	*P*	*HR*	*HR* 95% CI
Age	0.034	0.011	8.681	0.003	1.034	1.011-1.057
Histological subtype			23.628	<0.001		
Well-differentiated liposarcoma						1.000
Dedifferentiated liposarcoma	-2.044	0.763	7.178	0.007	0.130	0.029-0.578
Myxoid/round cell liposarcoma	-0.990	0.756	1.716	0.190	0.371	0.084-1.635
Pleomorphic liposarcoma	-1.737	0.812	4.574	0.032	0.176	0.036-0.865
Mixed-type liposarcoma	-0.233	0.827	0.079	0.799	0.793	0.157-4.008
Tumor stage	-0.820	0.275	8.886	0.003	0.440	0.257-0.755
Tumor differentiation grade	-0.929	0.263	12.495	<0.001	0.395	0.236-0.661

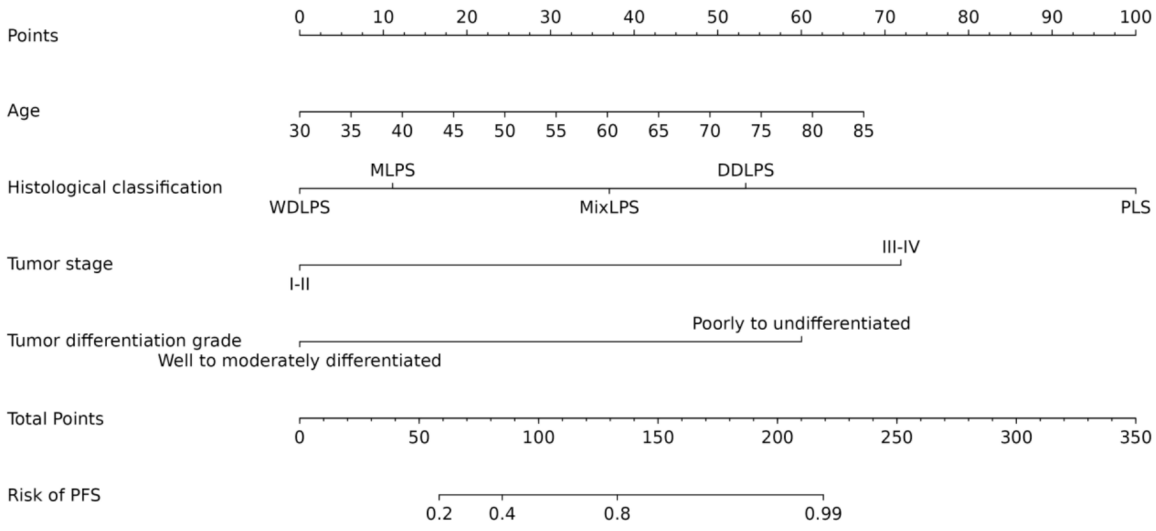

Figure 2. Nomogram incorporating significant prognostic factors. Note: WDLPS, well-differentiated liposarcoma; DDLPS, dedifferentiated liposarcoma; MLPS, myxoid/round cell liposarcoma; PLS, pleomorphic liposarcoma; MixLPS, mixed-type liposarcoma.

ease control following surgical resection and 1-year survival rates are relatively high, the 3-year survival rate declines significantly due to local recurrence and distant metastasis. The

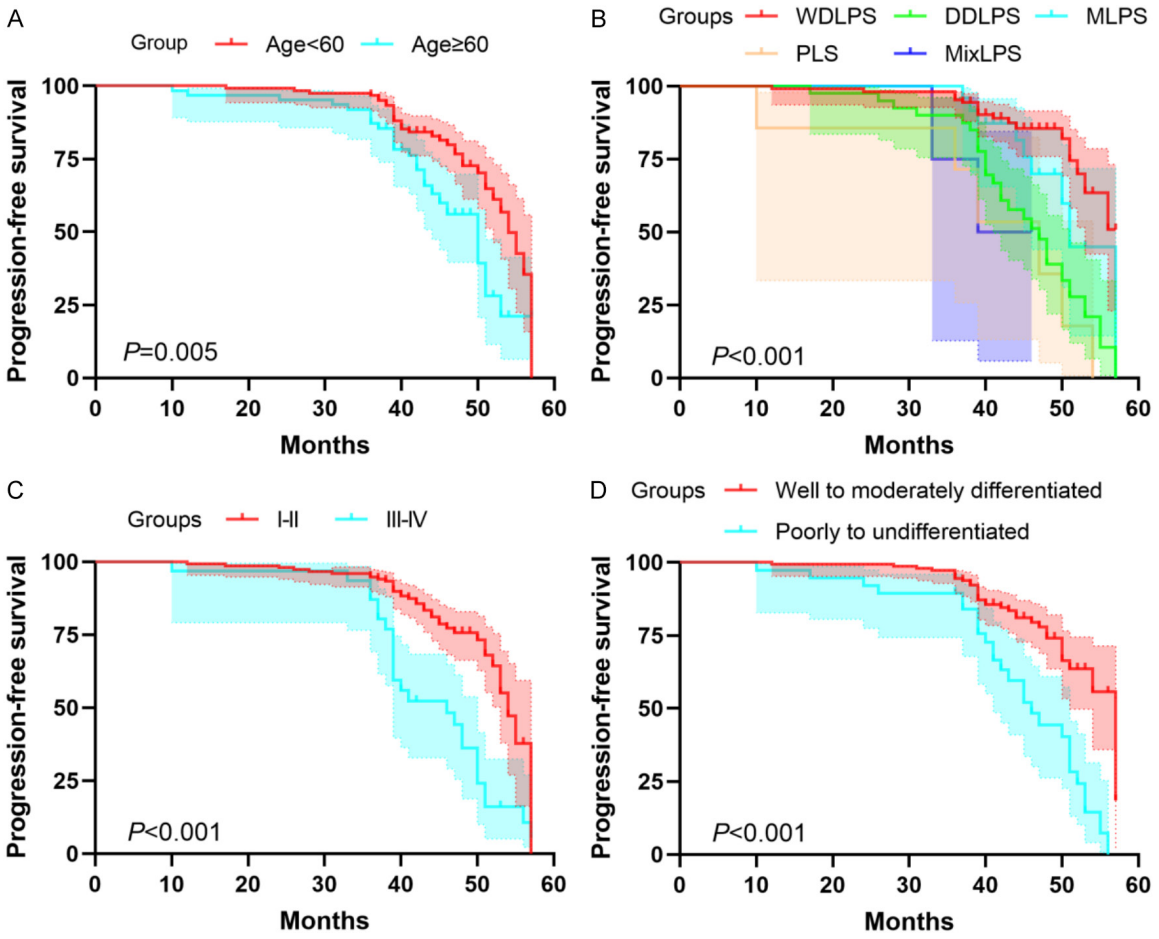

Figure 3. Survival analysis based on predictive variables. Note: A: Comparison of K-M curves among different age groups. B: Comparison of K-M curves among different histological subtypes. C: Comparison of K-M curves among different tumor stages. D: Comparison of K-M curves among different tumor differentiation grade.

5-year prognosis is even less optimistic, as the risk of late-phase recurrence persists [13]. The large retroperitoneal space provides an ideal environment for tumor concealment and growth. Even after R0 resection, microscopic residual cancer cells inevitably remain. Moreover, malignant cells exhibit a propensity for discontinuous spread along retroperitoneal fascial planes, collectively contributing to the heightened risks of intermediate-term recurrence and distant metastasis in RPLS patients [14]. For recurrent cases, the R0 resection rate in secondary surgeries is less than 20%, and the vast majority of patients are not candidates for reoperation, posing a significant threat to postoperative survival [15]. Consequently, the high recurrence rate and poor long-term prognosis have become major clinical concerns. This study analyzed patients' general information, clinicopathological data, and laboratory parameters to establish a prognostic prediction model, aimed at informing clinical treatment and management strategies. The model identified age, histological subtype, tumor stage, and tumor differentiation grade as independent prognostic factors.

Our results indicated that postoperative disease progression was more common in patients aged ≥60 years despite R0 resection. Previous studies have similarly demonstrated that age serves as an independent prognostic predictor for RPLS [16]. The inferior prognosis observed in elderly patients may be attributed to age-related declines in immune competence and tissue regenerative capacity, potentially impairing the clearance of micrometastatic lesions [17]. Additionally, undifferentiated liposarcoma, characterized by intrinsically aggressive biological behavior and higher recur-

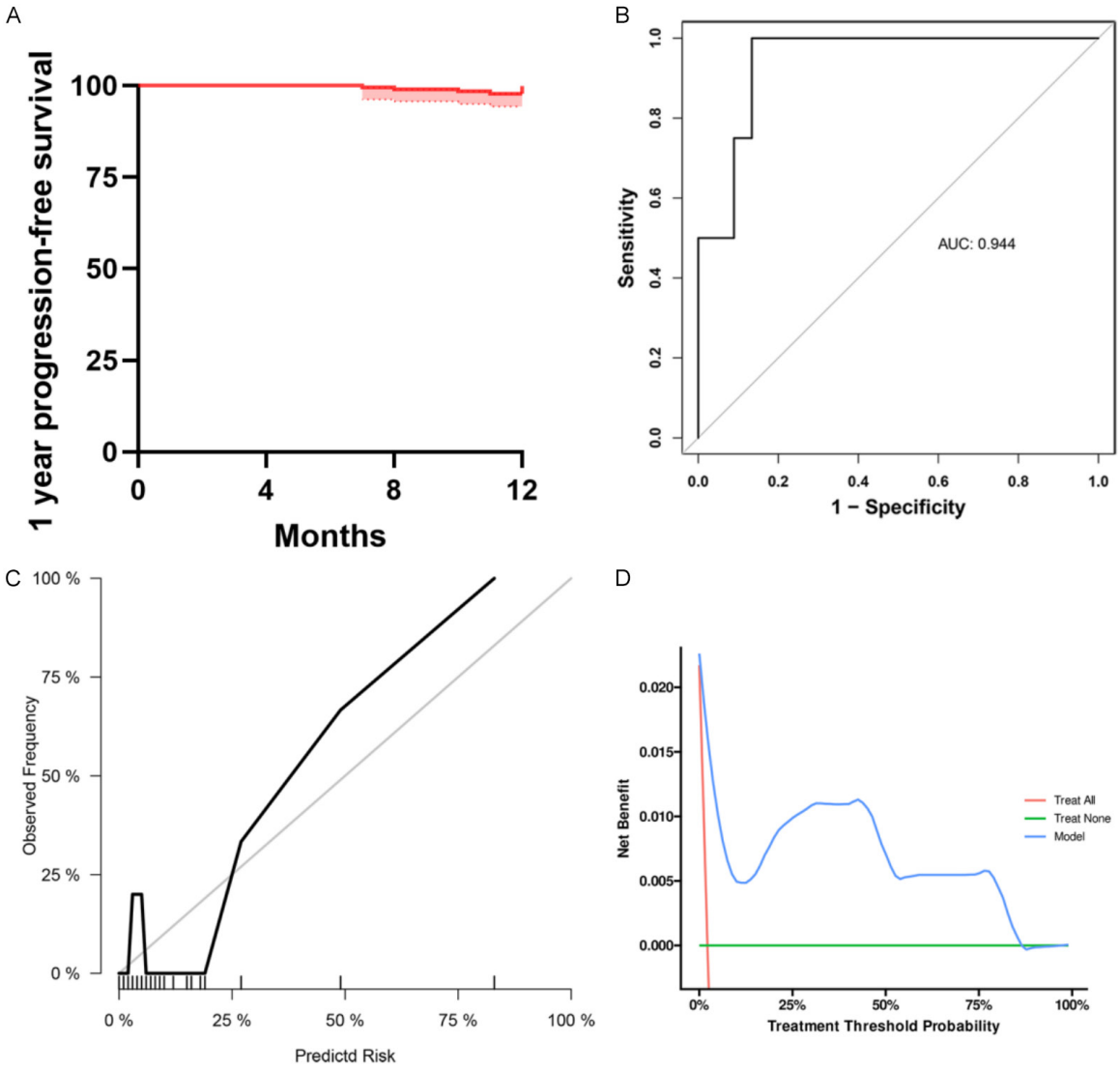

Figure 4. Evaluation and validation of the 1-year prognostic prediction model for RPLS patients. Note: A: 1-year K-M survival curves for all RPLS patients. B: ROC curve for 1-year PFS. C: Calibration curve analysis at 1 year. D: DCA at 1 year.

rence risk, is more prevalent among elderly patients [18]. In addition to the adverse prognostic impact of advanced age, patients with DDLPS and PLS subtypes were also found to have poorer clinical outcomes. These subtypes, according to clinicopathological features, typically present with larger tumor sizes and higher differentiation grades at diagnosis [19], and they exhibit genomic instability, further exacerbating their aggressive behaviors [20]. In this study, tumor stage emerged as another significant prognostic factor, with stage III-IV RPLS patients exhibiting significantly worse prognosis. A previous study has similarly confirmed that advanced tumor stage (≥ stage III) predicts poorer five-year survival in RPLS patients [21]. This may be attributed to greater genomic instability and enhanced activation of invasion and metastasis-related pathways in higher-stage tumors [22]. Additionally, stage III-IV tumors are often associated with more extensive infiltration of surrounding tissues [23]. Tumor differentiation grade was also identified as a critical prognostic factor. This phenomenon may be attributed to the distinct biological characteristics of poorly differentiated tumors. On one hand, low-grade tumor cells typically exhibit enhanced proliferative activity and invasive capacity [24]. On the other hand, poorly differentiated tumors frequently present with

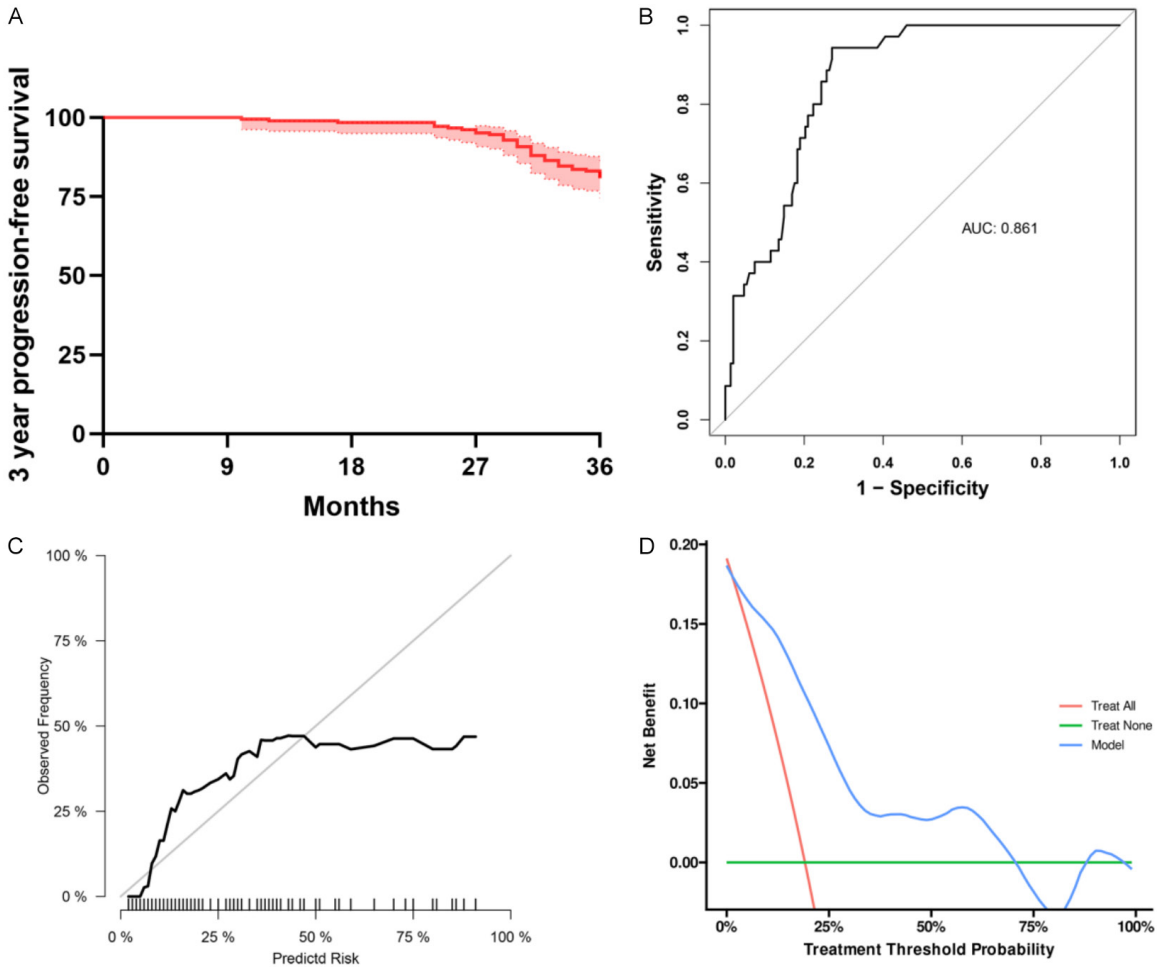

Figure 5. Evaluation and validation of the 3-year prognostic prediction model for RPLS patients. Note: A: 3-year K-M survival curves for all RPLS patients. B: ROC curve for 3-year PFS. C: Calibration curve analysis at 3 year. D: DCA at 3 year.

more extensive vascular invasion and neural infiltration, which may lead to residual micrometastases that are difficult to completely eradicate during surgery [25]. Therefore, for RPLS patients with high-risk features, including advanced age, DDLPS/PLS subtypes, stage III-IV disease, or poor differentiation, should undergo strict R0 resection followed by intensified postoperative imaging surveillance to mitigate unfavorable prognostic outcomes.

Based on these prognostic factors, the investigators developed predictive models for 1-year, 3-year, and overall survival in RPLS patients following R0 resection. The 1-year model demonstrated optimal predictive performance (AUC=0.944), with excellent calibration and strong clinical utility (NB=0.05-0.80). However, the 3-year model (AUC=0.861) showed modestly reduced calibration accuracy and clinical applicability (NB=0.05-0.73), suggesting temporal decay in predictive performance for intermediate-term outcomes. In contrast, the overall model (AUC=0.903) confirmed strong predictive capacity, with excellent calibration curve agreement, NB reaching 0.03-0.90 across clinically relevant probability thresholds. The concordant results across the three models highlight both the potential of these factors for risk stratification and the temporal heterogeneity in prognostic determinants for RPLS. A previous short-term prognostic study similarly identified the predictive potential of age and tumor stage [21]. These findings emphasize the need for enhanced early intervention and comprehensive treatment management throughout the clinical course for high-risk patients, including elderly individuals, those with DDLPS subtype, stage III-IV disease, and poorly differentiated tumors [26].

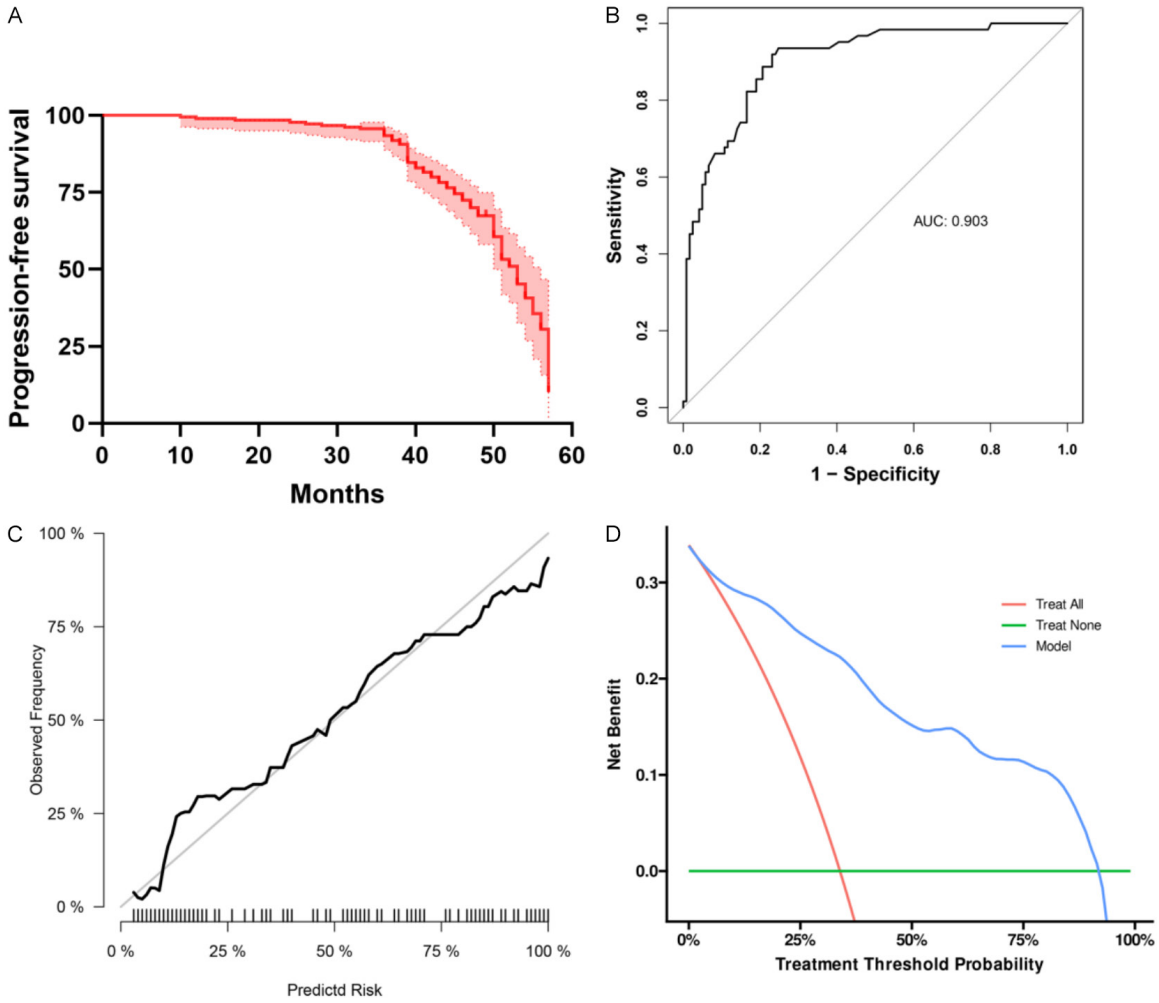

Figure 6. Evaluation and validation of prognostic prediction model for RPLS patients. Note: A: Overall K-M survival curve for the entire RPLS cohort. B: ROC curve for overall PFS. C: Overall calibration curve analysis. D: Overall DCA.

This investigation has several limitations that should be acknowledged. Firstly, as a single-center retrospective analysis, the relatively limited sample size may introduce selection bias, particularly in the evaluation of certain rare subtypes where statistical power may be insufficient. Secondly, the relatively short follow-up duration could compromise accurate assessment of long-term prognostic factors, which may partially account for the observed decline in predictive accuracy of the 3-year model. Future research should prioritize multicenter prospective designs and incorporate more comprehensive molecular characterization to further refine the predictive precision of the system.

Conclusion

Advanced age, DDLPS, PLS, stage III-IV disease, and poor tumor differentiation were identified as independent predictors of shorter PFS in RPLS patients following R0 resection, providing a validated predictive model to guide clinical management. These findings highlight the necessity of enhanced postoperative surveillance for high-risk patients to improve long-term outcomes.

Disclosure of conflict of interest

None.

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