Surgical role, prognostic factors, and outcome prediction in primary retroperitoneal sarcoma: a prospective large cohort study

Taha A. Baiomy[a], Ahmed R.A. El Fattah[a], Ahmed A. Obaya[b], Rham Z. Ahmed[c], Ola A. Harb[d], Ahmed Embaby[e], Dalia S. El Deen[f], Gamal Osman[a], Amr Ibrahim[a]

Departments of [a]General Surgery, [b]Clinical Oncology & Nuclear Medicine, [c]Medical Oncology, [d]Pathology, [e]Internal Medicine, [f]Radiology, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Correspondence to Ola A. Harb, e-mail: olaharb2015@gmail.com

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Background
Surgical resection with wide safety margins in addition to chemotherapy and radiotherapy has been considered now the best management strategy of retroperitoneal sarcomas (RPS) in case of absence of distant metastasis, but the rate of local recurrence is still high, which worsens patients' outcome.
The aim of this study was to detect postoperative short-term and long-term oncological outcomes of RPS, in addition to evaluating predictive factors related to recurrence, overall survival (OS), and disease-free survival rates in patients with RPS, to allow detection of patients who might have more benefits from aggressive therapeutic approaches and radical surgery.
Patients and methods
This was a prospective study of 80 patients with primary RPS who underwent curative resection. We followed up all patients for about 5 years with recording of all surgical and oncological details.
Results
After a median follow-up time of 34 months, with range 8–56 months, we showed that factors associated with poor OS and recurrence-free survival (RFS) rates in univariate analysis were tumor size, histopathological types, grade, stage, resection margins, adjacent organ infiltration, chemotherapy, radiotherapy ($P<0.001$), and vascular involvement ($P=0.003$). In multivariate analysis, grade ($P=0.001$) and vascular involvement (0.002) were the most important predictors.
Conclusion
We concluded that surgical excision with negative safety margins leads to reduction in local and distant recurrence and favorable RFS and OS rates. Grade, resection margins, and vascular involvement were predictors of RFS and OS rates.

Keywords:
recurrence, retroperitoneal sarcoma, surgery, survival

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Introduction

Retroperitoneal sarcomas (RPS) are rare different tumor groups that form about 15% of soft tissue sarcomas and have variable behavior and outcomes [1]. They affect any age group with a peak incidence in the 5th decade [2]. The retroperitoneum contains many vital structures, so management of RPS, establishment of free surgical margins, and patient outcomes could not be expected [3]. Surgical resection with wide safety margins in addition to chemotherapy and radiotherapy has been considered now the best management strategy in case of absence of distant metastasis [4]. Although there is marked improvement in diagnostic and therapeutic modalities, the rate of local recurrence is still high even after complete resection and that local recurrence worsens patients' outcome [5]. Patterns and sites of recurrences whether local or distant are related to tumor histology and grade.

Low-grade tumors were more liable to local recurrence. Distant recurrence mostly occurs in the lung, and ~10–15% of patients have synchronous metastases with unfavorable outcome [6].

Both patient-related and tumor-related pathological factors affect patient outcomes.

Status of resection margins and tumor grade remain important predictors of local recurrence and disease-free survival.

Some tumors with similar grade and resection margins have different outcomes, which signify searching for other prognostic parameters.

The aim of this study was to detect postoperative short-term and long-term oncological outcomes of RPS, in addition to evaluating predictive factors related to recurrence, overall survival (OS), and disease-free survival rates in patients with RPS, to allow detection of patients who might have more benefits from aggressive therapeutic approaches and radical surgery.

Patients and methods

This was a prospective study of 80 patients with RPS who underwent curative resection at Department of Surgery, Faculty of Medicine, Zagazig University Hospitals, from March 2012 to April 2017. We acquired an approval from the local ethical committee of Faculty of Medicine, Zagazig University, to perform the study.

Inclusion criteria

We included 80 cases of primary RPS in different age groups that were surgically managed, and written informed consents were acquired from all included patients.

Exclusion criteria

We excluded cases diagnosed with desmoid tumor, gastrointestinal stromal tumors, recurrent cases, and pediatric RPS.

All patients underwent complete clinical examination with recording of all surgical and oncological details.

Follow-up of patients in Clinical Oncology and Nuclear Medicine Department and Medical Oncology Department was done for about 34 months (range, 8–56 months) for detection of local recurrence, distant recurrence, 5-year recurrence-free survival (RFS) rate, and 5-year OS.

Preoperative workup included physical examination, laboratory testing, computed tomography, and MRI for accurate assessment of dimension and location of the sarcoma and presence of adherent tissues and organs. A multidisciplinary team formulated the therapeutic approach individually for every patient.

Excised samples were assessed, graded, and subtyped by a sarcoma pathologist.

The type of treatment whether surgery only or with adjuvant therapy depends on the site and size of the tumor and complete resection of the tumor and the state of surgical margin.

Surgical procedure

Perioperative intravenous antibiotics (Metronidazole 500 mg and Cefuroxime 1 g) were given. All procedures were done in an open surgical approach.

A midline incision was done to facilitate exposure and vascular control, then a complete abdominal cavity exploration was done to assess the degree and extent of local resectability of the sarcoma, particularly the need for multiorgan resection if adherent to the tumor or infiltrated by it [7].

Radiological evaluation and preoperative diagnosis were done in all patients in Radiology Department, Faculty of Medicine, Zagazig University (Fig. 1).

Histopathological reports were assessed to detect tumor size, histopathological subtype, nodal metastases, surgical margins, grade, and microscopic involvement of adjacent organs in Pathology Department, Faculty of Medicine, Zagazig University.

Histology was assessed according to classification of the WHO.

Grading of the tumor depends on differentiation, presence of necrosis, and mitotic rate per high-powered fields according to the system of Fédération Nationale des Centres de Lutte Contre Le Cancer (FNCLCC) [8]. Staging of the RPS was done according to the AJCC 8th, ed [9]. We counted each removed organ separately considering the kidney and ureter a single organ.

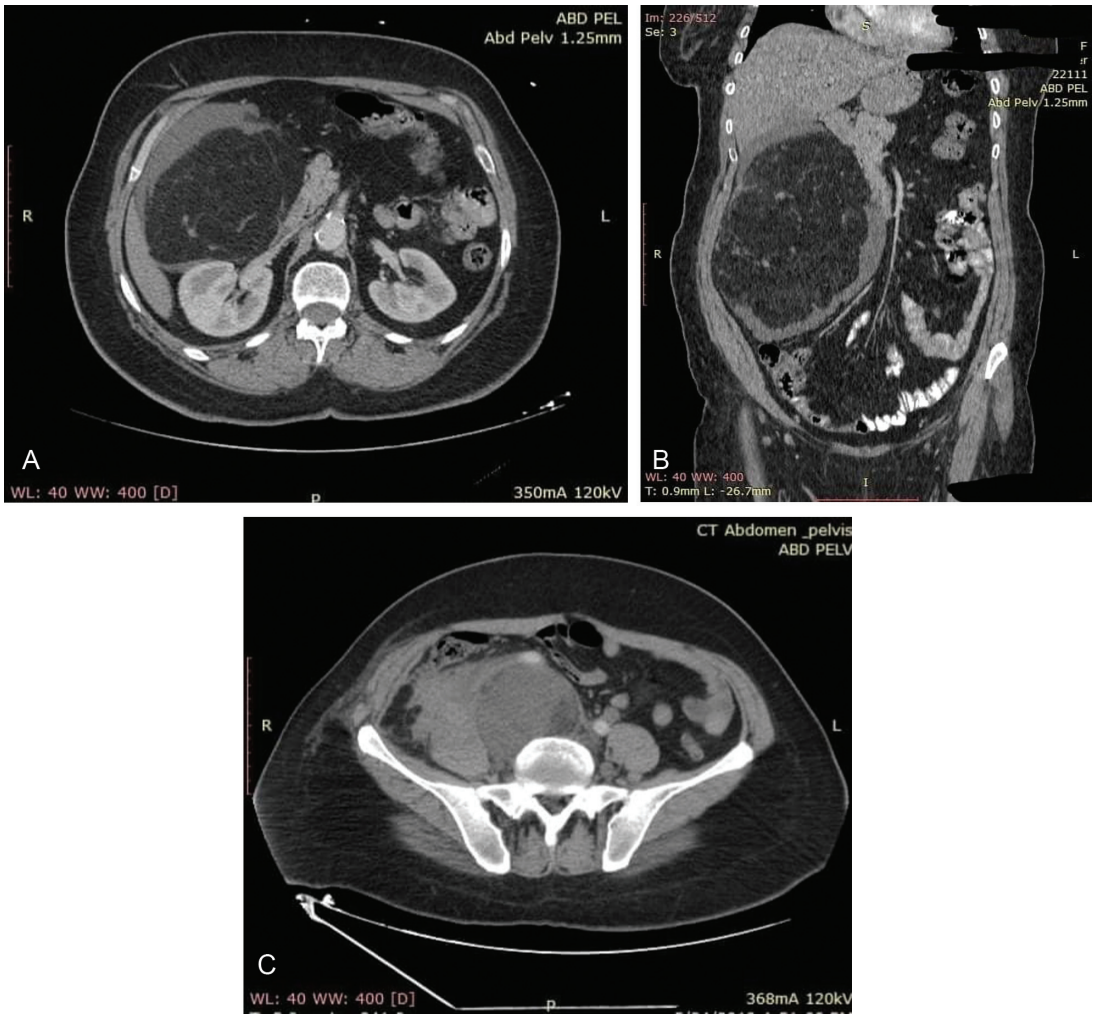
Surgical margins were evaluated grossly and microscopically and then divided into free, microscopically invaded, and grossly invaded. R0 is defined as no gross or microscopic evidence of the tumor. We classified and graded postoperative complications, morbidity, and mortality according to system of Clavien-Dindo grading [10].

Postoperative assessment

All patients were monitored at the surgical intensive care unit for 1–3 days.

We considered complications that occurred within 90 days as a postoperative morbidity. We considered any deaths occurred in the hospital as postoperative mortality.

Figure 1



Radiological images of retroperitoneal sarcoma. (a–c) CT images of the abdomen show large retroperitoneal fat containing mass seen at right side of the abdomen displacing the bowel loops to the left side the lesion containing fat attenuation and thick faintly enhancing (low vascular) septae. A well-differentiated retroperitoneal liposarcoma. (a) Axial view. (b) Coronal view. (c) Axial CT view of pleomorphic liposarcoma. CT, computed tomography.

We determined long-term patient outcome by assessment of tumor recurrence and patient survival.

Patients were followed up every 3 months for the first 2 years, and every 6 months for the following 3 years of the follow-up.

In each visit of the follow-up, we performed a complete physical examination and imaging of the abdomen and chest.

Recurrences that occurred in the retroperitoneum were defined as local recurrence, whereas we defined recurrences that occurred in the lung, liver, peritoneal lining, and nodes as distant recurrence.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software (IBM Corporation, New York; formerly SPSS Inc. Chicago, Illinois, USA). Descriptive statistics was used for categorical variables. We used the Kaplan–Meier curves with Cox logistic regression for survival assessment. Statistical significance was defined as P value less than 0.05. Univariate and multivariate analyses were used to identify prognostic variable that would affect recurrences and survival. OS was calculated as the period from surgical resection to last follow-up date or death, whereas we defined RFS as the time from surgical resection to time of disease clinical, pathologic, or radiographic recurrence.

Results

Table 1 shows the descriptive analysis of demographic, clinical, and pathological parameters and methods of management of all included RPS patients.

Table 1 Demographic, clinical, surgical, and pathological parameters of included patients with retroperitoneal sarcoma

Parameters	Total *N*=80 [*n* (%)]
Age	
Mean±SD	34±11
Median (range)	35 (15–55)
Sex	
Female	30 (37.5)
Male	50 (62.5)
BMI	
Mean±SD	30±7
Median (range)	30 (16–42)
Presenting symptoms	
Mass	18 (22.5)
Pain	28 (35.0)
Pain+mass	34 (42.5)
Grade	
High	31 (38.8)
Intermediate	28 (35.0)
Low	21 (26.3)
Size (cm)	
Mean±SD	16±10
Median (range)	14 (4–44)
AJCC stage	
I	21 (26.3)
II	32 (40.0)
III	21 (26.3)
IV	6 (7.5)
Chemotherapy	
No	55 (68.8)
Yes	25 (31.3)
Radiotherapy	
No	55 (68.8)
Yes	25 (31.3)
Resection margins	
R0	53 (66.3)
R1	17 (21.3)
R2	10 (12.5)
Days of hospital stay	
Median (range)	14 (8–24)
Vascular involvement	
No	49 (61.3)
Yes	31 (38.8)
Organ adhesion	
No	49 (61.3)
Yes	31 (38.8)
Organ type	
No	49 (61.3)
Colon	6 (7.5)
Gall bladder	1 (1.3)
Kidney	5 (6.3)
Kidney and adrenals	2 (2.5)
Kidney and liver	3 (3.8)
Kidney and small intestine	1 (1.3)
Kidney, adrenals. and colon	1 (1.3)
Kidney, liver, and colon	1 (1.3)
Kidney, small intestine and colon	1 (1.3)
Liver	1 (1.3)
Lung	2 (2.5)
Ovaries	1 (1.3)
Pancreas	5 (6.3)
Small intestine and stomach	1 (1.3)
Organs removed	
No	49 (61.3)
1	21 (26.3)
2	7 (8.8)
3	3 (3.8)
Organ infiltration	
No	64 (80.0)
Yes	16 (20.0)

The median age was 35 years and ranged from 15 to 55 years, and 50 (62.5%) patients were male.
Median size of the tumor was 14 cm and ranged from 4 to 44 cm.
Complete tumor removal (R0) was made in 53 (66.3%) patients.
Positive surgical margins (R1) was found in 17 (21.3%) patients.
Positive surgical margins (R2) was found in 10 (12.5%) patients.
Vascular involvement was found in 31 (38.8%) patients.
Vascular resection was planned in 12 cases preoperatively.

No adjacent organs were resected in 49 (61.3%) patients, whereas adjacent organ resections were done in 31 (38.7%) patients. After resection, adjacent organ infiltration was found in 16 (20.0%) patients, whereas just-adjacent organ adhesion was found in 15 (18.7%) patients.

Nephrectomy alone or with other organs was performed in 14 (17.5%) patients Nephrectomy facilitated radical removal of the tumor. It was found that high-grade tumors and tumors with dedifferentiated histologies had more liability for adjacent organ infiltration and the need for resection.

Histopathological subtypes were detailed in Table 2. Liposarcoma forms the commonest subtype, being diagnosed in 26 (32.50%) patients (Figs 2–4).

Table 3 shows the detailed clinical outcome of the included patients.

We showed that local recurrence of RPS occurs in 30 (37.5%) patients, whereas distant [12 (15.1%)] recurrence of RPS occurs in 30 (37.5%) patients. We found no need for intraoperative transfusion of

red blood cell concentrate during the surgical procedure, and we found no intraoperative mortality.

Postoperative morbidity, according to the Clavien-Dindo classification more than or equal to 3, was eight (10%) patients, and the 90-day mortality rate was four (5%) patients.

Long-term survival

After a median follow-up time of 34 months, range 8–56 months, the 5-year OS rate of patients was 63.7% and the 5-year RFS rate of patients was 62.5% (Table 4 and Fig. 5).

Predictors of overall survival

Factors associated with poor OS rate in univariate analysis were tumor size, histopathological types, grade, stage, resection margins, adjacent organ infiltration, chemotherapy, radiotherapy ($P<0.001$), and vascular involvement ($P=0.003$). In multivariate analysis, grade ($P=0.001$) and vascular involvement (0.002) were the most important predictors.

Table 2 Histological subtypes of included retroperitoneal sarcoma

Histopathological type	Total $N=80$ [n (%)]
Liposarcoma	26 (32.50)
Leiomyosarcoma	16 (20.00)
Pleomorphic sarcoma	12 (15.00)
Spindle cell sarcoma	12 (15.00)
Round cell sarcoma	8 (10.00)
Myxoid sarcoma	4 (5.00)
Myofibroblast sarcoma	2 (2.50)

Predictors of recurrence-free survival rate

Factors associated with poor RFS rate in univariate analysis were tumor size, histopathological types, grade, stage, resection margins, adjacent organ infiltration, chemotherapy, radiotherapy ($P<0.001$), and vascular involvement ($P=0.003$). In multivariate analysis, grade ($P=0.001$) and vascular involvement (0.002) were the most important predictors of RFS rate.

Correlations between survival rates and prognostic parameters is shown in Table 5.

We found no difference in OS rate or RFS rate between patients with organ adhesion and patients with organ infiltration (Table 6).

Discussion

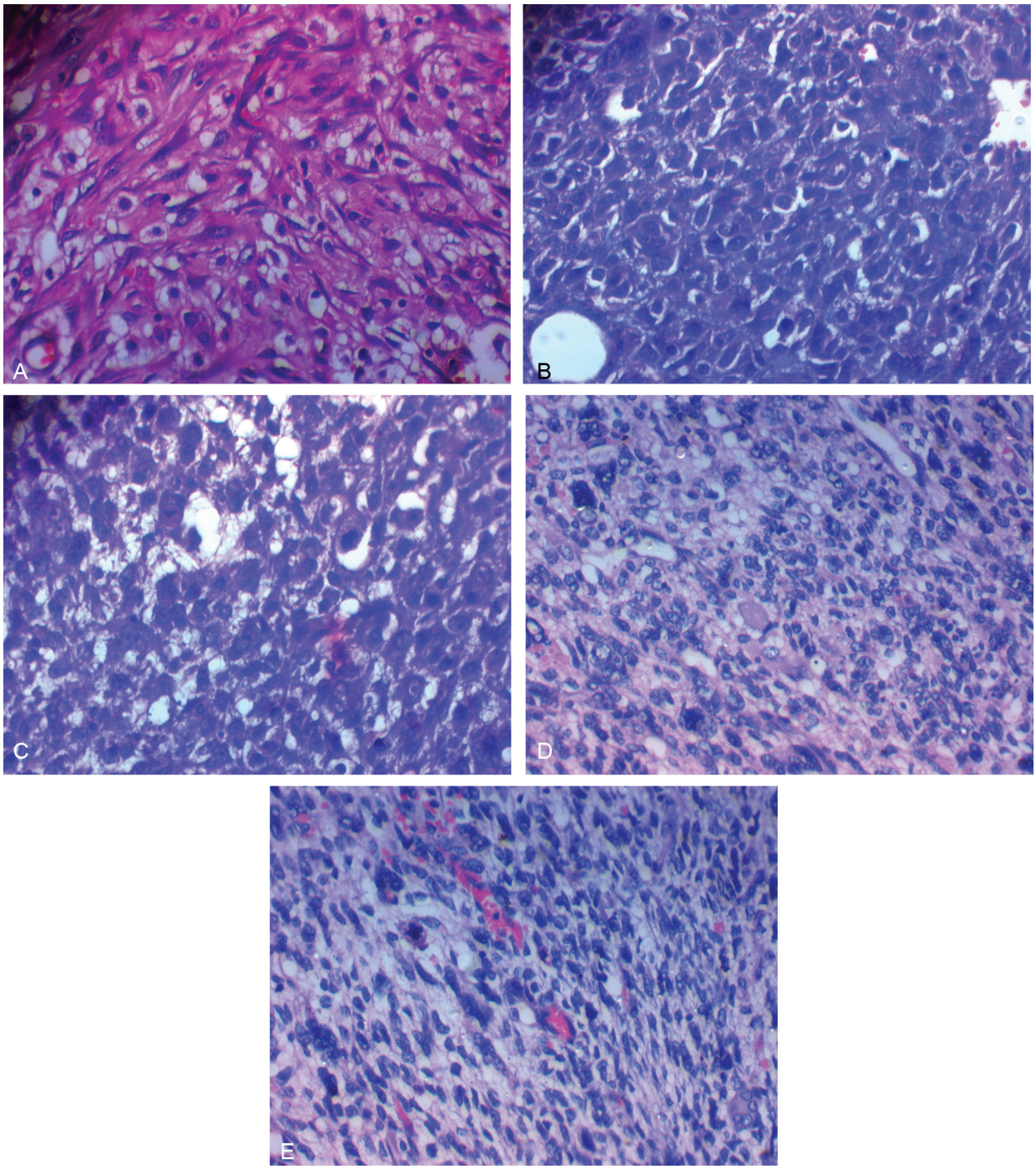
In the present study, we tried to assess the pathological, operative, postoperative, and long-term results of surgically operated patients with primary RPS, and we tried to detect factors responsible for prediction of recurrence, survival, and progression of RPS patients. Moreover, we found results similar to the results of Malinka *et al.* [3], and in line with Giuliano *et al.* [11], who aimed to identify predictive factors for improved OS rate in RPS patients.

Previous reports stated results near our results that complete surgical excision of the tumor and tumor grade were the most important predictors of tumor recurrence and RFS [12].

Figure 2

Gross description of some excised sarcoma subtypes: (a) liposarcoma and (b) leiomyosarcoma.

Figure 3



Histopathological types of surgically excised sarcoma. (a) High-grade round cell liposarcoma, (b) high-grade leiomyosarcoma, (c) pleomorphic sarcoma, (d) differentiated round cell sarcoma, and (e) differentiated spindle cell sarcoma high grade.

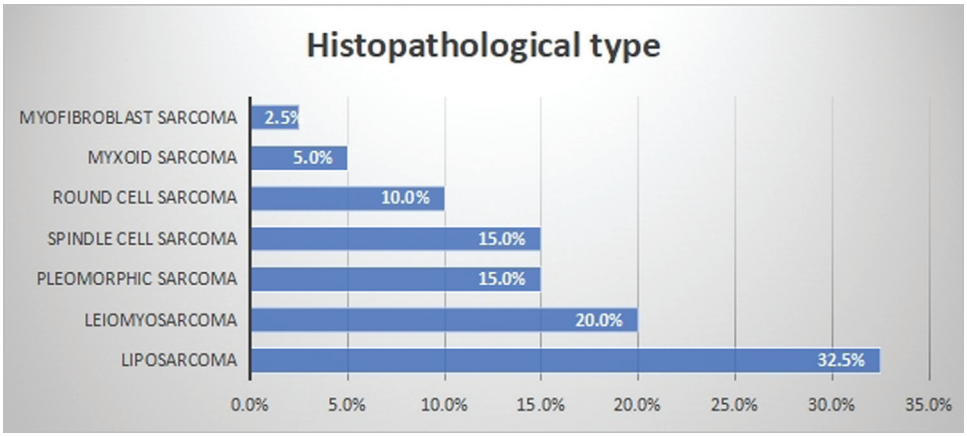
There are controversial results found by previous studies, which find no survival benefit of tumor size, grade, or vascular invasion [13].

The curative benefit of radiotherapy and chemotherapy is still under evaluation [14].

As we found that given data regarding prognostic factors of patients with RPS are heterogeneous and uncertain, we tried to clarify them.

Regarding tumor and patient data, we found that liposarcoma and leiomyosarcoma were the most common histologic tumor entities. Malinka *et al.* [3] showed similar findings to ours. In previous studies on this subject, Nathan *et al.* [13], who assessed 1365 patients with RPS, and Giuliano *et al* [11], who assessed 2920 patients with RPS, reported similar patient clinicopathological data to those reported in our study.

Figure 4



A diagram of distribution of the histopathological subtypes of resected sarcomas.

Table 3 Clinical outcome of included patients with retroperitoneal sarcoma

Clinical outcome	Total *N*=80 [*n* (%)]
Local recurrence	
No	50 (62.5)
Yes	30 (37.5)
Distant recurrence	
No	68 (85.0)
1 (lung and liver)	7 (8.8)
1 (other)	5 (6.3)
Death	
No	51 (63.8)
Yes	29 (36.3)
Follow-up period (months)	
Median (range)	34 (8–56)

We found that patients' age is younger than that was reported by former studies, denoting improvement in diagnostic modalities.

We reported a similar survival rate to previous reports and stated that tumor grade and histopathological subtype affects the survival, which is similar to the results of previous studies [1,12–15].

Regarding RFS, we identified patient age, tumor grade, AJCC stage, safety margins, and vascular invasion were the most important predictive factors, which is similar to Malinka *et al.* [3].

Previous studies demonstrated that free surgical safety margins are essential for the curative treatment for RPS [16]. Moreover, inability to achieve complete surgical excision of the tumor has an adverse effect on outcome and associated with occurrence of disease-related death [17].

Complete surgical resection with R0 is the most effective predictive parameter for the RPS, but the role of R1 or R2 resection is still controversial [3]. Shibata *et al.* [18] compared between incomplete resection and nonresection of RPS and found that in patients with unresectable RPS performing incomplete surgical resection produced a prolongation of survival rates and could allow better symptom palliation. Grobmyer *et al.* [19] showed similar results that in patients with RPS the OS rate was about 20 months in patients with R2 resection, whereas it was 10 months in patients who have biopsy and supportive care only [19,20].

Collectively these results showed that surgical resection in resectable RPS and tumor debulking or palliative resection could reduce the rate of recurrence of the tumor and prolong RFS and OS rates in selected cases.

Data regarding the association between vascular involvement and oncological outcomes after resection of RPS are still deficient, and relation between these complex procedures and degree of prolongation of patient survival is still unknown.

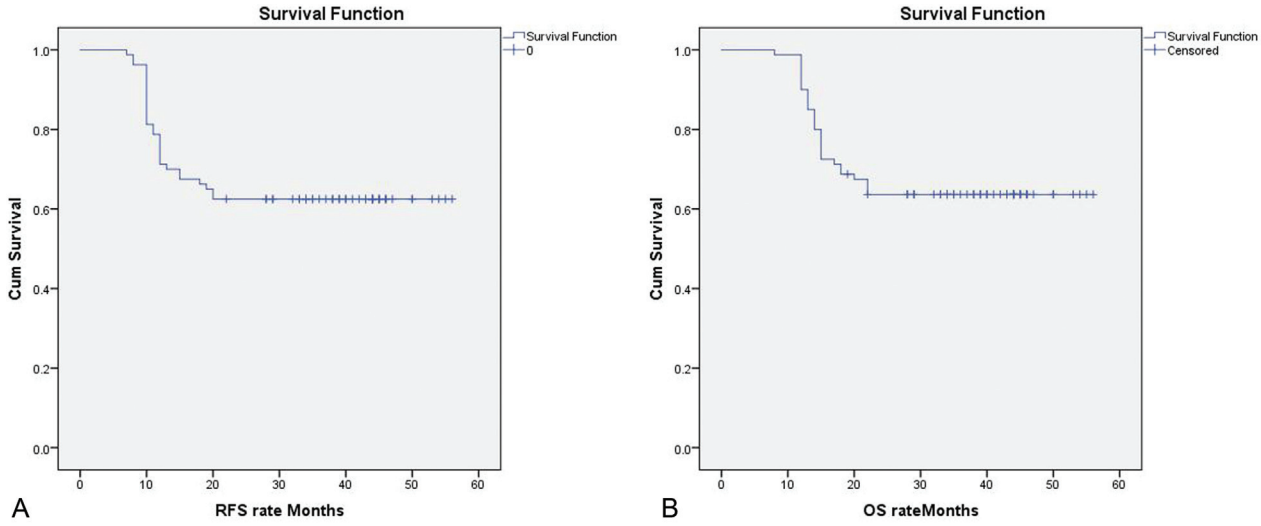
Although previous reports showed safety of vascular resection for RPS for achieving radical removal of the tumor needed [21], some other studies showed that vascular resection of RPS increased perioperative morbidity, had no survival benefits, and produced similar oncologic outcome to cases without vascular involvement [22]. We showed that patients with vascular involvement recurred faster, showing that the 5-year RFS rate was ~72 versus 28% in patients without vascular involvement and those with vascular infiltration, respectively, but the OS is not affected. These results were explained by that

Table 4 Overall survival and recurrence-free survival rates of included patients with retroperitoneal sarcoma regarding sarcoma subtype

Histopathological type	Total *N*	Number of events	Censored [*n* (%)]	OS (%)	*P*
Overall survival					
Leiomyosarcoma	16	5	11 (68.8)	68.2	
Liposarcoma	26	9	17 (65.4)	65.4	
Myofibroblast sarcoma	2	0	2 (100.0)	0.0	
Myxoid sarcoma	4	0	4 (100.0)	0.0	<0.001
Pleomorphic sarcoma	12	11	1 (8.3)	8.3	
Round cell sarcoma	8	0	8 (100.0)	0.0	
Spindle cell sarcoma	12	4	8 (66.7)	66.7	
Overall	80	29	51 (63.8)	63.7	
Histopathological type	Total *N*	Number of events	Censored [*n* (%)]	RFS%	*P*
Relapse-free survival					
Leiomyosarcoma	16	6	10 (62.5)	62.5	
Liposarcoma	26	9	17 (65.4)	65.4	
Myofibroblastic sarcoma	2	0	2 (100.0)	0.0	
Myxoid sarcoma	4	0	4 (100.0)	0.0	<0.001
Pleomorphic sarcoma	12	11	1 (8.3)	8.3	
Round cell sarcoma	8	0	8 (100.0)	0.0	
Spindle cell sarcoma	12	4	8 (66.7)	66.7	
Overall	80	30	50 (62.5)	62.5	

OS, overall survival; RFS, recurrence-free survival.

Figure 5



Kaplan–Meir survival curves of included patients: (a) recurrence-free survival (RFS) rate of included patients with sarcoma. (b) 5-year overall survival (RFS) rate of included patients with sarcoma.

vascular invasion was consequence of tumor aggressive behavior [23].

In the present study, we have demonstrated histopathological tumor subtype and tumor grade as essential predictors of OS, similarly to Poultsides *et al.* [22].

We showed that chemotherapy and radiotherapy have significant effect on improvement of survival rates. Moreover, although using neoadjuvant therapy was now considered an established line of treatment for many tumor entities, its preoperative role in management of RPS is still uncertain [24].

The previously detected limited effectiveness of chemotherapy in RPS may result from many reasons; first, retroperitoneum forms an ample anatomical space allowing growth of sarcoma to huge size before its diagnosis resulting in less effective chemotherapy. Second, adjuvant radiotherapy was not recommended

Table 5 Univariate and multivariate Cox regression for overall survival of myofibroblast included patients with retroperitoneal sarcoma

OS	Univariate			Multivariate		
	Significance	HR	95.0% CI for HR	Significance	HR	95.0% CI for HR
Age	0.646	1.01	0.97–1.04			
Sex	0.088	0.48	0.20–1.12			
BMI	0.052	0.95	0.90–1.00	NS		
G						
G	<0.001	36.14	4.85–269.34	0.002	0.001	0.0001–0.220
Size (cm)	<0.001	1.06	1.04–1.09	NS		
AJCC stage						
AJCC stage (1)	0.004	0.11	0.02–0.49	NS		
AJCC stage (2)	0.054	0.45	0.20–1.01	NS		
AJCC stage (3)	<0.001	3.39	1.72–6.66	NS		
Histopathological type						
Histopathological type (leiomyoma)	0.002	0.18	0.06–0.53	NS		
Histopathological type (liposarcoma)	<0.001	0.18	0.07–0.46	NS		
Histopathological type (others)	<0.001	0.08	0.02–0.26	NS		
Chemotherapy	<0.001	15.93	6.52–38.94	NS		
Radiotherapy	<0.001	15.93	6.52–38.94	NS		
Resection margins						
Resection margins (1)	<0.001	0.10	0.05–0.21	NS		
Resection margins (2)	<0.001	2.72	1.63–4.53	NS		
Vascular involvement	0.003	0.00	0.00–0.12	0.003	0.002	0.0001–0.120
Organ adhesion	0.003	0.00	0.00–0.12	NS		
No removed organ (≤1 vs. >1)	<0.001	0.16	0.07–0.35	NS		
Organ infiltration	<0.001	0.09	0.04–0.20	NS		

CI, confidence interval; HR, hazard ratio; OS, overall survival

Table 6 Univariate and multivariate Cox regression for recurrence-free survival rate of included patients with retroperitoneal sarcoma

RFS	Univariate			Multivariate		
	Significance	HR	95.0% CI for HR	Significance	HR	95.0% CI for HR
Age	0.866	1.00	0.97–1.04			
Sex	0.126	0.73	0.49–1.09			
BMI	0.119	0.94	0.90–0.99	NS		
G	<0.001	37.99	5.09–283.43	<0.001	0.001	0.0001–0.10
Size (cm)	<0.001	1.06	1.03–1.09	NS		
AJCC stage	<0.001	3.47	1.77–6.78	NS		
Histopathological type (leiomyoma)	0.005	0.23	0.08–0.63	NS		
Histopathological type (liposarcoma)	0.001	0.20	0.08–0.50	NS		
Histopathological type (others)	<0.001	0.08	0.03–0.27	NS		
Chemotherapy	<0.001	0.06	0.03–0.15	NS		
Radiotherapy	<0.001	0.06	0.03–0.15	NS		
Resection margins (R1)	<0.001	0.09	0.04–0.20	NS		
Resection margins (R2)	<0.001	2.82	1.69–4.70	NS		
Vascular involvement	0.002	0.00	0.00–0.10	0.002	0.002	0.0001–0.10
Organ adhesion	0.002	0.00	0.00–0.10	NS		
No removed organ (≤1 vs. >1)	<0.001	0.16	0.07–0.36	NS		
Organ infiltration	<0.001	0.10	0.04–0.22	NS		

CI, confidence interval; HR, hazard ratio; RFS, recurrence-free survival.

as a standard management owing to gastrointestinal toxicities [25].

The extensive radical surgery for resectable RPS and debulking operations in unresectable cases remain the main management strategies for RPS.

There are no clear data regarding the use of systemic chemotherapy and radiotherapy in RPS management

to guide the clinicians owing to the relative disease rarity [26].

Patkar *et al.* [1] showed that the patient prognosis in case of adjacent organ removal depends on whether the tumor directly infiltrated certain organ or just attached to it and found no significant differences in survival between patients with adhesive or infiltrative tumors.

We showed that prognosis of patients with infiltrative tumors was poorer than prognosis of patients with tumors just attached to the organ, and similarly, previous studies demonstrated the dismal outcomes of patients with infiltrative tumors [26–28] and found that such infiltrating tumors had poorer outcomes in comparison with tumors just adherent to organs. We showed that resection of infiltrated organs was not associated with significant morbidity. Similarly, Kim *et al.* [29] showed that resection of pancreatic head and duodenum was associated with serious morbidity, whereas resection of kidney, appendix, or spleen was not associated with serious complications.

We showed that higher grade of sarcoma was associated with more liability to infiltration, which was similar to the results of Fairweather *et al.* [26], who correlated histopathological subtype and invasiveness of sarcoma and showed that high-grade or dedifferentiated tumors have higher liability for adjacent organ infiltration.

Moreover, in line with most previous reports, we showed that extent of RPS resection, margins, resectability, and histopathological grade were the most important prognostic parameters for patients with RPS [30–32].

Regarding RPS recurrence, we showed that low-grade tumors were associated with local recurrence, whereas high-grade tumors were associated with distant recurrences.

Conclusion

RPS is a rare relatively aggressive tumor with uncertain treatment protocols. Surgical management of RPS remains the main line of treatment, even in infiltrative huge cases.

The best management strategy up till now is surgical excision with negative safety margins, which leads to less incidence of recurrence and favorable RFS and OS rates.

There was increasing rates of multiorgan and compartmental resection for achieving a complete excision and reaching R0.

In our study, we showed that liposarcoma and leiomyosarcoma form the commonest histopathological subtypes. Histopathological grade, resection margins, and vascular involvement were considered the most significant indicators of RFS and OS rates.

Preoperative and postoperative chemotherapy and radiotherapy still have uncertain effects on patient survival, but recent studies are needed to evaluate their benefits in patient management, particularly in patients with positive surgical margins.

There is a need for recent multicenter studies for development of multidisciplinary approach of RPS management for improving survival outcomes more than that could be produced by surgery alone.

Points of strengths of our study were that it is a single-center experience in RPS with relatively long follow-up time and emphasis on surgical management and outcomes. Points of weakness of our study were that it included a smaller patient number.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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