Original Article

A better overall survival (OS) for total (ipsilateral) retroperitoneal lipectomy than standard complete resection in patients with retroperitoneal liposarcoma: a comparative multi-institutional study

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Background: Complete resection (CR) serves as the standard of surgical treatment for retroperitoneal liposarcoma (RPLS). Unfortunately, even at referral centers, recurrence rates are high, and CR may not address multifocal diseases, which are a common phenomenon in RPLS. We sought to retrospectively compare the clinical outcomes of RPLS patients treated with total (ipsilateral) retroperitoneal lipectomy (TRL) and CR. Because TRL remove potentially multifocal tumors in the fat, patients may have a better prognosis than CR.

Methods: Patients with primary/first-recurrent RPLS who had been treated at 5 referral centers were recruited from December 2014 to June 2018. Multivariable Cox regression analyses were conducted to determine the effects of demographic, operative, and clinicopathological variables on the following primary endpoints: local recurrence (LR), local recurrence-free survival (LRFS), and overall survival (OS).

Results: A total of 134 patients were enrolled in this retrospective study, 53 of whom underwent TRL, and 81 of whom underwent CR. The 2 groups were comparable in terms of age, gender, presentation (primary *vs.* first-recurrent RPLS), number of tumors (unifocal *vs.* multifocal) at presentation, and Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grade. The TRL group had higher levels of preoperative hemoglobin (Hb) (13 *vs.* 12.5 g/dL; P=0.008) and a lower amount of intraoperative blood loss (400 *vs.* 500 mL; P=0.034), but there were no significant differences in the length of hospital stay (23 *vs.* 22 d; P=0.47) or complications (32 *vs.* 30; P=0.82) between the 2 groups. In a subset of patients with multifocal tumors at initial presentation, OS was more prolonged in those treated with TRL than those treated with CR (P=0.0272). Based on the multivariable analysis, primary liposarcoma and a low FNCLCC grade were associated with decreased LR and improved OS.

Conclusions: TRL is a safe procedure that positively affects the OS of patients with multifocal RPLS. This novel strategy deserves further investigation in prospective studies.

Keywords: Retroperitoneal liposarcoma (RPLS); total (ipsilateral) retroperitoneal lipectomy (TRL); complete R0/R1 resection; multifocal retroperitoneal liposarcoma

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Introduction

Retroperitoneal sarcoma (RPS) accounts for approximately 0.15% of all adult cancers and has an incidence of 0.5–1 case per 100,000 (1). Retroperitoneal liposarcoma (RPLS) is the most common subtype of RPS. RPLS creates significant challenges for treatment due to its large size and potential for adjacent organ involvement. The role of radiation and systemic therapy in RPLS is not well defined, and surgery is currently the only treatment choice. Macroscopic complete resection (CR) combined with the resection of involved adjacent organs has been recommended for the treatment of RPLS (2-4). CR improves survival more than incomplete resection (R_2); however, local recurrence (LR) remains common (40–85%) (3,5-7).

The inability to achieve a true R_0 resection with the susceptive microscopic involvement of adjacent organs, structures, and surfaces might contribute to the high rate of postoperative LR in RPLS. Multiple satellite tumor foci may exist in the perceived normal fat that can be separated from the visible tumor as a "field defect" (8). Notably, recurrence not only occurs at the site of resection but also at sites within the retroperitoneum and peritoneal cavity, distant from the resection site (8). This observation has been independently reported by several studies (2,9,10). Singer *et al.* at the Memorial Sloan Kettering Cancer Center recommend complete surgical resection with abnormal ipsilateral retroperitoneal fat from the diaphragm to the pelvis, including dis-contiguous fat in the independent space. However, Singer *et al.* only recommend the removal of abnormal retroperitoneal fat and do not provide any supporting evidence for their recommendation (11).

In this study, we propose total (ipsilateral) retroperitoneal lipectomy (TRL), a new concept of surgery for patients with RPLS. TRL involves the total resection of retroperitoneal adipose tissue ipsilateral to the tumor. Under this approach, tumor and ipsilateral fat are always resected *en bloc*. The contents resected during this procedure include liposarcoma, fat tissue (normal and abnormal), the perirenal fat capsule, and surrounding organs as appropriate, depending on the specific extent of tumor involvement (10).

TRL was first introduced by Dr. Chenghua Luo at Peking University International Hospital (PKUIH) (10). Since 2015, TRL has been implemented at 5 referral centers in China, including PKUIH, the Affiliated Hospital of Qingdao University (AHQU), the Yunnan Cancer Hospital (YCH), Zhongshan Hospital of Fudan University (ZHFU), and University of Southern California-Keck School of Medicine (USC-KSM). Through joint conferences, multidisciplinary therapy team discussions, hands-on courses, and extensive internal communication, this approach has been extensively explored and standardized among these Chinese centers. In this retrospective multi-center study, we tested our scientific hypothesis that TRL is safe and improves the outcomes of RPLS patients compared to conventional CR. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3332/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review boards of Peking University International Hospital (PKUIH, No. IRB-2021-079), Affiliated Hospital of Qingdao University (AHQU), Yunnan Cancer Hospital(YCH), Zhongshan Hospital of Fudan University (ZHFU), University of Southern California-Keck School of Medicine (USC-KSM). Individual consent for this retrospective analysis was waived. All participating hospitals/institutions were informed and agreed the study. Patients with unilateral primary or first-recurrent RPLS who underwent resection with curative intent between December 2014 and June 2018 were identified from prospectively maintained sarcoma databases at PKUIH, AHQU, YCH, ZHFU, and USC-KSM. Only patients with well-differentiated liposarcoma (WDLPS) or dedifferentiated liposarcoma (DDLPS) who were treated with R_0/R_1 resection were included in this study. Patients

with central (mesenteric) or primarily pelvic tumors, grossly incomplete (R_2) resection, missing clinical information, or a follow-up period of <6 months were excluded from this study. Notably, patients with giant tumors (8) (encompassing ≥6 compartments, as defined by Tseng *et al.*) were also excluded from this study.

Electronic medical records were retrieved from all 5 institutions to extract data on the following variables: (I) preoperative variables [i.e., age, gender, date of diagnosis, presentation (primary/first-recurrent tumor), symptoms, co-morbidity, hemoglobin (Hb), albumin (ALB), receipt of neoadjuvant therapy, tumor size (maximum diameter), tumor site, number of tumors (unifocal *vs.* multifocal), and American Society of Anesthesiologists (ASA) score]; (II) intraoperative variables [i.e., type of surgery (TRL *vs.* CR), organs resected, total period of surgery, and estimated blood loss]; and (III) postoperative variables [i.e., histologic subtype, Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grade (12), length of hospital stay, complications according to Clavien-Dindo classification (13), receipt of adjuvant therapy, dates of LR, and death]. To assess these variables, patients' medical history, radiologic imaging, operative notes, and pathological reports were reviewed and integrated by experienced multidisciplinary sarcoma specialists at each center. A unifocal tumor was defined as 1 solitary tumor in the retroperitoneum, while multifocal tumors were defined as the presence of 2 or more non-contiguous tumors in the retroperitoneum, as determined by preoperative computed tomography (CT) scans and confirmed by intraoperative findings. Patients who had both WDLPS and DDLPS components in their tumors were classified as DDLPS.

Surgical techniques

CR was defined as the surgical resection of the total tumor mass with grossly negative margins (R_0/R_1). To achieve this goal, *en-bloc* resection of the tumor with grossly involved adjacent organs and/or major vessels was carried out. In TRL, in addition to CR, all the ipsilateral retroperitoneal fat was removed. The anatomic extent of lipectomy in TRL was demarcated by the following 6 borders: anterior (the posterior surface of abdominal viscera); posterior (the psoas, iliopsoas, and other muscle surfaces); superior (the diaphragm surface); inferior (the iliac vascular surface); medial [the inferior vena cava surface (to the right) or abdominal aorta surface (to the left)]; and lateral (the lateral abdominal wall surface at mid-auxiliary line level) (see *Figure 1*).

Follow-up

Postoperative baseline CT/magnetic resonance imaging scans were performed to ensure the complete removal of gross visible fat in all RPLS patients. Patients continued to receive contrast-enhanced CT scans of the abdomen/pelvis every 3 months for 2 years, and then every 6 months for 5 years as recommended by the National Comprehensive Cancer Network (NCCN, United States of America) (14) and The Trans-Atlantic Retroperitoneal Sarcoma Working Group (TARPSWG) (2). For patients with high-grade DDLPS tumors, contrast-enhanced CT of the chest was added as a form of surveillance imaging.

Statistical analysis

The TRL- and CR-related parameters were compared by independent sample *t*-tests for the numerical variables and Wilcoxon rank-sum test for the categorical variables. Local recurrence-free survival (LRFS) and overall survival (OS) were defined as the time from the date of surgery to the date of recurrence, or to death/last at follow-up, respectively. LR, LRFS, and OS were identified to determine the safety and oncological outcomes of TRL and CR. Survival curves were obtained by means of Kaplan-Meier plots to estimate the LRFS and OS. The log-rank test was used to compare the survival outcomes. To identify the patient population that would benefit the most from TRL, univariable and multivariable Cox proportional-hazards regression models were used. All the statistical analyses were carried out using SAS software (version 9.4), and a P value <0.05 was considered statistically significant.

Results

In total, 134 patients from 5 referral centers met the inclusion criteria for this study. The number of patients from each center is listed in Table S1. The main characteristics are summarized in *Table 1*. The patients had a median age of 55 years (range, 29–81 years), and 68 (51%) of the patients were male. Both the TRL and CR groups were comparable in terms of age, gender, and presentation (primary/recurrent). The mean tumor size was 21.0 cm (range, 3.5–45 cm). A total of 60 (45%) patients had multifocal disease (i.e., ≥2 non-contiguous tumors). The mean preoperative Hb was 12.75 g/dL (range, 6.7–16.8 g/dL), and the baseline Hb was higher in the TRL group than the CR group (P=0.008).

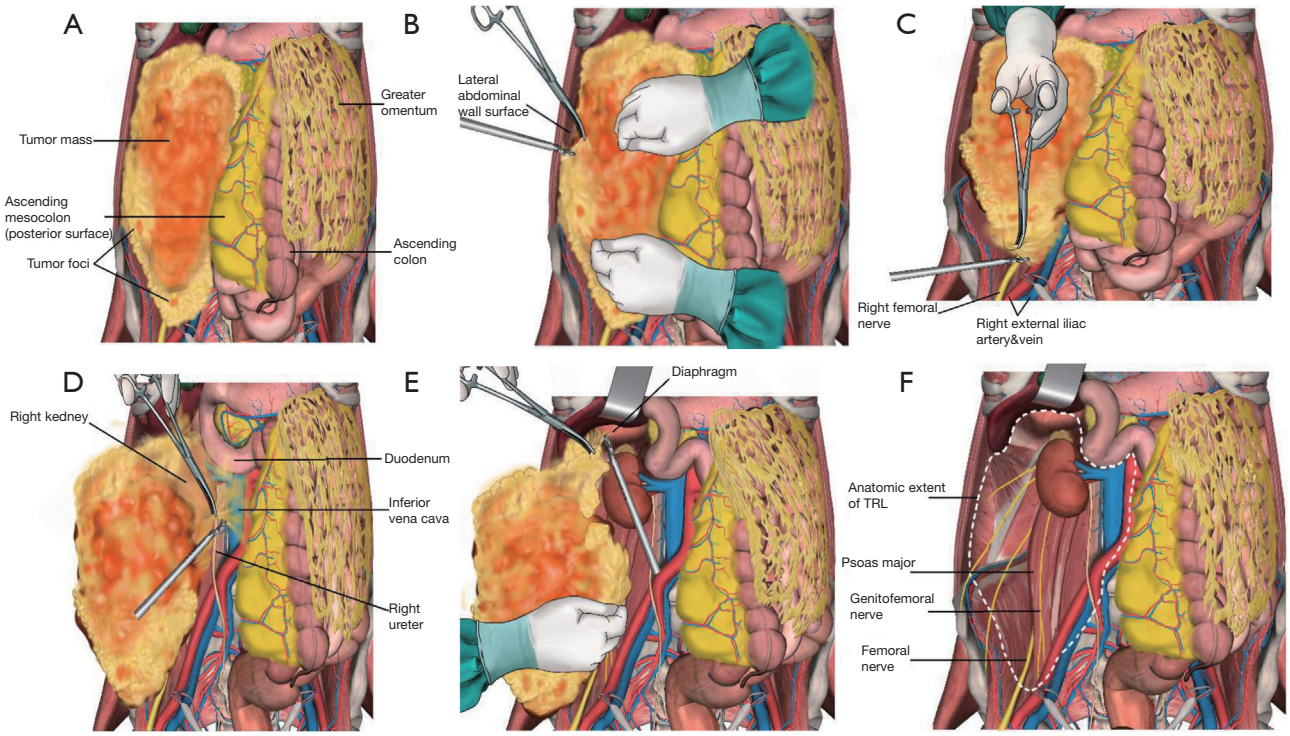

Figure 1 TRL. (A) Anterior border: posterior surface of abdominal viscera. (B) Lateral border: surface of lateral abdominal wall at mid-axillary line level. (C) Inferior border: surface of Iliac vessels. (D) Medial border for right RPLS: surface of inferior vena cava. (E) Superior border: surface of diaphragm. (F) Posterior border: surface of psoas, iliopsoas and other muscles. TRL, total (ipsilateral) retroperitoneal lipectomy; RPLS, retroperitoneal liposarcoma.

Table 1 Demographic, operative and clinicopathologic characteristics of RPLS patients

Variable	All patients (n=134)	CR (n=81)	TRL (n=53)	P value
Age, years [range]	55 [29–81]	56 [29–81]	53 [36–77]	0.890
Gender, n [%]				0.310
Male	68 [51]	44 [54]	24 [45]	
Female	66 [49]	37 [46]	29 [55]	
Presentation, n [%]				0.120
Primary	75 [56]	41 [51]	34 [64]	
First recurrence	59 [44]	40 [49]	19 [36]	
Tumor size (maximum diameter)*, n [%]				0.270
<21 cm	66 [49]	43 [53]	23 [43]	
≥21 cm	68 [51]	38 [47]	30 [57]	
Hemoglobin, g/dL [range]	12.75 [6.7–16.8]	12.5 [6.7–15.9]	13 [7.8–16.8]	0.008
Albumin, g/dL [range]	3.9 [1.7–5.3]	3.8 [1.7–4.7]	4 [2.6–5.3]	0.070
Neoadjuvant therapy, n [%]	9 [7]	8 [10]	1 [2]	0.070

Table 1 *(continued)*

Table 1 *(continued)*

Variable	All patients (n=134)	CR (n=81)	TRL (n=53)	P value
Tumor site, n [%]				0.690
Right retroperitoneum	66 [51]	40 [53]	26 [49]	
Left retroperitoneum	63 [49]	36 [47]	27 [51]	
No. of tumors, n [%]				0.130
Unifocal	74 [55]	49 [60]	25 [47]	
Multifocal	60 [45]	32 [40]	28 [53]	
Resected organs, n [%]				0.850
None	53 [40]	32 [40]	21 [40]	
1	40 [30]	25 [31]	15 [28]	
2	30 [22]	18 [22]	12 [23]	
≥3	11 [8]	6 [7]	5 [9]	
Operation time, minutes [range]	245 [92–689]	260 [92–689]	240 [101–625]	0.580
Estimated blood loss, mL [range]	455 [20–11,000]	400 [20–3,000]	500 [100–11,000]	0.034
Histologic subtype, n [%]				0.120
Well-differentiated	75 [56]	41 [51]	34 [64]	
Dedifferentiated	59 [44]	40 [49]	19 [36]	
FNCLCC grade, n [%]				0.410
Unknown	6 [5]	6 [9]	0 [0]	
Grade 1	64 [56]	35 [54]	29 [58]	
Grade 2	20 [17]	9 [14]	11 [22]	
Grade 3	25 [22]	15 [23]	10 [20]	
Complications, n [%]	42 [31]	26 [32]	16 [30]	0.820
Clavien-Dindo classification				0.250
None	69 [44]	41 [51]	18 [34]	
<3	57 [43]	27 [33]	30 [57]	
≥3	18 [13]	13 [16]	5 [9]	
Adjuvant therapy, n [%]	8 [6]	6 [7]	2 [4]	0.390
Length of hospital stay, days [range]	23 [3–143]	23 [3–143]	22 [7–45]	0.470
Recurrence	51 [38]	32 [40]	19 [36]	0.670
Deceased	17 [13]	14 [17]	3 [6]	0.049
Cause of mortality, n [%]				0.315
Recurrence	12 [9]	10 [12]	2 [4]	
Metastasis	5 [4]	4 [5]	1 [2]	

*, mean/median 21 cm. RPLS, retroperitoneal liposarcoma; CR, complete resection; TRL, total (ipsilateral) retroperitoneal lipectomy; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer.

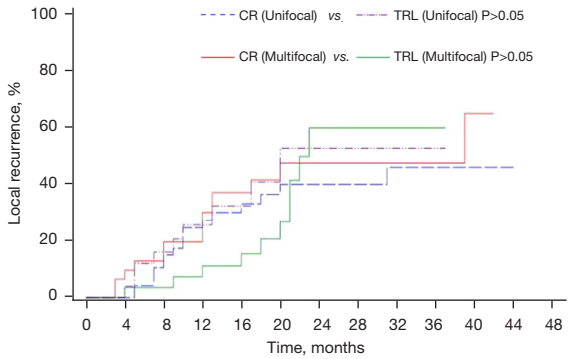

Figure 2 LR rate according to the unifocality and multifocality of tumors in RPLS patients treated with TRL or CR. CR, complete resection; TRL, total (ipsilateral) retroperitoneal lipectomy; LR, local recurrence; RPLS, retroperitoneal liposarcoma.

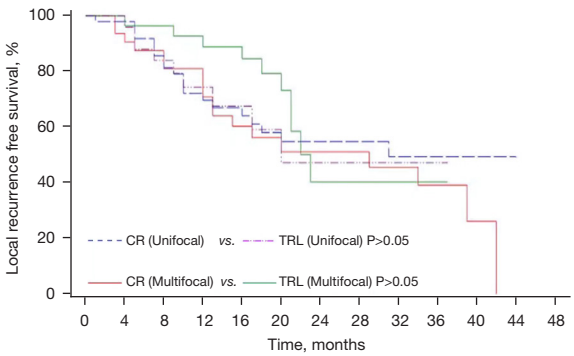

Figure 3 LRFS according to the unifocality and multifocality of tumors in RPLS patients treated with TRL or CR. CR, complete resection; TRL, total (ipsilateral) retroperitoneal lipectomy; LRFS, local recurrence-free survival; RPLS, retroperitoneal liposarcoma.

No adjacent organs were resected in 40% of the patients; however, 30% of the patients had 1 organ resected, 22% had 2 organs resected, and 8% had ≥3 organs resected. The colon and kidney were the most common organs resected *en bloc* with the tumor (see Table S2). In the TRL group, an ipsilateral colectomy was performed in 27 (51%) patients and a nephrectomy was performed in 18 (34%) patients. In the CR group, an ipsilateral colectomy was performed in 30 (37%) patients and a nephrectomy was performed in 29 (36%) patients. The Whipple procedure or pancreaticoduodenectomy was performed in 1 patient; and an inferior vena cava resection was performed in 1 patient in the CR group. The tumor site, number of adjacent organs resected, and operative time were comparable between the 2 groups (TRL *vs.* CR). Overall, 75 (56%) patients had WDLPS, and 59 (44%) had DDLPS. The TRL group tended to have a higher frequency of WDLPS and a lower frequency of DDLPS than the CR group.

Postoperative morbidity and mortality

Based on Clavien-Dindo classification (13), fewer patients in the TRL group developed grade-3 or higher complications compared to the CR group (9% *vs.* 15%). Because of postoperative complications, fewer patients were re-operated on in the TRL group than the CR group (1 *vs.* 4; see Table S3). The median length of hospital stay was comparable between the TRL and CR groups (22 *vs.* 23 days; P>0.05). There were no in-hospital deaths in the TRL group; however, 1 patient died in the CR group due to postoperative complications (multi-organ failure).

LRFS

Of the 134 RPLS patients, 51 (38%) experienced recurrence at a median follow-up period of 17 months (17 months in the TRL group and 17 months in the CR group). In relation to the recurrent diseases, 28 were locoregional (ipsilateral), 4 were remote (contralateral retroperitoneum), 6 were locoregional + remote, and 13 were unknown. There was no significant difference in LR between the 2 groups (see *Figure 2*). Recurrence resulted in the death of 12 (9%) patients, but only 2 (16.7%) were from the TRL group, and 10 (83.3%) were from the CR group. Among the patients with multifocal tumors, the 1- and 3-year estimated LRFS rates were 89% [95% confidence interval (CI), 69–96%] and 40% (95% CI, 15–65%) in the TRL group, respectively, and 71% (95% CI, 51–84%) and 39% (95% CI, 19–59%) in the CR group, respectively (see *Figure 3*). Based on the multivariable analysis, primary presentation was independently associated with a lower risk of LR, while a younger age and FNCLCC grade III were associated with a higher risk of LR (see *Table 2*).

OS

In total, 17 (13%) deaths were recorded during the study period. The major causes of death included postoperative complications in 1 patient, recurrence and/or metastasis in 12 patients, and late complications in 2 patients; the cause of death was unknown in 2 patients. Of the total 17 deaths, 3 patients were in the TRL group, and 14 patients were in the CR group (P=0.049). Only 5 (4%) patients developed

Table 2 Univariable and multivariable analysis of associations between clinicopathological factors and LR

Variable	Univariable analysis			Multivariable analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age, years	1.03	1.01–1.06	0.0144	1.05	1.02–1.09	0.0035
Gender (male *vs.* female)	1.24	0.71–2.17	0.4552	–	–	–
Presentation (primary *vs.* recurrence)	0.45	0.25–0.79	0.0057	0.35	0.18–0.70	0.0032
CR *vs.* TRL	2.67	0.76–9.40	0.1262	–	–	–
Hemoglobin, g/dL (≥12.75 *vs.* <12.75)*	0.40	0.14–1.13	0.0846	–	–	–
Albumin, g/dL (≥3.9 *vs.* <3.9)*	0.91	0.52–1.59	0.7359	–	–	–
Tumor size, cm (≥21 *vs.* <21)*	1.06	0.61–1.85	0.8301	–	–	–
No. of tumors (unifocal *vs.* multifocal)	1.02	0.59–1.78	0.9405	–	–	–
Resected organs						
1 *vs.* none	2.07	0.99–4.33	0.0545	–	–	0.5220
2 *vs.* none	2.79	1.32–5.91	0.0072	–	–	0.8679
≥3 *vs.* none	2.33	0.82–6.64	0.1125	–	–	–
Estimated blood loss, mL	1.00	1.00–1.00	0.0004	1.00	1.00–1.00	0.0001
FNCLCC grade						
II + III *vs.* I	2.99	1.57–5.69	0.0009	–	–	0.1895
III *vs.* I + II	3.39	1.72–6.71	0.0004	3.29	1.66–6.53	0.0007
Histologic subtype						
WDLPS *vs.* DDLPS	1.01	0.56–1.85	0.9632	–	–	–
CD classification (<3 *vs.* ≥3)	0.98	0.44–2.19	0.9700	–	–	–
Length of hospital stay, days	1.01	0.99–1.03	0.4224	–	–	–

*, median value. LR, local recurrence; HR, hazard ratio; CI, confidence interval; CR, complete resection; TRL, total (ipsilateral) retroperitoneal lipectomy; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer; WDLPS, well-differentiated liposarcoma; DDLPS, dedifferentiated liposarcoma; CD, Clavein-Dindo.

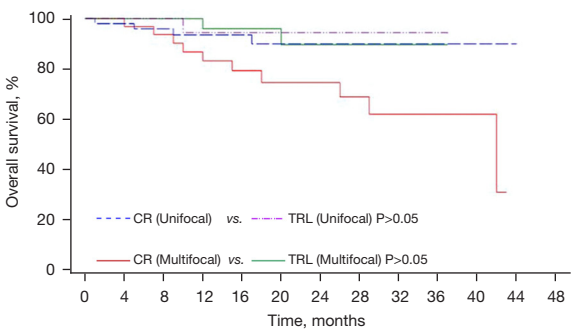

Figure 4 OS according to the unifocality and multifocality of tumors in RPLS patients treated with TRL or CR. TRL was associated with better OS for patients with multifocal tumors than CR (P=0.0272). CR, complete resection; TRL, total (ipsilateral) retroperitoneal lipectomy; OS, overall survival; RPLS, retroperitoneal liposarcoma.

metastases before death, of whom, only 1 (20%) was from the TRL group, and 4 (80%) were from the CR group. For those with multifocal tumors, the 1- and 3-year OS rates were 96% (95% CI, 75–99%) and 90% (95% CI, 63–97%) in the TRL group, respectively, and 83% (95% CI, 64–93%) and 62% (95% CI, 38–79%) in the CR group, respectively (P=0.0272). The OS rate was comparable between the 2 groups among patients with unifocal tumors (see *Figure 4*). Based on the multivariable analysis, primary disease was associated with better OS, while FNCLCC grade III was associated with poorer OS (see *Table 3*).

Discussion

Both the extent of the surgical resection and tumor

Table 3 Univariable and multivariable analysis of association between clinicopathological factors and OS

Variable	Univariable analysis			Multivariable analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age, years	1.03	0.99–1.08	0.1496	–	–	–
Gender (male *vs.* female)	1.64	0.60–4.52	0.3381	–	–	–
Presentation (primary *vs.* recurrence)	0.21	0.07–0.66	0.0071	0.17	0.04–0.68	0.0122
CR *vs.* TRL	2.67	0.76–9.40	0.1262	–	–	–
Hemoglobin, g/dL (≥12.75 *vs.* <12.75)*	0.40	0.14–1.13	0.0846	–	–	–
Albumin, g/dL (≥3.9 *vs.* <3.9)*	0.24	0.07–0.82	0.0234	–	–	0.5771
Tumor size, cm (≥21 *vs.* <21)*	0.89	0.34–2.32	0.8185	–	–	–
No. of tumors (unifocal *vs.* multifocal)	0.39	0.14–1.12	0.0793	–	–	–
Resected organs						
1 *vs.* none	3.21	0.62–16.61	0.1649	–	–	–
2 *vs.* none	7.37	1.56–34.78	0.0116	–	–	0.1478
≥3 *vs.* none	5.78	0.81–41.22	0.0798	–	–	–
Estimated blood loss, mL	1.00	1.00–1.00	<0.0001	1.00	1.00–1.00	<0.0001
FNCLCC grade						
II + III *vs.* I	6.85	1.86–25.22	0.0038	–	–	0.1530
III *vs.* I + II	7.57	2.31–24.80	0.0008	6.87	2.06–22.93	0.0017
Histologic subtype						
DDLPS *vs.* WDLPS	2.35	0.70–7.85	0.1647	–	–	–
CD classification (<3 *vs.* ≥3)	0.41	0.14–1.17	0.0845	–	–	–
Length of hospital stay, days	1.03	1.01–1.05	0.0008	–	–	0.1242

*, median value. OS, overall survival; HR, hazard ratio; CI, confidence interval; CR, complete resection; TRL, total (ipsilateral) retroperitoneal lipectomy; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer; DDLPS, dedifferentiated liposarcoma; WDLPS, well-differentiated liposarcoma; CD, Clavein-Dindo.

biology must be taken into account and balanced when treating patients with RPS (15). Clinically, the histologic subtype determines the pattern of recurrence and heavily influences the surgical and management approaches adopted (16). The standard of care for treatment in RPLS is CR; however, CR results in a high rate of recurrence, which requires more extended resection (17-19). Multifocal disease is common in RPLS (8,16). Indeed, multi-foci disease occurs in 34% of patients at initial presentation, and 57% of patients with unifocal disease progress to multifocal disease at recurrence after CR (8). As a newly developed surgical technique, TRL removes thoroughly ipsilateral retroperitoneal adipose tissue *en bloc* with the tumor. TRL not only achieves complete resection but also attempts to treat multifocal disease while sparing organs rather than liberally resecting them.

As far as we know, this is the first study to compare the clinical outcomes of patients with RPLS who were treated with TRL or CR. TRL is a relatively safe procedure compared to CR. In our study, patients who underwent TRL experienced more minor but fewer major or grade ≥3 complications compared to those who underwent CR. In fact, grade ≥3 postoperative morbidity occurred in only 5 (9%) patients in the TRL group, which was remarkably lower than the complication incidence (of approximately 16–21%) reported in recent studies that advocate for extended or compartmental resection (20,21). The amount of estimated intraoperative blood loss was significantly lower in the TRL group than the CR group. During TRL, the dissection of retroperitoneal adipose tissue was

carried out from borders with abdominal muscles, visceral organs, and other structures as appropriate. This method decreased the risk of intraoperative injury to blood vessels, which were embedded in adipose tissue. Thus, this technique reduced the amount of blood loss during surgery.

LR and LRFS were not affected by TRL; however, an improvement in OS was observed among patients with multifocal disease who underwent TRL. Multifocal disease has profound effects on the oncological outcomes of RPLS patients (see Table S4). In a recent study, 20% of patients presented with multifocal disease, and the 5-year OS rate was significantly lower in the multifocal group than the unifocal group (8,22-25). In another study, 25% of RPLS patients presented with multifocal disease with curtailed OS (24). In our series, the proportion of multifocal disease at initial presentation was 45% (23% for primary, 22% for first-recurrent RPLS), whereas the 3-year OS rate post-TRL was significantly higher than the 3-year OS rate post-CR in those with multifocal disease (95% CI, 63–97%; P=0.0272). TRL not only improves the OS of patients with multifocal RPLS, but also reduces overall deaths and recurrence- and/or metastasis- related deaths in RPLS patients (P=0.049). Our results suggest that TRL is indicated for multifocal RPLS.

Our study had several limitations. First, due to its retrospective nature, our study had inherent biases. Second, patients with first-recurrent RPLS were included in the data analysis, which might have generated a bias due to the lack of quality control over the original surgery for the primary disease. Third, as the median follow-up period was only 17 months, we could not assess LR, LRFS, and OS over a longer duration. Late recurrences occur after 5 years in RPLS (26). Finally, patient selection for surgical treatment was determined at each center, which introduced an unavoidable selection bias. It would have been more ideal if all 5 centers had jointly determined whether a given patient should undergo TRL or CR. However, ultimately, the critical clinicopathological characteristics were comparable between the 2 groups. Notably, one of the advantages of this study is the relatively low frequency of chemotherapy or radiation therapy in both the neoadjuvant and adjuvant settings; thus, we were able to more accurately compare these 2 surgical approaches with less confounding influence from nonsurgical therapies.

In conclusion, TRL is a relatively safe surgical approach for RPLS patients. Multifocal disease is an important histologic subtype. TRL was associated with a significantly higher OS than CR in this subset of patients. Future prospective studies at sarcoma referral centers with standardized selection criteria for TRL, larger sample sizes, and longer follow-up periods need to be conducted to validate these findings.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist Available at https://atm.amegroups.com/article/view/10.21037/atm-22-3332/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-3332/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3332/coif). GKZ and HYY are from HBR Data Science Ltd. The other 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 (as revised in 2013). The study was approved by the institutional review boards of Peking University International Hospital (PKUIH, No. IRB-2021-079), Affiliated Hospital of Qingdao University (AHQU), Yunnan Cancer Hospital (YCH), Zhongshan Hospital of Fudan University (ZHFU) and University of Southern California-Keck School of Medicine (USC-KSM). All participating hospitals/institutions were informed and agreed the study. Individual consent for this retrospective analysis was waived.

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