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ORIGINAL ARTICLE

Multivisceral resection of primary multifocal retroperitoneal sarcomas: a retrospective study from a high-volume sarcoma center

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Abstract

Background: Although surgery plays a key role in the treatment of the primary retroperitoneal sarcoma (RPS), there remain few reports on the primary multifocal RPS.
Aims: This study aimed to identify the prognostic factors for the primary multifocal RPS in an effort to optimize the clinical management of this malignancy.
Methods: A retrospective analysis was conducted on a cohort of 319 primary RPS patients who underwent radical resection from 2009 to 2021, with post-operative recurrence as the primary endpoint of this study. COX regression was performed to identify the risk factors for post-operative recurrence, and a comparison was made to baseline and prognostic differences between multivisceral resection (MVR) and non-MVR groups with multifocal disease.
Results: There were 31 (9.7%) patients with multifocal disease, the mean tumor burden placed on them was 24.1 ± 11.9 cm, and nearly half of the patients (48.4%) had MVR. Dedifferentiated liposarcoma, well-differentiated liposarcoma, and leiomyosarcoma accounted for 38.7%, 32.3%, and 16.1%, respectively. The 5-year recurrence-free survival rate reached 31.2% (95% CI, 11.2–51.2%) in the multifocal group and 51.8% (95% CI, 44.2–59.4%) in the unifocal group ($P = 0.010$). Age (heart rate [HR] = 0.916; $P = 0.039$) and complete resection (HR = 1.861; $P = 0.043$) were identified as the independent risk factors for the post-operative recurrence of multifocal primary RPS.
Conclusions: Regarding primary multifocal RPS, the overall treatment strategy can be adopted for the treatment of the primary RPS, and MVR remains effective in boosting the chance of disease control for a selected group of patients.
Relevance for Patients: This study is relevant to patients as it highlights the importance of receiving appropriate treatment for the primary RPS, especially for those with multifocal disease. The treatment options should be evaluated carefully to ensure that the patients receive the most effective treatment for their specific type and stage of RPS. The potential risk factors for post-operative recurrence should be well understood to minimize those risks. Ultimately, this study underscores the importance of ongoing research to optimize the clinical management of RPS and improve outcomes for patients.

1. Introduction

Retroperitoneal sarcomas (RPSs) account for 10–15% of all soft-tissue sarcomas [1]. With no effective adjuvant treatments currently available, surgery remains the most common approach to treating primary RPS [2]. In 2009, Gronchi *et al*. proposed that aggressive surgery significantly reduced the 5-year local recurrence rate from 48% to 28% [3]. In the same year, a retrospective multicenter study conducted in France revealed that compared those patients with simple tumor resection, complete chamber resection reduced the local

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recurrence rate of the primary RPS by 3 times [4]. It was also confirmed in subsequent studies that this more aggressive surgical strategy posed no safety risks [5,6]. Therefore, multivisceral resection (MVR), a way of treatment that relies on complete chamber resection to achieve the maximum negative margins and reduce the risk of intraoperative tumor rupture, is increasingly accepted in high-volume sarcoma centers [7].

On the other hand, multifocal RPS has a significant effect on the prognosis of patients 8, 9. More specifically, the probability of recurrence after multifocal RPS showed a two-fold increase compared with unifocal disease [8]. The incidence of multifocal disease varies approximately from 10% to 20% [8,9], a large proportion of which is in recurrent RPS. Given the rarity of multifocality, both primary and recurrent disease cohorts were included in the existing studies. However, there are still no studies that focus exclusively on the primary RPS multifocality.

Therefore, the present study aims to reveal the prognostic factors of the primary multifocal disease and to determine the therapeutic role that MVR plays in multifocal RPS.

2. Methods

2.1. Patient selection

This study included the RPS patients who underwent radical resection at South Hospital of the Zhongshan Hospital, Fudan University, Shanghai, China from 2009 to 2021. The inclusion criteria are as follows: (1) the primary tumor located in the retroperitoneum; (2) pathological conformance; (3) no previous surgical resection performed; (4) the absence of distant metastasis; and (5) the complete clinicopathological data. In the meantime, gastrointestinal stromal tumor and Ewing's sarcoma were excluded from the study. All recruited patients signed an informed consent form for the use of clinicopathological information during hospitalization. Approved by the Ethics Committee of South Hospital of Zhongshan Hospital, this study was conducted in strict accordance with the Declaration of Helsinki.

2.2. Clinicopathologic factors evaluation

All relevant details that might affect the outcome for patients were included, such as patient baseline, tumor baseline, and surgery-related conditions. The tumor burden was defined as the sum of the largest diameters of all tumors, multifocal disease was defined as the presence of more than one discrete lesion in the abdominal cavity or retroperitoneal space, and sarcomatosis was defined as disseminated lesions in the abdominal cavity, regardless of whether there are sub-lesions in the ipsilateral or contralateral retroperitoneum. MVR is defined as the removal of more than one organ in a single surgical procedure [4]. Complete tumor resection was defined as grossly negative margins, that is, R0 or R1 resection. Post-operative complications were graded in line with the Clavien–Dindo Classification, in which the severer post-operative complications than III were defined as serious complications [9].

The post-operative follow-up of patients included clinical and imaging examinations (enhanced computerized tomography [CT] or magnetic resonance imaging of chest, abdomen, and pelvis). The follow-up was performed every 3–4 months within 2 years after surgery, every 6 months for 2–5 years postoperatively, and once a year for 5 years after surgery. The recurrence of disease was defined as the new lesions or enlargement of pre-existing lesions (after R2 resection) revealed by imaging examination.

2.3. Statistical methods

Continuous variables were indicated by median, mean, interquartile range (IQR), or standard deviation and then compared by conducting independent sample t-test. Categorical variables were denoted as numbers and percentages and then compared using the χ^2 test and Fisher's exact. As for recurrence-free survival (RFS) time and overall survival (OS), they were calculated using Kaplan–Meier and compared by performing log-rank test. Univariate and multivariate analyses of disease recurrence were conducted using COX regression models. All tests were two-tailed, with $P \leq 0.05$ treated as statistically significant. All data were analyzed with the assistance of SPSS 22.0 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Baseline characteristics of multifocal and unifocal patients

A total of 319 patients were recruited for the study, with the median follow-up time reaching 45 (95% CI, 38–52) months for all patients. There were 31 patients with multifocal disease, accounting for 9.7% of the total. Of them, 17 were male (54.8%) and 14 were female (45.2%). The average age of multifocal patients was 59.0 (SD, 9.8) years. The proportion of symptomatic patients reached 41.9% (n = 13). The mean tumor burden was 24.1 (SD, 11.9) cm for those patients with multifocal disease. Among the histologic subtypes, dedifferentiated liposarcoma, well-differentiated liposarcoma, and leiomyosarcoma accounted for 38.7%, 32.3%, and 16.1%, respectively. A vast majority of the patients received no pre-operative adjuvant therapy. Complete resection was achieved for 83.9% (n = 26) of the patients. On average, the number of combined organ resections was 1 (IQR, 1–3). Severe post-operative complications occurred in 16.1% of the patients, with the median length of hospitalization reaching 16.0 (IQR, 13.0–24.0) days (Table 1).

The 5-year RFS rate was 31.2% (95% CI, 11.2–51.2%) in the multifocal group and 51.8% (95% CI, 44.2–59.4%) in the unifocal group (P = 0.010), while the 5-year OS rate was 48.7% (95% CI, 27.7–69.7%) and 64.7% (95% CI, 57.4–72.0%) (P = 0.065) among the two groups, respectively. Compared with unifocalty, the tumor burden placed on those patients with multifocalty was greater (mean, 24.1 vs. 16.7 cm; $P < 0.001$) and the rate of complete resection was lower among them (83.9% vs. 98.3%; P = 0.001). Although not statistically significant, the multifocal group had a longer operative time (mean, 4.1 vs. 3.6 h; $P = 0.120$), more bleeding (median, 500.0 vs. 400.0 ml; P = 0.165) and a larger proportion of packed RBC transfusion (48.4% vs. 29.5%; P = 0.031). There was similarity shown between the two groups in the proportion of patients undergoing MVR surgery, the

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Table 1. Patient and tumor characteristics in 319 patients with the primary retroperitoneal sarcoma

Characteristics	Multifocal (*n*=31)	Unifocal (*n*=288)	*P*-value
Gender			0.635
Male	17 (54.8)	145 (50.3)	
Female	14 (45.2)	143 (49.7)	
Age, years mean (SD)	59.0 (9.8)	55.8 (13.4)	0.198
ASA score			0.421
1	19 (61.3)	197 (68.4)	
>1	12 (38.7)	91 (31.6)	
Symptoms			0.875
Yes	13 (41.9)	125 (43.4)	
No	18 (58.1)	163 (56.6)	
Tumor burden, cm mean (SD)	24.1 (11.9)	16.7 (9.1)	<0.001
Histologic subtypes			0.410
WDLPS	10 (32.3)	112 (38.9)	
DDLPS	12 (38.7)	68 (23.6)	
LMS	5 (16.1)	47 (16.3)	
SFT	1 (3.2)	24 (8.3)	
Others	3 (9.7)	37 (12.8)	
FNCLCC			0.451
Grade 1	9 (29.0)	104 (36.1)	
Grade 2	13 (41.9)	91 (31.6)	
Grade 3	7 (22.6)	84 (29.2)	
Unknown	2 (6.5)	9 (3.1)	
Radiation			
Yes	1 (3.2)	24 (8.3)	0.315
(pre/post)	1 (3.2)/0 (0)	16 (5.6)/8 (2.7)	
No	30 (96.8)	264 (91.7)	
Chemotherapy			0.116
Yes	6 (19.4)	29 (10.1)	
(Pre/post)	3 (9.7)/3 (9.7)	20 (6.9)/9 (3.2)	
No	25 (80.6)	259 (89.9)	
Operation			0.417
Laparoscopic surgery	0 (0.0)	6 (2.1)	
Open surgery	31 (100.0)	282 (97.9)	
Complete resection			0.001
Yes	26 (83.9)	283 (98.3)	
No	5 (16.1)	5 (1.7)	
Major vascular surgery			0.215
Yes	1 (3.2)	29 (10.1)	
No	30 (96.8)	259 (89.9)	
Pancreaticoduodenectomy			0.562
Yes	1 (3.2)	5 (1.7)	
No	30 (96.8)	283 (98.3)	
Number of combined resections, median (IQR)	1 (1–3)	2 (0–3)	0.975
MVR			0.751
Yes	15 (48.4)	148 (51.4)	
No	16 (51.6)	140 (48.6)	
Operative time, hours mean (SD)	4.1 (2.1)	3.6 (1.5)	0.120
Estimated blood loss, ml median (IQR)	500.0 (200.0–1500.0)	400 (100–800)	0.165

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Table 1. *(Continued)*

Characteristics	Multifocal (*n*=31)	Unifocal (*n*=288)	*P*-value
Packed RBC transfusion			0.031
Yes	15 (48.4)	85 (29.5)	
No	16 (51.6)	203 (70.5)	
ICU Stay			
Yes	19 (61.3)	140 (48.6)	0.180
No	12 (38.7)	148 (51.4)	
Severe post-operative adverse events			
Yes	5 (16.1)	32 (11.1)	0.381
No	26 (83.9)	256 (88.9)	
Post-operative hospital stay, days median (IQR)	16.0 (13.0–24.0)	14.0 (11.0–21.0)	0.622

IQR: Interquartile range

proportion of serious post-operative complications, and post-operative hospitalization.

3.2. Baseline characteristics for MVR and non-MVR in multifocal patients

The 5-year RFS rate for MVR and non-MVR was 40.6% (95% CI, 0.0–82.1%) and 21.9% (95% CI, 0.1–43.7%), respectively. Despite the MVR group showing a trend of better prognosis from the survival curve, it failed to reach a statistically significant level due to the small sample size (P = 0.076). The 5-year OS was 68.6% (95% CI, 41.6–95.6%) and 34.6% (95% CI, 7.6–61.6%) among the two groups, respectively, with no statistical significance shown either (P = 0.775).

Compared with the non-MVR group, the MVR group had more liposarcoma (100% vs. 43.8%; P = 0.012), greater tumor burden (mean, 30.1 vs. 18.5 cm; P = 0.005), and higher ipsilateral disease rates (46.7% vs. 31.3%; P = 0.379). Despite no statistical difference observed, a larger proportion of patients from the MVR group had complete tumor resection (93.3% vs. 75.0%; P = 0.333). This is because MVR is a more aggressive surgical strategy. Consequently, there were more combined organ resections, longer operative times, and more packed RBC transfusion (P < 0.05) (Table 2).

3.3. RFS analysis for multifocal disease

COX univariate analysis revealed that younger age (P = 0.015) and incomplete resection (P = 0.032) were the risk factors for post-operative recurrence. Furthermore, the variables (age, complete resection, and MVR) with univariate analysis P < 0.1 were factored into multivariate analysis. In multivariate analysis, age (heart rate [HR] = 0.916; P = 0.039) and complete resection (HR = 1.861; P = 0.043) were the independent risk factors for post-operative recurrence of multifocal primary RPS (Table 3).

4. Discussion

At present, surgical resection remains essential for the treatment of the primary RPS[2]. The retrospective studies conducted by Bonvalot *et al*., and Gronchi, in 2009, confirmed the role of MVR in the treatment of the primary RPS [3,4]. However, the above studies included no indicators for the assessment of multifocal disease. In subsequent reports, multifocal disease was further identified as a risk factor for the recurrence of disease after RPS [8,10]. In some nomogram prediction models, the multifocality of disease has also been included as prognostic evaluation indicators, which is sufficient to show that disease multifocality is an important influencing factor for the prognosis of patients with the primary RPS [11,12]. In view of no studies on multifocal primary RPS at present, this study is the first one to explore the risk factors for post-operative recurrence, revealing the potential of aggressive surgical approach to deliver benefit to the selected patients with multifocal primary RPS.

Despite few studies on the multifocality of the primary RPS, three of them cannot be ignored. The earliest one was William's report in 1998, including 29 patients with the primary RPS. Among them, 7 (24.1%) had multiple lesions on pre-operative CT. Although the study was limited by sample size and no risk factor analysis was performed, all seven patients suffered recurrence within 1 year after surgery [13]. Anaya *et al*. conducted retrospective analysis of a cohort of 393 patients with the primary or recurrent RPS, revealing that 79 (20%) of them developed multifocal disease. Among them, the primary RPS multifocal disease accounted for 10.8%, which is similar to the cohort of this study (9.7%). Despite no distinction between primary or recurrent disease, the risk factor analysis of greater than seven tumors was a risk factor for poor prognosis, which was defined as sarcomatosis [8]. In 2015, Tseng *et al*. conducted analysis of the locoregional disease patterns of 247 patients with the primary and recurrent retroperitoneal liposarcoma [14]. In their study, the proportion of multifocal disease reached as high as 34%, but no patients underwent extended resection. It was found out that those patients with retroperitoneal liposarcoma may have metastatic tumors in the abdominal cavity far away from the primary one, and the unifocal tumors recurring in multifocality accounted for a large proportion. Therefore, for complete resection, the combination with peritoneal resection may be required with posterior space adipose tissue, and even with intramesenteric adipose tissue. All patients in this cohort underwent no combined organ resection, which led to the conclusion that extended resection (MVR) is worth considering with caution in liposarcoma.

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Table 2. Patient and tumor characteristics in MVR and non-MVR group with multifocal disease

Characteristics	MVR (*n*=15)	Non-MVR (*n*=16)	*P*-value
Gender			0.576
Male	9 (60.0)	8 (50.0)	
Female	6 (40.0)	8 (50.0)	
Age, years mean (SD)	61.6 (11.0)	56.6 (8.2)	0.161
ASA score			0.552
1	10 (66.7)	9 (56.3)	
>1	5 (33.3)	7 (43.7)	
Symptoms			0.833
Yes	9 (60.0)	9 (56.3)	
No	6 (40.0)	7 (43.7)	
Tumor burden, cm mean (SD)	30.1 (11.4)	18.5 (9.6)	0.005
Number of tumors >2			0.576
Yes	6 (40.0)	8 (50.0)	
No	9 (60.0)	8 (50.0)	
Ipsilateral tumor			0.379
Yes	7 (46.7)	5 (31.3)	
No	8 (53.3)	11 (68.7)	
Sarcomatosis			0.347
Yes	5 (33.3)	8 (80)	
No	10 (66.7)	8 (80)	
Histologic subtypes			0.012
WDLPS	8 (53.3)	2 (12.5)	
DDLPS	7 (46.7)	5 (31.3)	
LMS	0 (0.0)	5 (31.3)	
SFT	0 (0.0)	1 (6.3)	
Others	0 (0.0)	3 (18.8)	
FNCLCC			0.363
Grade 1	3 (20.0)	6 (37.5)	
Grade 2	7 (46.7)	6 (37.5)	
Grade 3	3 (20.0)	4 (25.0)	
Unknown	2 (13.3)	0 (0.0)	
Radiation			1.000
Yes	0 (0.0)	1 (6.36)	
No	15 (100.0)	15 (93.8)	
Chemotherapy			0.654
Yes	2 (13.3)	4 (25.0)	
No	13 (86.7)	12 (75.0)	
Complete resection			0.333
Yes	14 (93.3)	12 (75.0)	
No	1 (6.7)	4 (25.0)	
Major vascular surgery			0.484
Yes	1 (6.7)	0 (0.0)	
No	14 (93.3)	16 (100.0)	
Pancreaticoduodenectomy			0.484
Yes	1 (6.7)	0 (0.0)	
No	14 (93.3)	16 (100.0)	
Number of combined resections, median (IQR)	3.0 (2.0–4.0)	1.0 (0.0–1.0)	<0.001
Operative time, hours mean (SD)	5.2 (2.4)	2.4 (1.3)	0.005
Estimated blood loss, ml median (IQR)	1000.0 (500.0–1500.0)	200 (125.0–1025.0)	0.068

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Table 2. *(Continued)*

Characteristics	MVR (*n*=15)	Non-MVR (*n*=16)	*P*-value
Packed RBC transfusion			0.049
Yes	10 (66.7)	5 (31.3)	
No	5 (33.3)	11 (68.7)	
ICU Stay			0.066
Yes	12 (80.0)	7 (43.7)	
No	3 (20.0)	9 (56.3)	
Severe post-operative adverse events			0.172
Yes	4 (26.7)	1 (6.3)	
No	11 (73.3)	15 (93.7)	
Post-operative hospital stay, days median (IQR)	20.0 (14.0–29.0)	13.0 (9.0–22.0)	0.054

Table 3. Univariable and multivariable analyses to determine independent predictors of recurrence-free survival of the primary multifocal retroperitoneal sarcoma

Variables	Univariate analysis		Multivariate analysis	
	Hazard ratio (95%CI)	*P*-value	Hazard ratio (95%CI)	*P*-value
Gender male versus female	1.121 (0.689–1.825)	0.645		
Age (continuous)	0.929 (0.876–0.986)	0.015	0.916 (0.842–0.996)	0.039
ASA score>1 versus 1	0.761 (0.263–2.198)	0.614		
Symptoms yes versus no	1.699 (0.661–4.371)	1.699		
Tumor burden (continuous)	0.992 (0.955–1.030)	0.674		
Number of tumors>2 yes versus no	1.478 (0.551–3.968)	0.438		
Ipsilateral tumor yes versus no	0.492 (0.173–1.396)	0.182		
Sarcomatosis yes versus no	1.930 (0.744–5.005)	0.176		
Histologic subtypes		0.395		
DDLPS versus WDLPS	6.116 (0.000–1E+25)			
LMS versus WDLPS	18.408 (0.000–3E+25)			
SFT versus WDLPS	0.000 (0.000–1E+93)			
Others versus WDLPS	8.878 (0.000–1E25)			
FNCLCC		0.204		
Grade 2 versus Grade 1	0.968 (0.331–2.826)			
Grade 3 versus Grade 1	2.056 (0.461–9.165)			
Unknown versus Grade 1	13.169 (1.017–170.502)			
Radiation yes versus no	2.016 (0.254–16.025)	0.507		
Chemotherapy yes versus no	2.381 (0.621–9.125)	0.206		
Complete resection no versus yes	1.868 (1.056–3.305)	0.032	1.861 (1.021–3.392)	0.043
Number of combined resections (continuous)	0.846 (0.570–1.255)	0.407		
MVR yes versus no	0.402 (0.142–1.138)	0.086	1.286 (0.331–4.994)	0.716
Operative time (continuous)	1.182 (0.856–1.632)	0.309		
Estimated blood loss (continuous)	1.000 (1.000–1.001)	0.131		
Packed RBC transfusion yes versus no	1.728 (0.598–4.997)	0.312		
ICU Stay yes versus no	1.004 (0.954–1.056)	0.890		
Severe post-operative adverse events yes versus no	1.018 (0.228–4.547)	0.981		

In contrast, 48.4% of the patients with multifocal disease in this study underwent MVR. Despite a greater tumor burden among the MVR group, the MVR group showed a trend toward improved oncological outcomes. Notably, all patients in the MVR group were liposarcoma, which is related to our selection of surgical patients. Because primary multifocal RPS is an uncommon and poorly documented disease, our treatment principles still reference the treatment principles for unifocal diseases, specifically speaking well-differentiated liposarcoma and low-grade dedifferentiated liposarcoma are mainly local recurrence, so we implement a more aggressive surgical strategy (even if the surrounding organs of the tumor are not violated by the naked eye, they will be resected together); for high-grade dedifferentiated liposarcoma, if it is evaluated that there is

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invasion of surrounding organs, complete radical resection should be attempted; leiomyosarcoma often presents as a tumor with clear borders, and if the surrounding organs not invaded, it should be preserved; for pleomorphic undifferentiated sarcoma, malignant peripheral nerve sheath tumor, and solitary fibrous tumor, complete resection with negative margins is enough [2,7,15,16]. For this reason, the combination of organ resection in patients with liposarcoma is preferable in our daily practice. Although there was no statistical difference in the multivariate analysis between whether the patients underwent MVR or not, it is now widely believed MVR is effective in improving the local control on the disease for the following two reasons. On the one hand, the possible micrometastatic lesions are removed. On the other hand, wider negative margins are obtained [17]. Since the condition of the resection margin is an independent risk factor for the post-operative recurrence of multifocal disease, it is still believed that even with multifocal disease, a selected group of patients may still benefit from the more aggressive surgical approaches. However, it must be noted that due to the complexity of RPS pathology and the specificity of surgery, MVR is not a universally applicable rule for either multifocal or unifocal disease, and each patient should have a surgical strategy tailored to their individual circumstances.

In this study cohort, only one patient (3.2%) received radiation therapy, while six patients (19.4%) received chemotherapy. The low proportion of patients receiving adjuvant therapy is largely due to the lack of sensitivity of retroperitoneal tumors to radiation and chemotherapy. The efficacy of new adjuvant radiotherapy remains controversial [18]. The STRASS study is the only completed randomized controlled trial (n = 266 patients) comparing pre-operative radiotherapy plus surgery with surgery alone for the primary RPS. Although subgroup analysis suggests potential benefit for WDLPS, overall study results indicate no difference in 3-year disease-free survival between the combined radiotherapy group and the surgery alone group [19]. In addition, the presence of multiple lesions increases the difficulty of radiation therapy target localization, so only one patient in this study received pre-operative adjuvant radiation therapy. Post-operative radiation therapy is not commonly recommended due to its toxicity effects [20]. For chemotherapy, both neoadjuvant chemotherapy and adjuvant chemotherapy do not seem to benefit patients who undergo complete surgical resection [21,22], so we do not recommend routine chemotherapy for patients with multifocal disease who can undergo complete resection.

In an analysis of the risk factors for post-operative recurrence of multifocal disease, it was found out that age was an independent risk factor for post-operative recurrence. More specifically, contrary to our previous conclusion, younger patients are at higher risk of post-operative recurrence. As reported from previous large cohorts, increasing age was a risk factor for poor prognosis [11,23]. However, there is also a trend of worse prognosis among the younger patients in some studies [24,25]. In the present study, the data were reviewed again, with the average age of 60 years as the cutoff value, revealing that only four cases (26.7%) of 15 patients aged over 60 had sarcomatosis. In comparison, the proportion of 16 patients aged below 60 reached as high as 43.8% (n = 7). Despite the limited sample size, the difference between the two groups was not statistically significant (P = 0.176). However, a higher proportion of sarcomatosis may indicate that younger patients have more aggressive tumors and thus a worse prognosis.

Are satellite lesions of multifocal RPS metastatic or multifocal? Should treatment follow the treatment of the primary disease or metastatic disease? Although pathological examinations are required for exploring answers to the above questions, some clues can be obtained by comparing the patients with the first local recurrence treated in our center [26]. It was discovered that the median RFS in the primary RPS for unifocal and multifocal and for first local recurrent RPS of unifocal and multifocal with complete resection was 62.7 (95% CI, 41.8–83.5), 55.5 (14.0–96.7) months, 23.4 (15.2–31.6), and 12.6 (8.9–16.4) months, respectively. From above, it can be seen that the prognosis is similar and better than that of recurrent disease if complete resection is achievable in the primary RPS, regardless of whether it is unifocal or multifocal. Therefore, the treatment strategy can still refer to the treatment of the primary RPS, even in multifocal disease.

There are some limitations on this study. First, this study is a retrospective one, which makes it inevitable for selection bias to arise. Second, despite more than 300 patients with the primary RPS included in this cohort, there were 31 patients with multifocal disease, and the relatively small sample size also constrained this study. Third, as mentioned earlier, it was pointed out in the study of Anaya *et al*. that the larger number of tumors than 7 is an independent risk factor for poor prognosis. However, due to the lack of information, it is only indicated in this study whether the number of tumors exceeds 2. Fourth, due to the limitation of sample size, it was not identified in this study whether recurrence was local recurrence or distant metastasis. Fifth, whether the lesions of the multifocal disease are in the same compartment or not may be a variable affecting clinical decision making and prognosis, but due to information missing, this was not included in the study.

5. Conclusion

This study is the first cohort study of the primary multifocal RPS. In this study, it was discovered that young patients and incomplete resection were the risk factors for post-operative recurrence. For the primary multifocal RPS, the overall treatment strategy can be referred to the treatment of the primary RPS, and MVR still boosts the chance of survival for a selected group of patients.

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Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflicts of interest.

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Ethics Statement

This study was approved by the Ethics Committee of South Hospital of Zhongshan Hospital/Shanghai Public Health Clinical Center.

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