Surgically resected retroperitoneal sarcoma: a high-volume center outcome

Mohammad Taher[a], Rasha M. Allam[b], Ibrahim Abdelrahman[a], Mohamed A. ElKordy[a]

Departments of [a]Surgical Oncology, [b]Biostatistics & Cancer Epidemiology, National Cancer Institute, Cairo University, Cairo, Egypt

Correspondence to Mohammad Taher, MD, Department of Surgical Oncology, National Cancer Institute, Cairo University, Cairo 11796, Egypt. Tel (off): 02-23664690; Fax: 02-23644720; e-mail: mohammed.taher@nci.cu.edu.eg

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Background
Local recurrence is the main cause of treatment failure in retroperitoneal sarcoma (RPS). Surgical gross tumor resection with negative margins in a high-volume hospital is the hope for cure. We aimed to evaluate the surgical and oncological outcomes of RPS in our high-volume cancer center.

Patients and methods
This retrospective study included all patients who underwent surgical resection of RPS who presented to the National Cancer Institute, Cairo University, Egypt, from January 2010 to December 2019, and follow-up until December 2021.

Results
he study included 109 patients who underwent surgical resection. The most common histological type was liposarcoma in 74 (67.9%) patients. Eighty-four (77%) patients received macroscopic gross resection (R0/R1). Contiguous organ resection when invaded was done in 51 (46.8%) patients. The 60-day mortality rate was 9.2% (10 patients). The 60-day morbidity rate was 26.6% (29 patients). The lethal complications were the secondary hemorrhage (three, 10.3%) and intestinal leakage (five, 17.2%). The cumulative overall survival of the whole cohort was 70.5, 58.6, and 57.4% at 3, 5, and 10 years, respectively. The independent prognostic factors were the type of resection and the tumor grade. The cumulative disease-free survival of the whole cohort was 53, 47, and 44% at 3, 5, and 10 years, respectively. The independent prognostic factor was the type of resection.

Conclusions
Primary surgical resection of RPS should be aggressive with excision of frankly invaded nearby organs. Obtaining R0 resection is the hope for cure. Debulking surgery is considered in the setting of palliation. Serving RPS patients in high-volume centers is the key to a better outcome and life quality.

Keywords:
contiguous organ resection, debulking surgery, high-volume hospital, margin status, retroperitoneal sarcoma

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Introduction

Primary retroperitoneal sarcomas (RPS) are rare potentially lethal tumors of mesenchymal origin, accounting for about 10–15% of all soft tissue sarcomas [1,2].

Between 40 and 80% of treatment failures are due to local recurrence, and 75% of fatalities are due to uncontrolled local recurrence [3–8]. Furthermore, locoregional recurrence is common (up to 50% of cases) even after complete tumor resection [3,9,10]. Thus, the mainstay of treatment is surgery with the intent of complete gross tumor resection with negative margins [1] with stress on the importance of an optimal first resection [11].

From the issued series, the gross complete resection rate is 80%, and this rate further declines for recurrent disease to 55% [11]. For this, an aggressive surgical approach by multivisceral (compartmental) has been strongly recommended by many authors, and its rates much increased recently, particularly at high-volume centers [2,9,12–15].

High-volume centers could obtain more R0 resections, with resultant reduced local recurrence rates, and improved overall survival (OS) in most series [1–3,13] and this suggests further centralization of RPS care [2]. High-volume centers were defined in many series as those with more than 10 cases per year [16,17].

Patients and methods

Our retrospective case-series study included all patients who underwent surgical resection of RPS in the period from January 2010 to December 2019, at the National Cancer Institute, Cairo University, Egypt, considering it as a high-volume center with an average of 13 cases presenting to us per year, and an average of 11 surgeries annually.

Ethical approval and consent to participate: a retrospective study. The patients have already consented to the surgery type and complications as usually adopted by our hospital (IBR No. 2211-510-016). All patients have provided acceptance and consent for publishing their data. All personal information has been made anonymous.

In that period, 131 cases presented to our institute, of which 120 cases underwent surgical exploration, and 11 cases were considered inoperable (eight cases with major medical comorbidities and three cases had radiological clear evidence of major vascular involvement beyond resection). Of the 120 cases that underwent surgical exploration, 11 cases were considered irresectable for either major vascular involvement or fixation to vertebral or pelvic bones, and 109 cases had tumor resection. Exclusion was done for the 22 cases (11 inoperable and 11 irresectable), and analysis was done for the 109 cases that underwent tumor resection.

Patient data were collected from medical records, and the following items were obtained and analyzed: age, sex, tumor grade, maximum diameter, pathology, operative details including organs resected, R-type of resection, postoperative complications, neoadjuvant and adjuvant treatment, and outcome (recurrence and survival). Follow-up was continued until December 2021.

The type of resection was categorized as R0 (no microscopic residual if the circumferential negative margins were >0.1 mm), R1 (tumor extends to or within 0.1 mm of resection margins), and R2 (gross residual disease documented by the surgeon). R0 and R1 were considered complete resection, while R2 was considered incomplete resection (debulking) [2].

The grade was determined using the French Federation of Cancer Centres Sarcoma Group Grading System (Fédération Nationale des Centres de Lutte Contre le Cancer, FNCLCC) [18].

Statistical analysis

Data were analyzed using IBM SPSS, version 24 (Statistical Package for Social Sciences; SPSS Inc., Chicago, Illinois, USA). Qualitative data were described as numbers and percentages. McNemar's test was used to evaluate the concordance between categorical variables, and Cohen's kappa was used to assess the interrater agreement for qualitative (categorical) items. The survival analysis was performed using the Kaplan–Meier method. A P value less than or equal to 0.05 was considered statistically significant; all tests were two-tailed. OS was calculated from the day of diagnosis until the day of death or the latest follow-up. Disease-free survival (DFS) was calculated from the day of surgery until the day of recurrence, death, or the latest follow-up.

Results

The study included 109 patients who underwent surgical resection, 89 (81.7%) after neoadjuvant radiotherapy and 20 (18.3%) as upfront surgery. The median length of follow-up was 45.8 (range, 2–142) months. Patients' demographics, clinicopathological features, and operative characteristics are shown in Table 1.

The most common histological type was liposarcoma in 74 (67.9%) patients. Leiomyosarcoma occurred in 24 (22%) patients. Most tumors had a high grade: G3 (76 patients, 69.7%). In 84 (77%) patients, a macroscopically complete resection (R0/R1) was achieved.

Table 1 Patients and tumor characteristics and treatment details

Items	Frequency	Percent
Sex		
Female	54	49.5
Male	55	50.5
Age (years)		
<55	55	50.5
≥55	54	49.5
Grade		
G1	6	5.5
G2	27	24.8
G3	76	69.7
Recurrence		
No	63	57.8
Yes	46	42.2
Type of recurrence		
Distant	16	34.8
Local	14	30.4
Local+distant	16	34.8
Total	46	100

(*Continued*)

Table 1 (*Continued*)

Items	Frequency	Percent
Pathology		
Liposarcoma	74	67.9
Leiomyosarcoma	24	22
Chondrosarcoma	2	1.8
Malignant peripheral nerve sheath tumor	3	2.8
Undifferentiated pleomorphic sarcoma	6	5.5
Type of resection		
R0	52	47.7
R1	32	29.4
R2	25	22.9
Number of resected organs		
0	58	53.2
1	17	15.6
2	20	18.3
3	10	9.2
4	4	3.7
Neoadjuvant radiotherapy		
No	20	18.3
Yes	89	81.7
Final status		
Alive	65	59.6
Dead	44	40.4
Tumor maximum diameter (cm)		
<40	55	50.5
≥40	54	49.5
Surgery complications		
Yes	29	26.6
No	80	73.4
Type of surgical complications (*n*=29)		
Secondary hemeorrhage	3	10.3
Burst abdomen	3	10.3
DVT/PE	3	10.3
Intestinal fistula	5	17.2
Pelvic abscess	2	6.9
Pneumonia	3	10.3
Wound infection	10	34.5

DVT, deep vein thrombosis; PE, pulmonary embolism.

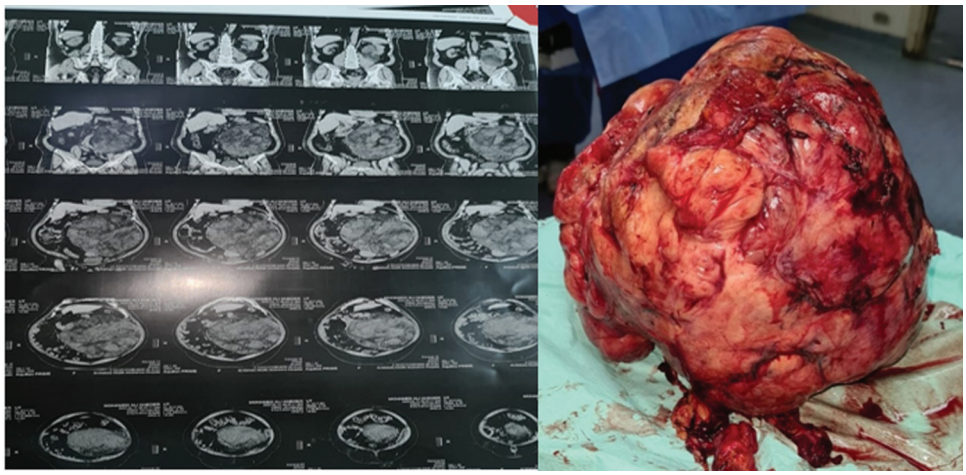
Contiguous organ resection when invaded was done in 51 (46.8%) patients, with the number of resected organs in a patient ranging from one to four organs. The resected organs were the kidney (33 patients, 64.8%), colon/rectum (25, 49%), urinary bladder partially or totally (12, 23.5%), uterus (three, 5.9%), spleen (six, 11.8%), liver (three, 5.9%), and pancreas (three, 5.9%). Excision of the invaded abdominal wall was performed in 15 (29.4%) patients. Excision and grafting of inferior vena cava were done in two (3.9%) cases. Part of our work is shown in Figs 1 and 2.

Morbidity and mortality

Eight (7.3%) patients died within 30 days of surgery. Three died of secondary hemorrhage, three died of deep vein thrombosis and massive pulmonary embolism, and two died of major intestinal leakage with consequent peritonitis and sepsis. Two more patients died in the following 30 days, thus, we had a 60-day surgery-related mortality rate of 9.2% (10 patients). Two more deaths, one died of intestinal leakage and peritonitis, and the other died of severe chest infection and pneumonia.

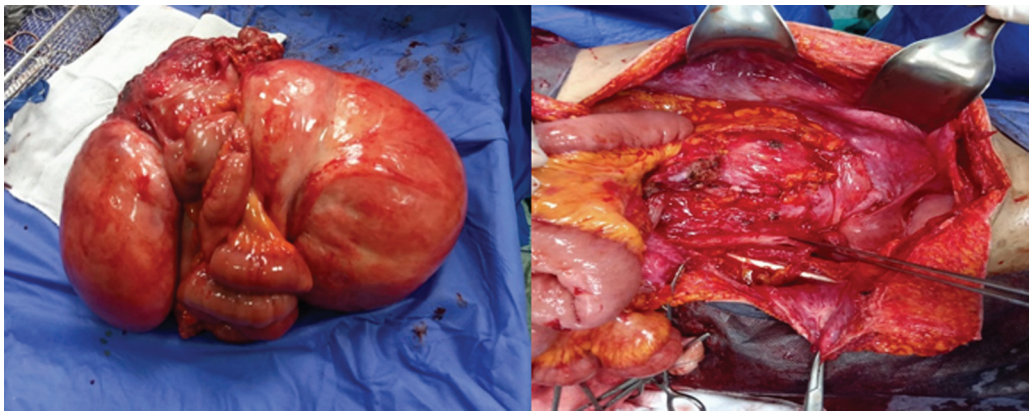
The 60-day morbidity rate was 26.6% (29 patients). The lethal complications were the secondary hemorrhage (three, 10.3%), and those patients died immediately before any intervention, and intestinal leakage (five, 17.2%). The commonest complication was wound infection (10, 34.5%), and all fully recovered on repeated dressings and antibiotics. Burst abdomen occurred in three (10.3%) patients, all were explored and their abdomens closed. Pelvic abscesses developed in two (6.9%) patients and were drained under sonar guidance.

Figure 1



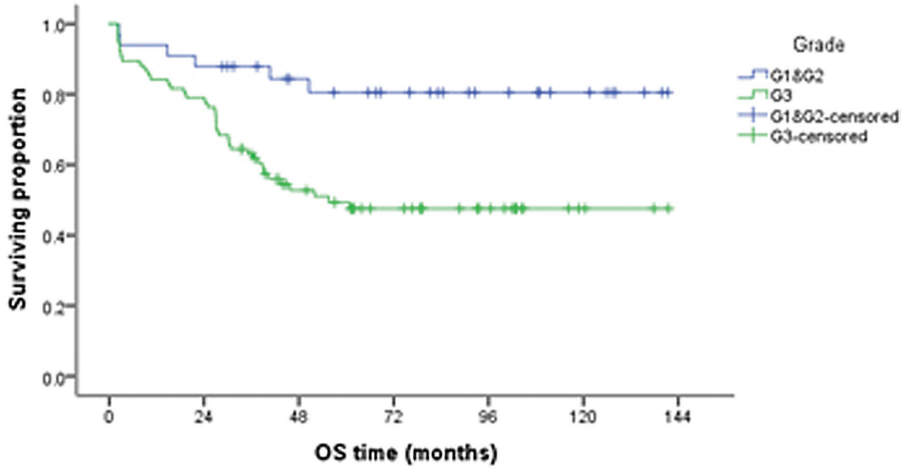
Liposarcoma (coronal CT and the specimen). CT, computed tomography.

Figure 2



Leiomyosarcoma (specimen with involved colonic resection and the operative field).

Figure 3



Overall survival (OS) and tumor grade.

Seven (6.4%) patients required a return to the theater. These were the four patients with major intestinal leaks and the three patients who had burst abdomen. One patient with burst abdomen required a second operation to reclose the abdomen.

Intestinal anastomotic leaks

Of the 109 operations performed, 25 (22.9%) had some sort of colorectal excision. Intestinal anastomosis was constructed in 23 cases, two of which had two anastomoses, and both received a diverting ileostomy. Two cases had undergone abdominoperineal resection with no anastomoses done. A total of five anastomotic leaks occurred, with a leak rate of 21.7%.

Four out of the five patients had a major leak. They were explored, and a diverting ileostomy was done. Unfortunately, three of them died of the consequences of peritonitis. The fifth patient had a minor leak and went smoothly on conservative measures.

Overall survival

The median OS was not reached. The cumulative OS of the whole cohort was 70.5, 58.6, and 57.4% at 3, 5, and 10 years, respectively. On univariate analysis, the factors that showed significant association with OS were tumor grade, pathology, type of resection, and the number of resected organs with a *P* value of 0.004, 0.029, less than 0.001, and 0.002, respectively.

Low-grade (G1, G2) tumors collectively had an OS rate of 88, 80.5, and 80.5% at 3, 5, and 10 years, respectively. High-grade tumors (G3), however, had a poor OS rate of 63, 49, and 48% at 3, 5, and 10 years, respectively, as shown in Fig. 3.

Liposarcoma histopathology had the best OS rate of 77, 66, and 66% at 3, 5, and 10 years, respectively. A fair OS rate was found with leiomyosarcoma histopathology, and the worst outcome was observed with other types as illustrated in Fig. 4.

R0 resection had the best OS rate of 83, 80, and 80% at 3, 5, and 10 years, respectively. R1 showed an inferior OS of 59, 32, and 28% at 3, 5, and 10 years, respectively. R2, however, showed an intermediate outcome with an OS rate of 60, 46, and 46% at 3, 5, and 10 years, respectively, as seen in Fig. 5.

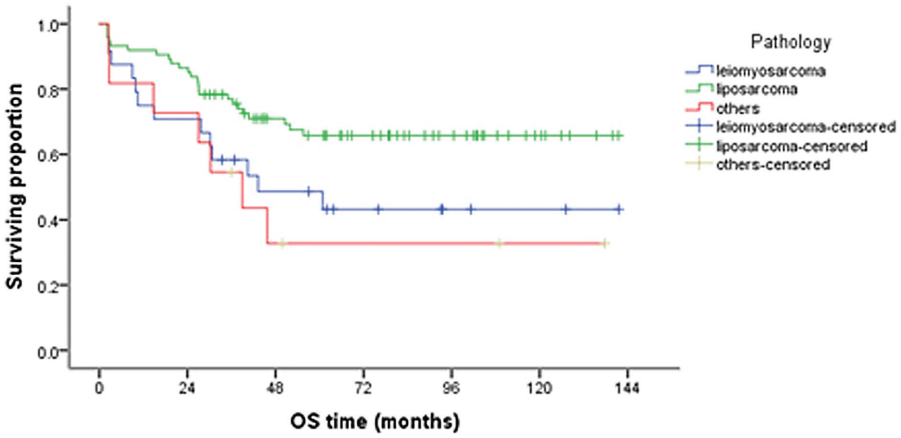
Resection of less than or equal to two organs showed a better outcome when compared with more than two organs resected. The first group had an OS rate of 73, 64, and 64% at 3, 5, and 10 years, respectively, while the other group had an OS rate of 50 and 27% at 3 and 5 years, respectively, and none of them reached 10 years.

The independent prognostic variables in multivariate analysis were only the type of resection and the tumor grade. R1/R2 were associated with more risk (four times as those with R0) with a hazard ratio (HR) of 4.2, 95% confidence interval (CI) of 2.1–8.6, and a *P* value of less than 0.001. High-grade tumors (G3) were three times more risky than low-grade tumors (G1, G2) with HR of 3.4, 95% CI 1.4–8, and a *P* value of 0.006.

Disease-free survival

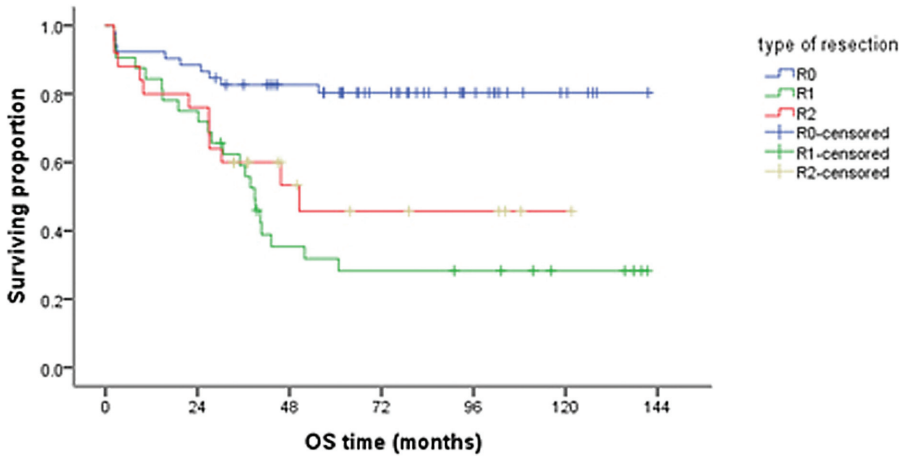
The median DFS was 43.6 months, with the cumulative DFS of the whole cohort being 53, 47, and 44% at 3, 5, and 10 years, respectively. On univariate analysis, the factors that showed significant association with DFS were pathology, type of resection, and the number of resected organs with a *P* value of 0.013, 0.029, less than 0.001, and 0.025, respectively.

Figure 4



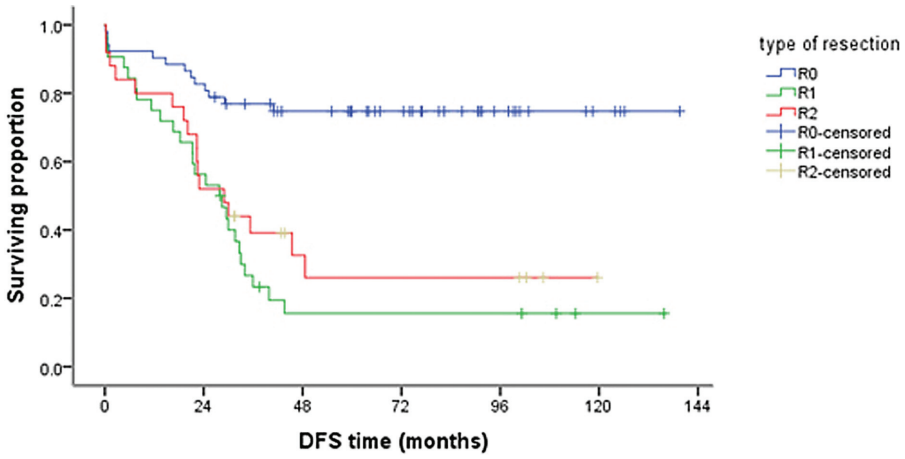
Overall survival (OS) and tumor histopathology.

Figure 5



Overall survival (OS) and type of resection (R).

Figure 6



Disease-free survival (DFS) and type of resection (R).

Liposarcoma histopathology had the best DFS rate of 62, 55, and 55% at 3, 5, and 10 years, respectively. A fair DFS rate was found with leiomyosarcoma histopathology, and the worst outcome was observed with other types.

R0 resection had the best DFS rate of 77, 75, and 75% at 3, 5, and 10 years, respectively. R1 showed an inferior DFS rate of 23, 16, and 16% at 3, 5, and 10 years, respectively. R2, however, showed an intermediate outcome with a DFS rate of 39 and 26% at 3 and 5 years, respectively, with no further free patients reaching 10 years. This is shown in Fig. 6.

Resection of less than or equal to two organs showed a better outcome when compared with more than two organs resected. The first group had EFS rates of 56, 53, and 53% at 3, 5, and 10 years, respectively, while the other group had DFS rates of 43 and 14% at 3 and 5 years, respectively, and no further free patients reached 10 years.

On multivariate analysis, the lone independent prognostic factor was the type of resection. R1/R2 were associated with more risk (4.5 times as those with R0) with a HR of 4.5, 95% CI of 2.4–8.4, and a *P* value of less than 0.001.

Discussion

Until recently, about 10% of primary RPS cases are still considered inoperable even in large referral centers. Mostly, this is related to the presence of locally aggressive disease with involvement of major vessels, and less commonly is related to associated comorbidities. These patients used to be offered palliative treatment [19].

Incomplete surgical resection (debulking) provided a survival benefit compared with laparotomy and open biopsy [20,21]. This, however, was of value in liposarcoma cases rather than in other pathology types, in those who undergo a primary resection rather than surgery for recurrence, and when adequate palliation is rather considered [8,11,22].

A debulking surgery could apply with the assumption concluded from a prospective large single institutional study held by Singer *et al.* [9], and supported in different other studies later on [23,24]. According to Singer *et al.* [9], there was no difference between microscopic positive margins (R1) and uninvolved margins (R0), and only macroscopic positive margins (R2 resection) were predictive of recurrence. Others, however, have shown a prognostic difference between R0 and R1 resection [14,25].

Current publications have defined an invasive behavior of RPS, helping to explain the tendency to local recurrence even in low-grade tumors [26]. Mussi *et al.* [27] and Toulmonde *et al.* [6] found invasive behavior in 25 and 33%, respectively, of well-differentiated liposarcomas. Hogg *et al.* [26] reported that 50% of the excised tumors proved invasive behavior, but only 35% when considering well-differentiated liposarcoma.

An aggressive surgical approach that involves resection of adjacent noninvaded ‘disposable’ organs was considered to improve microscopic margins and thus

outcome [14,15]. Opponents of this approach claim that resecting these organs with the preservation of vital structures that similarly are close to the tumor is not expected to improve outcome, but rather increases morbidity [28]. However, still broadly accepted that routine compartmental resection is not recommended, and excision of adjacent organs is justified only with evidence of direct invasion to avoid R2 resection [22].

High-volume centers being more adherent to applying treatment guideline protocols (such as neoadjuvant radiotherapy) have shown to provide better OS, fewer R2 resections, and less morbidity and mortality rates [1,17,29–34]. Restricting RPS care to high-volume centers that have the surgical experience, infrastructure, and processes to provide oncological care of high quality should be advocated [1].

In our study, the most common histological type was liposarcoma followed by leiomyosarcoma. This was quite similar to most series such as in Hogg *et al.* [26] as they had 60/90 (66.7%) liposarcoma and 12 (13.3%) leiomyosarcoma, and also in Smith *et al.* [2] where they had 233/362 (64.3%), liposarcoma, and 71 (19⊠6%) patients leiomyosarcoma.

Most cases in our series presented with high-grade; G3 tumors were documented in 76 (69.7%) patients. This was much higher than in the literature. Hogg *et al.* [26] documented G3 in 38/90 (42.2%), and Smith *et al.* [2] reported G3 in 77/362 (21.3%).

In our study, contiguous organ resection was done in 51 (46.8%) patients, including one or more organs, up to four organs. This was much lower when compared with other series. Hogg *et al.* [26] reported 62 (70.0%) resections, including one or more organs, and Smith *et al.* [2] reported 292 (80.7%) resections, including up to six organs. In our study, the most commonly resected organs were the kidney and the colon, which was similar to what has been reported in different series.

In 84 (77%) patients, a macroscopically complete excision (R0/R1) could be achieved in our study, which is similarly considered a high rate as other authors documented. Hogg *et al.* [26] reported that 80/90 (88.9%) had R0/R1, while Smith *et al.* [2] reported that 348/362 (96.1%) had R0/R1 resection.

Morbidity and mortality

We had a rather high mortality rate, with a 30-day mortality of eight (7.3%) patients and a 60-day mortality of 10 (9.2%) patients. Compared with ours, Smith *et al.* [2] reported that five (1.4%) patients died within 30 days of operation, and their 60-day mortality rate was 1.9% (seven patients). In a systematic review conducted by Peacock *et al.* [3], the overall 30-day mortality was 278/10181 (3%).

We had a 60-day morbidity rate of 26.6% (29 patients). Seven (6.4%) patients required a return to the theater. Smith *et al.* [2] stated that their 30-day morbidity rate was 15.7% (57 patients), and a minimum of one return to the theater was required in 27 (7.5%) patients, with two patients who needed a second operation. Peacock *et al.* [3] reported that the overall 30-day morbidity was 191/846 (23%).

We reported a high leak rate in patients who underwent bowel anastomosis in our study, as it occurred in 5/23 (21.7%). Smith *et al.* [2] reported four leaks out of 189 anastomoses, with a low leak rate of 2.2%. In Smith and colleagues' study, all patients with a leak were managed surgically. They had one patient who passed away, and the other three patients recovered totally.

Overall survival

In our study, the median OS was not reached as more than 50% of the recruited patients remained alive till the end of the study. The cumulative OS of the whole cohort was 70.5 and 58.6% at 3 and 5 years, respectively. Different other series showed similar results, as Peacock *et al.*'s [3] systematic review reported that 5-year survival ranged from 52 to 62%, and Hogg *et al.*'s [26] study where the 5-year OS rate was 55.3%. However, in Smith *et al.* [2] study, a 3-year disease-specific survival rate for the whole cohort was 81.2%, which is rather higher.

In our study, and on a univariate level, the liposarcoma histopathology, R0 resection, low-grade tumors, and less than or equal to two organs resected were associated with better OS. However, on multivariate analysis, the statistically significant independent predictors of OS were the tumor grade and resection status (R) as illustrated in the 'Results' section.Hogg *et al.* [26] showed that statistically significant independent predictors of worse OS were invasive phenotype (P=0.003), patient age (P=0.001), presence of distant metastasis at the time of resection (P=0.014), and high-grade tumors (P=0.015). Similarly, in Peacock *et al.*'s [3] systematic review, independent predictors of OS were the age of the patient, resection status, tumor grade and size, histological subtype, and receipt of radiotherapy. Smith *et al.* [2] found that better OS was associated with low-grade tumors and liposarcoma

histopathology, however, on multivariate analysis, they found the only factor to be significantly predictive of disease-specific survival was tumor grade.

Disease-free survival

In our study, the median DFS was 43.6 months, with the cumulative DFS of the whole cohort that was 53 and 47% at 3 and 5 years, respectively. Hogg *et al.* [26] reported a 5-year DFS of 30.8%. In Peacock *et al.* [3] systematic review, they found no study reported locoregional recurrence rates.

In our study on the univariate level, a better DFS was associated significantly with liposarcoma histopathology, R0 resection, and less than or equal to two organs resected. However, on multivariate analysis, the only independent predictor of better DFS was R0 resection.

Hogg *et al.* [26] documented that receipt of chemotherapy or radiotherapy, invasive phenotype, piecemeal excision, and histological subtype demonstrated significance as predictors of DFS following univariate analysis, but only tumor grade was statistically significant following multivariate analysis.

Smith *et al.* [2] have stratified the DFS into local recurrence-free survival and metastasis-free survival. For local recurrence, they have found that better outcomes showed significant associations with liposarcoma histopathology and low-grade tumors [2]. Following multivariable analysis, the only factors that predicted poorer local recurrence-free survival were high tumor grade and macroscopically incomplete tumor resection. Tumor grade and histology were predictive of 3-year distant metastasis-free survival, with leiomyosarcoma having a higher risk than dedifferentiated liposarcoma [2].

Conclusions

Primary surgical resection of RPS should be aggressive with excision of frankly invaded nearby organs. The hope for cure is to obtain R0 resection whenever feasible. Excision of uninvolved organs still is not justified. Debulking surgery still has a role in the setting of palliative resection. Serving RPS patients in high-volume centers is the key to a better outcome and a better life quality.

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Conflicts of interest

There are no conflicts of interest.

References

1 Maurice MJ, Yih JM, Ammori JB, Abouassaly R. Predictors of surgical quality for retroperitoneal sarcoma: volume matters. J Surg Oncol 2017; 116:766–774.

2 Smith HG, Panchalingam D, Hannay JAF, Smith MJF, Thomas JM, Hayes AJ, *et al.* Outcome following resection of retroperitoneal sarcoma. Br J Surg 2015; 102:1698–1709.

3 Peacock O, Patel S, Simpson JA, Walter CJ, Humes DJ. A systematic review of population-based studies examining outcomes in primary retroperitoneal sarcoma surgery. Surg Oncol 2019; 29:53–63.

4 Stahl J, Corso C, Park H, An Y, Rutter C, Han D, *et al.* The effect of microscopic margin status on survival in adult retroperitoneal soft tissue sarcomas. Eur J Surg Oncol 2017; 43:168–174.

5 Gronchi A, Strauss DC, Miceli R, Bonvalot S, Swallow CJ, Hohenberger P, *et al.* Variability in patterns of recurrence after resection of primary retroperitoneal sarcoma (RPS). Ann Surg 2016; 263:1002–1009.

6 Toulmonde M, Bonvalot S, Méeus P, Stoeckle E, Riou O, Isambert N, *et al.* Retroperitoneal sarcomas: patterns of care at diagnosis, prognostic factors and focus on main histological subtypes: a multicenter analysis of the French Sarcoma Group. Ann Oncol 2014; 25:735–742.

7 van DT, Plooij J, Van CF, Geel A, Hoekstra H, Albus-Lutter PC. Long-term prognosis of primary retroperitoneal soft tissue sarcoma. Eur J Surg Oncol 2007; 33:234–238.

8 Lewis J, Leung D, Woodruff J, Brennan M. Retroperitoneal soft-tissue sarcoma: analysis of 500 patients treated and followed at a single institution. Ann Surg 1998; 228:PMC1191491.

9 Singer S, Antonescu CR, Riedel E, Brennan MF, Pollock RE. Histologic subtype and margin of resection predict pattern of recurrence and survival for retroperitoneal liposarcoma. Ann Surg 2003; 238:358–371.

10 Stoeckle E, Coindre J, Bonvalot S, Kantor G, Terrier P, Bonichon F, *et al.* Prognostic factors in retroperitoneal sarcoma: a multivariate analysis of a series of 165 patients of the French Cancer Center Federation Sarcoma Group. Cancer Interdiscip Int J Am Cancer Soc 2001; 92:359–368.

11 Gyorki DE, Brennan MF. Management of recurrent retroperitoneal sarcoma. J Surg Oncol 2014; 109:53–59.

12 Gronchi A, Miceli R, Colombo C, Stacchiotti P, Collini L, Mariani C, *et al.* Frontline extended surgery is associated with improved survival in retroperitoneal low-to intermediate-grade soft tissue sarcomas. Ann Oncol 2012; 23:1067–1073.

13 Gronchi A, Bonvalot S, Le Cesne A, Casali PG. Resection of uninvolved adjacent organs can be part of surgery for retroperitoneal soft tissue sarcoma. J Clin Oncol 2009; 27:2106–2107.

14 Bonvalot S, Rivoire M, Castaing M, Stoeckle E, Le Cesne A, Blay JJ, *et al.* Primary retroperitoneal sarcomas: a multivariate analysis of surgical factors associated with local control. J Clin Oncol 2009; 27:31–37.

15 Gronchi A, Vullo S Lo, Fiore M, Mussi C, Stacchiotti S, Collini P, *et al.* Aggressive surgical policies in a retrospectively reviewed single-institution case series of retroperitoneal soft tissue sarcoma patients. J Clin Oncol 2009; 27:24–30.

16 Adam MA, Moris D, Behren S, Nussbaum DP, Jawitz O, Turner M, *et al.* Hospital Volume Threshold for the Treatment of Retroperitoneal Sarcoma. Anticancer Res 2019; 39:2007–2014.

17 Keung EZ, Chiang YJ, Cormier JN, Torres KE, Hunt KK, Feig BW, *et al.* Treatment at low-volume hospitals is associated with reduced short-term and long-term outcomes for patients with retroperitoneal sarcoma. Cancer 2018; 124:4495–4503.

18 Trojani M, Contesso G, Coindre JM, Rouesse J, Bui NB, De Mascarel A, *et al.* Soft-tissue sarcomas of adults; study of pathological prognostic variables and definition of a histopathological grading system. Int J Cancer 1984; 33:37–42.

19 Perhavec A, Provenzano S, Sangalli C, Morosi C, Barisella M, Baia M, *et al.* Inoperable primary retroperitoneal sarcoma: clinical characteristics and reasons against resection at a single referral institution. Eur J Surg Oncol 2020; 46:e29.

20 Lehnert T, Cardona S, Hinz U, Willeke F, Mechersheimer G, Treiber M, *et al.* Primary and locally recurrent retroperitoneal soft-tissue sarcoma: local control and survival. Eur J Surg Oncol 2009; 35:986–993.

21 Shibata D, Lewis J, Leung D, Brennan M. Is there a role for incomplete resection in the management of retroperitoneal liposarcomas? J Am Coll Surg 2001; 193:373–379.

22 Guo Q, Zhao J, Du X, Huang B. Survival outcomes of surgery for retroperitoneal sarcomas: a systematic review and meta-analysis. PLoS ONE 2022; 17:e0272044.

23 Gronchi A, Miceli R, Shurell E, Eilber FC, Eilber FR, Anaya DA, *et al.* Outcome prediction in primary resected retroperitoneal soft tissue sarcoma: histology-specific overall survival and disease-free survival nomograms built on major sarcoma center data sets. J Clin Oncol 2013; 31:1649–1655.

24 Anaya DA, Lahat G, Wang X, Xiao L, Pisters PW, Cormier JN, *et al.* Postoperative nomogram for survival of patients with retroperitoneal sarcoma treated with curative intent. Ann Oncol 2010; 21:397–402.

25 Singer S, Corson JM, Demetri GD, Healey EA, Marcus K, Eberlein TJ. Prognostic factors predictive of survival for truncal and retroperitoneal soft-tissue sarcoma. Ann Surg 1995; 221:PM C1234952.

26 Hogg HDJ, Manas DM, Lee D, Dildey P, Scott J, Lunec J, *et al.* Surgical outcome and patterns of recurrence for retroperitoneal sarcoma at a single centre. Ann R Coll Surg Engl 2016; 98:192–197.

27 Mussi C, Colombo P, Bertuzzi A, Coladonato M, Bagnoli P, Secondino S, *et al.* Retroperitoneal sarcoma: Is it time to change the surgical policy? Ann Surg Oncol 2011; 18:2136–2142.

28 Raut CP, Swallow CJ. Are radical compartmental resections for retroperitoneal sarcomas justified?. Ann Surg Oncol 2010; 17:1481–1484.

29 Hoekstra HJ, Haas RLM, Verhoef C, Suurmeijer AJH, van Rijswijk CSP, Bongers BGH, *et al.* Adherence to guidelines for adult (Non-GIST) soft tissue sarcoma in the netherlands: a plea for dedicated sarcoma centers. Ann Surg Oncol 2017; 24:3279–3288.

30 Gladdy RA, Gupta A, Catton CN. Retroperitoneal sarcoma: fact, opinion, and controversy. Surg Oncol Clin N Am 2016; 25:697–711.

31 Mullinax JE, Zager JS, Gonzalez RJ. Current diagnosis and management of retroperitoneal sarcoma. Cancer Control 2011; 18:177–187.

32 Ray-Coquard I, Thiesse P, Ranchère-Vince D, Chauvin F, Bobin JY, Sunyach MP, *et al.* Conformity to clinical practice guidelines, multidisciplinary management and outcome of treatment for soft tissue sarcomas. Ann Oncol 2004; 15:307–315.

33 Meric F, Hess KR, Varma DGK, Hunt KK, Pisters PWT, Milas KM, *et al.* Radiographic response to neoadjuvant chemotherapy is a predictor of local control and survival in soft tissue sarcomas. Cancer 2002; 95:1120–1126.

34 Nijhuis P, Schaapveld M, Otter R, Hoekstra H. Soft tissue sarcoma – compliance with guidelines. Interdiscip Int J Am Cancer Soc 2001; 91:2186–2195.