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Resection of retroperitoneal sarcoma en-bloc with inferior vena cava: 20 year outcomes of a single institution

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Abstract

Background: Margin negative resection offers the best chance of long-term survival in retroperitoneal sarcoma (RPS). En-bloc resection of adjacent structures, including the inferior vena cava (IVC), is often required to achieve negative margins. We review our 20-year experience of en-bloc IVC and RPS resection.

Methods: Retrospective review of patients with RPS resection involving the IVC were matched 1:3 by age and histology to RPS without IVC resection. Prognostic factors for overall survival (OS) and disease free survival (DFS) were assessed.

Results: Thirty-two patients underwent RPS resection en-bloc with IVC. They were matched with 96 cases of RPS without IVC resection. Median OS of 59 months and DFS 18 months in IVC resection group was comparable to RPS resection without vascular involvement: median OS 65 months, DFS 18 months ($P = 0.519$, $P = 0.604$). On multivariate analyses, R2 margin (OS: HR = 6.52 [95% CI: 1.18–36.09], $P = 0.032$) was associated with inferior OS. R2 margin and increased number of organs resected (DFS: HR = 5.07, [1.15–22.27], $P = 0.031$, HR = 1.28 [1.01–1.62], $P = 0.014$) were associated with inferior DFS. Reconstructions included graft ($n = 19$, 59%), patch ($n = 4$, 13%), primary repair ($n = 6$, 19%), and ligation ($n = 4$, 13%).

Conclusions: RPS resection en-bloc with IVC can achieve equivalent rates of DFS and OS to patients without vascular involvement.

Keywords

inferior vena cava; sarcoma; survival; vascular resection

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CONFLICTS OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

1 | INTRODUCTION

Soft tissue sarcomas (STS) represent a rare group of tumors constituting 1% of solid malignancies. STS present with over 50 histologic subtypes with a wide variance of tumor locations throughout the body.¹ Retroperitoneal sarcomas (RPS) represent 15–20% of STS and present with less heterogeneity in histology, predominately represented by leiomyosarcoma and liposarcoma.² Complete surgical resection of RPS with negative margins is associated with the best chance for long term disease free and overall survival (OS).^{3–5} Due to the anatomy of the retroperitoneal space, these tumors often remain asymptomatic and undetected until they have reached a large size or have extended into adjacent organs. Because of these unique anatomic challenges, even with resection, local recurrence remains high and 5-year survival low, ranging from 35% to 65%.^{5–7}

Aggressive multivisceral resection of involved organs is often necessary in order to achieve complete RPS extirpation with negative margins and the greatest chance for cure.^{8,9} Most frequently this includes retroperitoneal structures such as ipsilateral colon, kidney or psoas muscles/fascia. However, major vascular structures such as the inferior vena cava (IVC) may also be involved, posing a more technically challenging surgical approach.¹⁰ While tumor resection en-bloc with major vascular structures increases case complexity, studies in numerous other malignancies have shown survival rates following major vascular resection that are comparable to those without vascular involvement.^{11–14} Similar findings have been reported in multiple small case series of multivisceral RPS resections performed at high volume institutions.^{15–21} However, due to the rarity of this disease, present existing series are often small in size, include extremity sarcomas in analyses, or investigate primary leiomyosarcoma of the IVC only.

The primary aim of this study is to investigate outcomes following en-bloc resection of RPS and IVC using a robust clinical database from a single institution. We additionally compare these patients' OS and disease free survival (DFS) using a matched case-control method with patients during the same period with resected RPS without IVC involvement.

2 | MATERIALS AND METHODS

2.1 | Patient selection

Patients undergoing resection of RPS en-bloc with the IVC between the years 1995–2015 were identified from a prospectively maintained institutional database and included for review. These patients were matched in a 1:3 ratio according to continuous age and histopathology (leiomyosarcoma or de-differentiated liposarcoma) with cases of RPS without IVC resection. Patients with primary renal or uterine malignancies, as well as well differentiated liposarcomas were excluded from analysis. The need for en-bloc IVC resection was determined by the operating surgeon at the time of the operation. Compartmental retroperitoneal resection, or the systematic en-bloc extirpation of uninvolved contiguous organs, has been advocated by several centers to maximize local control.^{4,22} This compartmental technique is not routinely performed at our institution for RPS. Instead, additional organs are resected if noted to be involved by tumor or deemed necessary intraoperatively to achieve complete resection with negative oncologic margins. All

resections were performed at the Johns Hopkins Hospital, although neoadjuvant and adjuvant chemotherapy or radiation was permitted at outside institutions if received. Institutional Review Board approval was obtained for this study.

2.2 | Demographics and clinicopathological characteristics

The following demographic and clinicopathologic features were included for analysis in all patients: age, sex, recurrent or primary resection, receipt of neoadjuvant radiation, neoadjuvant chemotherapy, tumor pathology, tumor size, grade, resection margin, and the number of organs resected other than the IVC at the time of reported surgery. Within the RPS-IVC cohort, additional clinicopathologic characteristics included: type and details of vascular reconstruction, IVC patency, intraoperative bypass technique, presence of tumor thrombus, estimated blood loss, intraoperative transfusion data, length of stay, and postoperative complications including presence of leg swelling or venous thromboembolism (VTE) event. Perioperative complications within 90 days from resection, including symptoms of leg swelling or VTE, were obtained via individual chart review and scored by the Clavien-Dindo grading system with grade III or greater considered severe complications.²³ Resected organs included: colon, small bowel, liver, adrenal gland, kidney, diaphragm, gallbladder, spleen, pancreas, and uterus. All resection margins were assessed by pathologists experienced in sarcoma with an R0 resection defined as a distance of tumor cells ≥ 1 mm from the margin. An R1 resection was defined as distance of tumor cells < 1 mm from the margin and grossly positive margins deemed as R2. Intraoperative frozen section vascular margin were assessed in cases where significant length of IVC remained allowing for potential re-resection. In cases where large portions of IVC required resection, maximal resection margins were obtained and frozen section was not assessed.

2.3 | Follow-up and survival

Following RPS resection, patients at our institution are followed approximately every 3–6 months for the first 2 years, every 6 months for the next 3 years, and yearly thereafter with computed tomography (CT) scans of the chest, abdomen, and pelvis. IVC patency was determined with the use of surveillance CT images. Additional vascular duplex ultrasound was obtained in cases with concern for thrombosis or unclear patency. DFS was calculated from the time of surgery to the date of recurrence defined as the observation of progressing radiographic change locoregionally or at a distant site. Tissue confirmation of recurrence was not routinely obtained. OS was calculated from the date of diagnosis to the date of death, or censored until the date of last follow-up. The date of death was obtained from medical records, local obituary query or the Social Security Death Index.

2.4 | Statistical analysis

The primary outcomes of interest were OS and DFS. Categorical variables were expressed as percentages of the group they were derived from and were compared using a chi-squared or Fisher's exact test. Continuous variables were presented as median with interquartile range (IQR), and were compared using a Kruskal-Wallis test. Patients with RPS en-bloc with IVC were matched with three additional patients who underwent RPS resection without vascular involvement. Case matching was performed by: (i) continuous age and (ii) histologic type. Kaplan-Meier survival curves and a log-rank test were used to estimate

median survival and analyze survival outcomes between subgroups. All factors with a P -value of <0.10 in univariate analysis were included as a covariate in a Cox proportional-hazards multivariate regression model. For all other analyses, a two-tailed P -value of less than 0.05 was considered statistically significant. Statistical analysis was performed using Stata/MP 14.0 (Stata Corp, College Station, TX).

3 | RESULTS

3.1 | Patient demographics and clinicopathological characteristics

A total of 264 patients with primary or recurrent RPS were resected at Johns Hopkins Hospital between 1995 and 2015. Of these, 32 patients (12%) underwent en-bloc IVC resection. These cases were matched by patient age and tumor histopathologic type at a 1:3 ratio to 96 cases of RPS without IVC resection (Table 1). The groups were well matched, with no differences in patient age or sex. After matching, equivalent rates of leiomyosarcoma and dedifferentiated liposarcoma were found in each group ($P = 1.000$). The majority of resections were for initial primary tumors (84% with IVC resection vs 78% without, $P = 0.447$), with a median of two organs resected in both groups. The total time period for this study was divided into 5-year intervals, with a similar distribution of case number in each group (Table 1). No significant differences were noted among clinicopathologic characteristics between the two groups for the remaining pathologic factors: tumor size, grade, and resection margin.

Both neoadjuvant and adjuvant therapy are considered for patients as part of the evaluation in a multidisciplinary conference. Neoadjuvant chemotherapy was given to 22% of patients within the total study and was more likely offered for patients with high grade disease and leiomyosarcoma. No difference was noted between rates of neoadjuvant chemotherapy or radiation therapy between those with IVC resection and those without (Table 1). Following resection, no difference was noted in the rate of patients that received chemotherapy between the two groups. Moreover, these rates remained similar when stratified by pathology (Leiomyosarcoma: 42% with IVC resection vs 30% without, $P = 0.227$; Liposarcoma: 33% vs 17%, $P = 0.384$).

3.2 | Operative details and outcomes

Operative characteristics and perioperative outcomes of the IVC resected cohort can be found in Table 2. Within the cohort of patients that underwent RPS with IVC resection, multiple vascular reconstructions were performed: a graft was used most frequently (59% of cases), followed by primary repair in 19%, patch repair in 13% and no reconstruction, secondary to the presence of collaterals, in 9% of cases (Figure 1). Of graft reconstructions, a synthetic graft was used in 79% of cases. Bypass support was used in 22% of all resections, with veno-veno bypass the most common approach. Veno-veno bypass was typically utilized in patients that could not tolerate a test clamping of the IVC prior to resection. A tumor thrombus was appreciated intraoperatively in 16% of all cases. At a median follow up of 37 months, 92% of reconstructed IVCs remained patent. Postoperative leg swelling was observed in 16% of patients with IVC resection with no association between repair technique: 25% of patients without reconstruction versus 21% with graft

reconstruction ($P = 0.502$). The overall incidence of postoperative VTE was 9%. Patients who suffered from VTE had similar demographics and clinicopathologic features as those without VTE, age, sex, histopathology, grade, and margin (Supplemental Table S1). While use of intraoperative bypass support and reconstruction technique did not significantly affect VTE rate, the presence of a tumor thrombus was significantly associated with postoperative VTE events (67% vs 11%, $P = 0.012$).

3.3 | Survival

Figures 2 and 3 depict the Kaplan-Meier DFS and OS curves for patients undergoing RPS resection with or without en-bloc IVC resection. Median DFS was not significantly different in patients with RPS resected en-bloc with IVC compared to those without (Median DFS 18 months with IVC resection vs 18 months without, $P = 0.604$) (Figure 2). Likewise, median OS was similar, with a median OS of 59 months in IVC resection group versus 65 months in those without IVC resection ($P = 0.519$) (Figure 3).

Supplemental Figure S1 depicts the Kaplan-Meier DFS and OS curves for RPS with or without en-bloc IVC resection when divided by histologic subtype. DFS and OS was not significantly different in patients with RPS resected en-bloc with IVC compared to those without for both the liposarcoma (DFS: $P = 0.901$; OS: $P = 0.332$) and leiomyosarcoma subgroups (DFS: $P = 0.712$; OS: $P = 0.959$).

Results of a multivariate Cox regression model generated to describe the strength of association between different clinicopathologic variables and survival in the IVC resected cohort are shown in Tables 3 and 4. An increased number of organs resected, a positive resection margin (R1 or R2) and lack of reconstruction secondary to collaterals were included in the model due to an unadjusted univariate association with inferior DFS. On multivariate analysis, an increased number of organs resected ($HR = 1.28$, $P = 0.014$) and R1 ($HR = 3.66$, $P = 0.012$) or R2 resection ($HR = 5.07$, $P = 0.031$) were independently associated with inferior DFS (Table 3). Similarly, an R2 resection ($HR = 6.52$, $P = 0.032$) was independently associated with inferior OS along with the presence of tumor thrombus ($HR 4.91$, $P = 0.025$) (Table 4). Increased number of organs resected also trended toward inferior OS, although significance was not reached likely due to limited sample size ($HR 1.28$, $P = 0.073$).

4 | DISCUSSION

Surgical resection with negative margins offers the best chance for long term survival in patients with primary and recurrent RPS. Complete R0 resections can be difficult to obtain without aggressive resection of adjacent clinically involved viscera, including the IVC. In our 20-year experience, we found equivalent overall and disease-free survivals of patients with and without IVC resection in two well matched groups. Within the cohort of patients with IVC resections, increasing concomitant multivisceral resections and positive margins (R1/R2) were independently associated with inferior survival on multivariate analyses.

Studies have continually supported the feasibility of surgical intervention with durable oncologic outcomes in various tumor pathologies with major vascular involvement,

including: pancreatic cancer, renal cell carcinoma, and intrahepatic cholangiocarcinoma.^{11–14} In addition, several prior studies have specifically reported on major vascular resection en-bloc with soft tissue sarcoma. However, many of these studies were heterogeneous with respect to tumor location (intraabdominal and extremity), and type of vascular resection (arterial vs venous, central vs peripheral). Table 5 reports the results of 14 contemporary case-series and multi-institutional collaborations with 10 or more cases of RPS and en-bloc IVC resection published within the last 15 years. Of the 486 reported cases of RPS with vascular involvement in 14 studies, only 277 patients underwent en-bloc IVC resection (sample sizes ranging from 10 to 42 patients), which emphasizes the rarity of this presentation, the difficulty of resection and may highlight a potential bias against pursuing resection in patients with major vascular involvement. Of those reporting only RPS and IVC resection, 5-year OS ranged from 33% to 78%, and median OS ranged from 31 to 71 months, which is consistent with our current findings of a 5-year OS of 41% and a median OS of 59 months. Poultides et al,¹⁹ for example, reported equivalent OS in 15 patients undergoing en-bloc IVC resection, compared to 35 matched patients not undergoing resection. Our study reinforces this finding of equivalent OS and DFS within a larger focused cohort of RPS and en-bloc IVC resection.

Though dedifferentiated liposarcoma and leiomyosarcoma are two distinct histologies with varying biologic activity, both were included in this study given the rare nature of these diagnoses. While involvement of the IVC by liposarcoma is often from local invasion, leiomyosarcoma frequently arises directly from the muscle of the vessel wall. Recurrence patterns are also different, with distant failure much more common in leiomyosarcoma.²⁴ Despite this, significant differences in DFS and OS were still not noted in subgroup analyses of IVC resection versus no vascular resection when divided by histologic subtype (Supplemental Figure S1). Recurrence patterns in this study were consistent with those previously described, with only 10% of patients having distant recurrence for liposarcoma compared to 46% with leiomyosarcoma ($P = 0.002$). En-bloc IVC resection did not significantly alter these recurrence patterns for leiomyosarcoma ($P = 0.182$) or liposarcoma ($P = 0.471$).

The approaches for surgical reconstruction of the IVC reported in the literature are not standardized. Synthetic graft reconstruction was the most common approach reported in reviewed literature at approximately 62%, followed by primary repair in 18% and patch repair in 7% (Table 5). A similar breakdown was observed in our series with graft reconstruction in 19 (59%) cases, primary repair in 6 (19%) cases and patch repair in 4 (13%) (Table 2). The use of graft reconstruction increased throughout our 20 year period from 43% from 1995 to 2005 up to 72% from 2006 to 2015. This is likely influenced by advances in technology increasing the availability and selection of reconstructive graft options. Despite this, graft reconstruction did not influence DFS or OS (Tables 3–4).

VTE events are a common complication following IVC reconstruction. Previous reports have associated a higher risk of VTE with polytetrafluoroethylene (PTFE) graft reconstruction compared to patch or primary repair.^{25,26} However, this association was not appreciated in our series, with VTE observed in 13% of PTFE graft reconstructions compared to 17% of primary repairs ($P = 0.345$). While patients who suffered from VTE had

similar demographics and clinicopathologic features as patients without VTE, an intraoperative tumor thrombus was associated with increased risk of postoperative VTE ($P=0.019$). Residual tumor thrombus following resection of renal cell carcinoma has previously been associated with an increased risk of postoperative VTE, but has not been described in RPS.²⁷ Unrecognized residual tumor thrombus could feasibly play a similar role in our findings. Despite these events, no patients died or developed significant long-term morbidity as a result of VTE in our study.

In cases of chronic IVC occlusion, extensive venous collaterals may develop. In these cases, IVC ligation can be performed without reconstruction, resulting in similar postoperative outcomes.^{28–30} In our series, 3 (9%) cases did not undergo reconstruction. Of interest, lack of reconstruction was associated on univariate analysis with inferior DFS, conceivably inferring more aggressive tumor biology at the time of resection. This association, however, was not found to be an independent predictor in our multivariate cox regression model, perhaps due to the limited number of cases (Table 3).

Receipt of adjuvant chemotherapy was not different between the two groups (Table 1). The physiologic stress associated with a potentially more complex operation involving major venous resection thus did not significantly impact the ability to receive adjuvant therapy. Unfortunately, however, adjuvant chemotherapy did not impact DFS or OS (Tables 3–4). Recent studies querying the National Cancer Database have similarly demonstrated that chemotherapy did not improve survival for resected retroperitoneal soft tissue sarcoma.^{31,32} This further highlights the need for the identification or development of more effective systemic therapies for sarcoma.

Multivariate analyses within the IVC cohort identified an increased number of organs resected and positive margins (R1/R2) to be independently associated with inferior DFS (Table 3). Similarly, an R2 resection was independently associated with inferior OS with a trend toward R1 resection and an increase in number of organs resected and inferior OS (Table 4). A complete resection with negative margins has repeatedly been shown to be essential to maximize the chance for long term survival in RPS.^{3–5,15,21,25,33–36} As seen in our study, prior reports have also associated multivisceral resection with inferior survival for RPS.^{5,36} It could be inferred that the necessity of a more radical surgical approach may indicate worse tumor biology, with IVC invasion representing more aggressive tumor behavior. Furthermore, secondary to the risk of enteric leak, concerns may be raised with vascular reconstruction and concomitant colon resection. If possible, synthetic graft reconstruction is avoided in these patients, however the need for colonic resection should not preclude operative intervention. Within this study, five patients had concomitant colon and IVC resection, of which two underwent primary repair, one venous ligation, and two graft reconstruction.

Despite equivalent outcomes, IVC resection increases the complexity of the operation, thus increasing the risk of morbidity and mortality.^{19,37} However, literature suggests experienced surgeons can perform these complex IVC resections and reconstructions safely.²⁶ Due to increased complication risks, previous reports have recommended the utilization of intraoperative vascular consultation in cases requiring major vascular resection, reporting

fewer vascular injuries and a trend toward lower blood loss and improved survival.³⁸ While direct comparison of complications was beyond the scope of this study, 16% of patients with en-bloc IVC resection in our series had a severe postoperative complication as deemed by a Clavien-Dindo score of >IIIa.²³ This rate was similar to the 16.4% rate observed by the Transatlantic Retroperitoneal Sarcoma Working Group's collaborative of 1007 consecutive primary RPS cases.³⁷ There were no serious postoperative complications in patients that received neoadjuvant radiation in our study.

Pre-operative consultation with a vascular surgeon is ideal if IVC involvement is suspected on diagnostic imaging. All IVC resections in our series included intraoperative vascular surgery or transplant surgery assistance, even if vascular resection was not planned preoperatively. The complex interventions necessary to safely obtain a complete oncologic resection further support consideration for referral to centers with experience and resources to handle such patients.

Multiple limitations of this study deserve mention. First, as with any retrospective study, our data may be subject to patient selection biases. Second, the presented study population is a reflection of our institution's experience with this rare disease presentation, and thus is heterogeneous including different histologies and both primary and recurrent disease. Additionally, while the ratio of resected IVC cases per year remained consistent, this study spans two decades and we cannot quantify with our data the variation in practice patterns or reconstruction approaches that may have changed over time. With the limited numbers of events in this study, conclusions should be drawn cautiously, even with significant associations. This is further underlined with subgroup analyses such as groups receiving neoadjuvant therapy or tumor histology. Nevertheless, we present one of the largest, single institution studies of IVC resection and RPS. Future studies with greater power will provide superior clarity to many of these additional questions and associations. Finally, the endpoints of recurrence or death may hold inaccuracies as recurrence was determined radiographically, often without tissue confirmation, and precise cause of death was often unavailable.

5 | CONCLUSION

En-bloc resection of RPS and IVC in a high volume tertiary sarcoma center can be performed safely with equivalent disease free and OS to a matched cohort without vascular involvement. Survival or VTE risk was not associated with various reconstruction techniques including: graft, patch, primary repair, and ligation. Positive margins (R1/R2) and increased number of contiguous organs resected, were independently associated with inferior survival among the IVC resected cohort. The complex multivisceral resections necessary to safely obtain a complete oncologic resection in cases with IVC involvement support consideration for referral to centers with the experience and resources necessary for the management of these patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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SYNOPSIS

This study describes the survival outcomes of patients that underwent retroperitoneal sarcoma resection en-bloc with the IVC over a 20-year period at a single institution. When matched 1:3 to sarcoma resections without vascular involvement, patients undergoing en-bloc resection of the IVC had equivalent disease free and overall survival outcomes. Within the cohort of IVC resected patients, positive margins and increasing concomitant multivisceral resections were associated with inferior survival.

FIGURE 1.

Depiction of reconstruction techniques for patients with retroperitoneal sarcoma resection with en-bloc inferior vena cava. This image is reproduced with permission of the Department of Art as Applied to Medicine in the Johns Hopkins University School of Medicine

FIGURE 2.
Kaplan-Meier disease free survival (DFS) estimates for resected retroperitoneal sarcoma with and without en-bloc inferior vena cava (IVC) resection

FIGURE 3.

Kaplan-Meier overall survival (OS) estimates for resected retroperitoneal sarcoma with and without en-bloc inferior vena cava (IVC) resection

Clinicopathologic characteristics of patients with retroperitoneal sarcoma (RPS) resection with ($n = 32$) and without ($n = 96$) en-bloc inferior vena cava (IVC) resection

Table 1

Variable	RPS & IVC resection ($n = 32$)	RPS without IVC resection ($n = 96$)	P-value
Age, median years (IQR)	63 (52–68)	63 (51–68)	0.934
Male, n (%)	13 (41%)	44 (46%)	0.608
Recurrent tumor resection, n (%)	5 (16%)	21 (22%)	0.447
Neoadjuvant radiation, n (%)	7 (22%)	28 (29%)	0.423
Neoadjuvant chemotherapy, n (%)	6 (19%)	22 (23%)	0.621
Pathology, n (%)			1.000
Leiomyosarcoma	26 (81%)	78 (81%)	
Dedifferentiated liposarcoma	6 (19%)	18 (19%)	
Postoperative chemotherapy, n (%)			
Leiomyosarcoma	11 (42%)	23 (30%)	0.227
Dedifferentiated liposarcoma	2 (33%)	3 (17%)	0.384
Number of organs resected, ^a median (IQR)	2 (1–4)	2 (1–3)	0.731
Tumor size, median cm (IQR)	11.3 (6.5–14.7)	10.2 (7.0–15.0)	0.972
Grade			0.686
Low	2 (6%)	11 (12%)	
Moderate	10 (31%)	27 (28%)	
High	20 (63%)	57 (60%)	
Resection margin, n (%)			0.825
R0	14 (44%)	37 (39%)	
R1	15 (47%)	47 (49%)	
R2	3 (9%)	12 (12%)	
Time period of operation			0.973
1995–2000	7 (22%)	22 (23%)	
2001–2005	7 (22%)	18 (19%)	
2006–2010	8 (25%)	27 (28%)	
2011–2015	10 (31%)	29 (30%)	

^aOrgans include: colon, small bowel, liver, adrenal, kidney, diaphragm, gallbladder, spleen, pancreas, uterus.

Table 2

Operative characteristics and post-operative outcomes of retroperitoneal sarcoma (RPS) resection en-bloc with the inferior vena cava (IVC)

Variable	RPS & IVC resection (<i>n</i> = 32)
Reconstruction type, <i>n</i> (%)	
None	3 (9%)
Primary	6 (19%)
Patch	4 (13%)
Graft	19 (59%)
Graft reconstruction detail, <i>n</i> (%)	
Autologous vein	1 (5%)
Allograft	3 (16%)
Synthetic graft	15 (79%)
Bypass, <i>n</i> (%)	
Venovenous bypass	6 (19%)
Cardiopulmonary bypass ^a	1 (3%)
Tumor thrombus	5 (16%)
EBL, median mL (IQR)	2500 (1000–7000)
Transfusion, median units (range)	0 (0–55)
0 units, <i>n</i> (%)	14 (44%)
<5 units	8 (25%)
5 units	10 (31%)
LOS, median days (IQR)	8 (7–14)
Severe postoperative complication, <i>n</i> (%)	
Clavien-Dindo grade IIa	5 (16%)
Postoperative VTE, <i>n</i> (%)	3 (9%)
Postoperative leg swelling, <i>n</i> (%)	5 (16%)
IVC patency ^b , <i>n</i> (%)	27 (92%)

^aCardiopulmonary bypass for intracardiac extension of tumor.

^bAt median 37 month follow up.

Univariate and multivariate Cox regression analyses of disease-free survival in patients with retroperitoneal sarcoma resection en-bloc with inferior vena cava (IVC)

Table 3

Clinical characteristics	Cohort (n = 32)	Univariate P-value	HR	95%CI	Multivariate P-value
Age, n (%)					
Age <65	18 (56%)	ref.			
Age >65	14 (44%)	0.945			
Male, n (%)	13 (41%)	0.232			
Recurrent tumor resection, n (%)	5 (16%)	0.982			
Neoadjuvant radiation, n (%)	7 (22%)	0.749			
Neoadjuvant chemotherapy, n (%)	6 (19%)	0.676			
Postoperative chemotherapy, n (%)	13 (41%)	0.473			
Pathology, n (%)					
Leiomyosarcoma	26 (81%)	ref.			
Dedifferentiated liposarcoma	6 (19%)	0.558			
Number organs ^a resected, median (IQR)	2 (1–4)	0.018	1.28	1.01–1.62	0.014
Tumor size, n (%)					
10 cm	15 (47%)	ref.			
>10 cm	17 (38%)	0.196			
Grade					
Low	2 (6%)	ref.			
Moderate	10 (31%)	0.764			
High	20 (63%)	0.421			
Resection margin, n (%)					
R0	14 (44%)	ref.			
R1	15 (47%)	0.021	3.66	1.33–10.05	0.012
R2	3 (9%)	0.023	5.07	1.15–22.27	0.031
Estimated blood loss, n (%)					
EBL <2500	11 (61%)	ref.			
EBL >2500	7 (39%)	0.380			
Severe postoperative complication, n (%)					

Clinical characteristics	Cohort (<i>n</i> = 32)	Univariate <i>P</i> -value	HR	95%CI	Multivariate <i>P</i> -value
>Clavien-Dindo grade IIIa	5 (16%)	0.736			
Reconstruction type, <i>n</i> (%)					
Graft	19 (59%)	ref.	ref.		
None	3 (9%)	0.031	0.76	0.12–4.96	0.772
Primary	6 (19%)	0.123	0.23	0.03–1.61	0.137
Patch	4 (13%)	0.396	0.36	0.07–1.76	0.208
Bypass, <i>n</i> (%)	7 (22%)	0.176			
Tumor thrombus	5 (16%)	0.340			
Postoperative VTE, <i>n</i> (%)	3 (9%)	0.676			

^d Organs include: colon, small bowel, liver, adrenal, kidney, diaphragm, gallbladder, spleen, pancreas, uterus.

Significant *P* values <0.05. are indicated in bold.

Univariate and multivariate Cox regression analyses of overall survival in patients with retroperitoneal sarcoma resection en-bloc with inferior vena cava (IVC)

Table 4

Clinical characteristics	Cohort (n = 32)	Univariate <i>P</i> -value	HR	95%CI	Multivariate <i>P</i> -value
Age, <i>n</i> (%)					
Age <65	18 (56%)	ref.			
Age ≥65	14 (44%)	0.234			
Male, <i>n</i> (%)	13 (41%)	0.396			
Recurrent tumor resection, <i>n</i> (%)	5 (16%)	0.927			
Preoperative radiation, <i>n</i> (%)	7 (22%)	0.455			
Neoadjuvant chemotherapy, <i>n</i> (%)	6 (18%)	0.624			
Postoperative chemotherapy, <i>n</i> (%)	13 (41%)	0.209			
Pathology, <i>n</i> (%)					
Leiomyosarcoma	26 (81%)	ref.			
Dedifferentiated liposarcoma	6 (19%)	0.856			
Number organs resected, ^a median (IQR)	2 (1–4)	0.042	1.28	0.98–1.67	0.073
Tumor size, <i>n</i> (%)					
≤10 cm	15 (47%)	ref.			
>10 cm	17 (38%)	0.557			
Grade					
Low	2 (6%)	ref.			
Moderate	10 (31%)	0.668			
High	20 (63%)	0.631			
Resection margin, <i>n</i> (%)					
R0	14 (44%)	ref.			
R1	15 (47%)	0.140	2.75	0.85–8.85	0.090
R2	3 (9%)	0.028	6.52	1.18–36.09	0.032
Estimated blood loss, <i>n</i> (%)					
EBL <2500	11 (61%)	ref.			
EBL ≥2500	7 (39%)	0.194			
Severe postoperative complication, <i>n</i> (%)					

Clinical characteristics	Cohort (n = 32)	Univariate <i>P</i> -value	HR	95%CI	Multivariate <i>P</i> -value
Clavien-Dindo grade IIIa	5 (16%)	0.100	1.91	0.47–7.72	0.367
Reconstruction type, <i>n</i> (%)					
Graft	19 (59%)	ref.			
None	3 (9%)	0.438			
Primary	6 (19%)	0.733			
Patch	4 (13%)	0.324			
Bypass, <i>n</i> (%)	7 (22%)	0.615			
Tumor thrombus	5 (16%)	0.017	4.91	1.22–19.72	0.025
Postoperative VTE, <i>n</i> (%)	3 (9%)	0.120			

^aOrgans include: colon, small bowel, liver, adrenal, kidney, ureter, diaphragm, gallbladder, spleen, duodenum, pancreas, uterus.

Significant *P* values <0.05, are indicated in bold.

Literature review of large contemporary reports of patients with retroperitoneal sarcoma resection en-bloc with inferior vena cava (IVC)

Table 5

Reference	Institute(country)	Inclusion period	Total no. malignant vascular involvement	RPS with IVC resection	Reconstruction technique	Survival status and associations
Hollenbeck et al ²⁵	Memorial Sloan Kettering (USA)	1982–2002	21	21	Synthetic graft: 2 (10%) Patch: 1 (5%) Primary: 7 (33%) Ligation: 11 (52%)	5 year OS 33% Median OS: 58 months Shorter survival with positive margin status
Kieffer et al ³⁹	Pitie-Salpetriere University (France)	1979–2004	19	19	Synthetic graft: 13 (68%) Patch: 1 (5%) Ligation: 5 (26%)	5 year OS 35% Median OS: 36 months
Schwarzbach et al ¹⁵	University of Heidelberg (Germany)	1988–2004	25	11	Synthetic graft: 6 (55%) Patch: 3 (27%) Primary: 2 (18%)	5 year OS 67% ^a Shorter survival with positive margin status
Kuehnl et al ³³	Ludwig Maximilians University (Germany)	1991–2006	35	10	Synthetic graft: 8 (80%) Patch: 2 (20%)	Median OS: 34 months Shorter survival with positive margin status
Ito et al ¹⁶	Brigham and Women's Hospital (USA)	1990–2006	20	20	Synthetic graft: 5 (25%) Primary: 12 (60%) Ligation: 3 (15%)	5 year OS 62% Median OS: 71 months No prognostic association with OS Shorter DFS with tumor size >9 cm
Fiore et al ¹⁷	IRCCS (Italy)	2004–2011	15	15	Synthetic graft: 2 Homograft: 8 Patch: 1 Ligation: 4	OS 80% at 31 month median follow up
Mann et al ⁴⁰	University of Washington & Wake Forest (USA)	1984–2009	17	17	Synthetic graft: 7 (41%) Primary: 5 (33%) Ligation: 5 (33%)	5 year OS 56%
Quinones-Baldrich et al ¹⁸	UCLA (USA)	1990–2011	47	36	Synthetic graft: 27 ^a Patch: 9 ^a Primary: 11 ^a	5 year OS 45% ^a Shorter survival with extensive IVC replacement compared to primary or patch
Poultides et al ¹⁹	Stanford University (USA)	2000–2014	50	15	Synthetic graft: 8 (53%) Allograft: 2 (13%) Patch: 2 ^a Primary: 5 ^a	5 year OS 59% ^a Shorter survival with high tumor grade and presence of synchronous metastases. Equivalent OS to RPS without vascular resection
Illuminati et al ⁴¹	University of Rome (Italy)	1993–2014	27	18	Synthetic graft: 18 (100%)	5 year OS 54%
Cananzi et al ³⁴	HCRC Rozzano (Italy)	2000–2012	11	11	Synthetic graft: 4 (36%) Primary: 4 (36%)	5 year OS 78% Median OS: 71 months

Reference	Institute(country)	Inclusion period	Total no. malignant vascular involvement	RPS with IVC resection	Reconstruction technique	Survival status and associations
Radaelli et al ²⁰	IRCCS (Italy)	2000–2013	105	29	Ligation: 3 (27%) Synthetic graft: 11 (38%) Allograft: 14 (48%) Primary: 1 (3%) Ligation: 3 (10%)	Shorter survival with presence of residual disease Median OS: 120 months ^a Shorter survival with older age, higher grade and larger tumor diameter
Bertrand et al ²¹	ICM (France) Saifee Hospital (India)	2000–2013	31	13	Synthetic graft: 31 ^a Primary: 3 ^a Ligation: 3 ^a	3 year OS 61% ^a Shorter survival with positive margin status
Roland et al ⁴²	MD Anderson (USA)	1993–2012	63 ^b	42 ^b	Reconstruction ^c : 30 (71%) Ligation: 12 (29%)	5 year OS 65% Shorter survival with high expression of cytoplasmic β -catenin and insulin growth factor 1 receptor

NR, not reported; OS, overall survival.

^aUnable to differentiate IVC specific details among a total cohort of vascular resections with sarcoma surgery.

^b26 of initial 63 resected at MDACC.

^cNo differentiation between primary repair, patch or graft.