# Sarcoma Resection With and Without Vascular Reconstruction: A Matched Case-Control Study

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## INTRODUCTION

Sarcomas are a heterogeneous group of rare malignancies with variable presentation, behavior and outcome. Although our understanding of their natural history following resection has evolved considerably over the recent years,[1] these tumors are still in many cases resistant to standard chemotherapy or radiotherapy modalities and surgical resection remains the cornerstone of treatment.[2] Often, the ability to completely remove the tumor is affected by its relationship to major blood vessels. Traditionally surgeons have been reluctant to perform major vascular resections for this disease, due to the inherently increased complexity of these operations and the uncertainty about the long-term oncologic benefit. Over the last decade, several case series have established the feasibility and safety of en bloc vascular resection for sarcomas of the extremity,[3-7] retroperitoneum,[8-10] or specifically the inferior vena cava (IVC).[11-18] What remains unknown is whether these complex procedures are associated with a durable prolongation of survival that justifies their morbidity. Our institution has previously reported our findings with major blood vessel reconstruction on 14 sarcoma patients undergoing surgical resection.[19] The current study provides an update on this initial experience and attempts to further compare these patients in a matched case-control fashion with a separate cohort of sarcoma patients during the same time period who did not require en bloc vascular resection but had similar clinicopathologic characteristics.

## METHODS

The study population includes patients who underwent surgical resection for sarcoma of any anatomic site between 2000 and 2014 at our institution. Patients were identified from the

Stanford Cancer Registry through the appropriate use of ICD-9 (International Classification of Diseases) and CPT **(**Current Procedural Terminology) codes, following Institutional Review Board approval. The patients who underwent sarcoma resection with vascular reconstruction were matched with 2 additional patients who underwent sarcoma resection without vascular reconstruction. Case matching was performed on 6 established clinocopathologic predictors of outcome for sarcoma: anatomic site, histologic type, grade, size, presence of synchronous metastasis, and whether resection was performed for primary versus recurrent disease (primary vs. repeat resection). Patients with R2 resections (macroscopically positive margins) were excluded, but patients who had M1 disease at operation were included. Data on patient demographics, clinicopathologic characteristics, and intraoperative variables were collected. Endpoints included perioperative morbidity, mortality, margin status, local recurrence, and survival. Surgical complications were graded using the modified Clavien-Dindo classification.[20]

Repeat review of pathology slides of the VASC patients was undertaken by a single sarcoma-dedicated pathologist, to assess the level of histologic infiltration (if any) of the resected vascular structures by the tumor. The pathologist was blinded to the survival outcome. This retrospective study was approved by the Stanford Hospital and Clinics Institutional Review Board.

In general, our institutional practice when vascular involvement is suspected on preoperative contrast-enhanced cross-sectional imaging (Computed Tomography or Magnetic Resonance Imaging) is for patients to be referred by the surgical or orthopedic oncologist to the vascular surgeon for a preoperative discussion and assessment of vascular reconstruction options and conduit selection. Postoperatively, the two teams follow the patients jointly both throughout their hospitalization and outpatient follow-up. Cross-sectional imaging used to detect tumor

recurrence is also utilized to monitor vascular patency, in addition to the use of vascular ultrasound.

Categorical variables were presented as absolute counts (percentages) and compared using the Mantel-Haenszel test. Continuous variables were presented as medians (range) and compared using within-subjects ANOVA (analysis of variance).[21] Survival probabilities were calculated using the Kaplan-Meier method and compared using the log-rank test. Univariate and multivariate Cox proportional hazard models were created to identify prognostic factors associated with overall survival (OS). A two-sided P value of $< 0.05$ was considered statistically significant.

## RESULTS

From 2000 to 2014, 50 patients (cases) who underwent sarcoma resection with vascular reconstruction (VASC) were identified, representing 5% of 1,009 patients undergoing sarcoma resection at our institution during the same time period. Slightly more than half (54%) of these 50 patients (cases) were for retroperitoneal sarcomas and four representative cases are illustrated in **Figure 1**. Overall, 69 vessels were reconstructed in these 50 patients: 14 patients had arterial, 19 arterial and venous and 17 venous only reconstructions. The distribution of vessels reconstructed is shown in **Table 1** and the types of reconstruction (interposition graft, patch repair, or primary repair) and choice of conduit are shown in **Table 2**.

The 50 VASC cases were matched in a 1:2 ratio with 100 patients (controls) who underwent resection of sarcomas with similar clinicopathologic characteristics but did not require vascular reconstruction (NO VASC). A comparison of basic clinicopathologic

characteristics between the two groups is shown in **Table 3** and confirms that the two groups were adequately matched for site, histology, grade, size, synchronous metastasis, and primary versus repeat resection. The two groups were eventually found to be comparable by age, gender, margin positivity, and presence of comorbidities. Neoadjuvant chemotherapy and radiotherapy was more commonly utilized for VASC patients, whereas the rates of intraoperative radiotherapy and adjuvant chemotherapy or radiotherapy did not differ between the two groups.

A comparison of perioperative morbidity and mortality is shown in **Table 4**. The VASC group had approximately twice the estimated blood loss, operative time and intraoperative transfusion rate of the NO VASC group. Similarly, the rates of any (74% vs. 44%, P = 0.002) and of major (Clavien grade 3 or higher, 38% vs. 18%, P = 0.024) complications within 30 days were significantly higher in the VASC group. As a result, median length of stay was longer by 3 days. Return to the operating room within 30 days was twice as common for the VASC group (18% vs. 9%), however this difference did not reach statistical significance. Reasons for 30-day reoperation in the VASC group included acute limb ischemia (n=3, two requiring graft thrombectomy and one hip disarticulation), intestinal perforation (n=2, one leading to a prosthetic iliofemoral graft infection), postoperative bleeding (n=2, both unrelated to the vascular reconstruction) and extremity wound dehiscence (n = 2). In the NO VASC group, reasons for reoperation included: intestinal perforation (n=2), extremity wound hematoma (n=2), extremity wound infection (n=2), wound dehiscence (n=2, one abdominal and one trunk incision), and orthopaedic hardware infection (n=1).

The 2% 30-day and 6% 90-day mortality in the VASC group were not significantly different than the corresponding rates seen in the NO VASC group (0% and 2%). The single 30-day mortality in the VASC group was secondary to postoperative bleeding, which was unrelated

to the vascular reconstruction (primary repair of the juxtarenal IVC in this case). The two additional 90-day mortalities in the VASC group occurred after discharge from the hospital (to skilled nursing facilities) but appeared to be related to postoperative complications. The two 90-day mortalities in the NO VASC group included a death at home of unknown etiology and a death from rapid progression of disease postoperatively.

Median follow-up was 24 months for the VASC and 28 months for the NO VASC patients. Overall survival after resection was similar between the VASC and NO VASC groups (5-year 59% vs. 53%, P = 0.67, **Figure 2A**). Similarly, when various subset analyses were performed, no subgroup of patients was identified (retroperitoneum or extremity/trunk, high or low/intermediate grade, R1 or R0, tumor size > 10 cm or < 10 cm, synchronous M1 or M0, primary surgery or for recurrence) in whom a difference in overall survival was noted between the VASC and NO VASC patients (data not shown). Furthermore, on multivariate analysis, high tumor grade and presence of synchronous metastases were independent predictors of overall survival, however there was still no association between the need for vascular reconstruction and overall survival (**Supplemental Table**). Last, as local control is another significant endpoint in the assessment of the efficacy of surgical resection for any given tumor we specifically evaluated the time to local recurrence between the two groups: again, 5-year local recurrence rates were similar between the two groups (51% vs. 54%, P = 0.119, **Figure 2B**).

We sought to examine whether specific factors within the VASC cohort, such as the type of vessel involved or the presence of true pathologic vessel invasion, were predictive of long-term outcome. We found no association between the type of vascular involvement (arterial vs. venous) and overall survival (**Figure 2C**). Furthermore, pathology slides for 34 of the 50 VASC cases were available for re-review to specifically assess vessel wall invasion histologically.

Histologic vessel wall invasion by sarcoma was noted in 21 (62%) of 34 patients and was more common in resected veins (18/26, 69%) than resected arteries (3/16, 19%). When stratified by sarcoma type, histologic vessel invasion was noted in all 10 leiomyosarcomas, 3 out of 7 liposarcomas, 2 out of 4 undifferentiated pleomorphic sarcomas and 1 out of 4 synovial sarcomas. Overall survival after resection did not appear to be associated with the presence of histology proven vessel wall invasion by the tumor (**Figure 2D**).

The patency rates of the vascular reconstructions are shown in **Figure 3**. The 5-year primary and assisted primary patency of arterial reconstructions for retroperitoneal sarcoma was 86% and 92%, and for extremity/trunk sarcoma 56% and 56%. There were three amputations among the 19 extremity patients (limb salvage rate of 84%). The 5-year primary patency of venous reconstructions for retroperitoneal sarcoma was 86% and for extremity/trunk sarcoma 63%. Graft infection was noted in three patients. A popliteal artery cryopreserved allograft had to be replaced by autologous vein 6 months postop due to the presence of an infected pseudoaneurysm. This patient had a free myocutaneous flap at the time of the initial operation for coverage of the resection bed, but flap ischemia required flap revision early in the postoperative period and likely contributed to the graft infection. The second case of graft infection was an iliac artery Dacron graft that got secondarily infected postoperatively after the patient developed colonic perforation. This graft was removed and replaced with contralateral superficial femoral vein. The third case of graft infection was an SMA Dacron graft that was noted 7 years postoperatively to erode through the posterior wall of the stomach on endoscopy. The graft had thrombosed, but the patient had developed collateral circulation to the midgut through the inferior mesenteric artery and did not have any signs of intestinal ischemia. The graft was removed without reconstruction. Long-term follow-up is not yet available for this case.

## DISCUSSION

The objective of our study was to examine the impact of concomitant vascular reconstruction on sarcoma resection outcomes. Given the fact that sarcomas involving major blood vessels are usually more extensive than ones without vascular involvement, we utilized a matched case-control methodology. The main finding was that the need for vascular reconstruction almost doubled the morbidity of these resections, but was associated with a comparable oncologic outcome (local recurrence and overall survival) to matched cases without vascular involvement. Our study reinforces previously reported findings of a smaller case-control study on 19 extremity sarcoma patients who underwent vascular reconstruction and were matched with 38 patients of similar age, tumor size, anatomic location, depth, and timing of radiotherapy, but without vascular involvement.[5] Although cases and controls in this previous study were not matched for the presence of synchronous metastases, when only M0 patients (n=40) were examined, the 5-year disease-free survival rates were similar at 83% and 74%. Our study corroborated this finding on a larger cohort of patients, with retroperitoneal and truncal in addition to extremity sarcomas as well as patients undergoing resection of both primary and recurrent disease.

The concept that long-term survival after resection may not be affected by the need for vascular resection and reconstruction has been demonstrated for a variety of other solid tumors. Specifically, several single-institution[22-25] and multi-institutional series[26] have demonstrated that patients with pancreatic adenocarcinoma who require portal vein resection have similar survival to resected patients not requiring portal vein resection. Similarly, our group has previously reported our experience on outcomes after resection of pancreatic neuroendocrine tumors with major vascular involvement,[27] and others have reported on outcomes after resection of locally

recurrent rectal cancer involving the aortoiliac axis,[28] with both studies showing long-term survival rates comparable to historical controls with locally advanced disease but not involving vascular structures. Taken together, these data indicate that major vascular involvement is not necessarily a predictor of aggressive tumor biology but rather a reflection of tumor size and location.

Histologically proven invasion of the resected vessel wall by sarcoma was noted in 62% of 34 patients at dedicated pathologic re-review. This number is higher than previously reported studies examining the frequency of histologic vessel infiltration found at concomitant vascular resection for retroperitoneal (32%),[10] and extremity sarcoma (43%),[7] and similar to corresponding studies on pancreatic adenocarcinoma (61%).[25,29] Histologic vessel invasion was less frequently noted in resected arteries (19%) than veins (69%) in our study, and the finding on arterial invasion is identical to a previous study of 37 sarcoma patients who underwent arterial resection and in whom the frequency of true pathologic invasion was 19%.[8] In the absence of clear-cut encasement or intraluminal tumor thrombus, our practice has been to initially attempt to dissect the tumor off the surrounding vessels. However, as noted herein and in several other studies,[7,8,10,25,29] true vascular invasion is difficult to differentiate intraoperatively from peri-tumoral inflammation and desmoplastic reaction. In addition, dissection of arteries and veins from abutting tumors can threaten their integrity, and formal vascular resection is sometimes necessary to prevent inadvertent venotomy or arteriotomy even in the absence of true invasion. Nonetheless, as reported by others specifically for pancreatic adenocarcinoma,[25] histologically proven vessel wall involvement was not associated with worse survival in our study.

Perhaps more controversial is the necessity, if any, to reconstruct a major vein that has been resected. In particular, the optimal management of the IVC after resection is debatable, with

some advocating ligation,[14,30] others selective,[12,31,32] and others routine reconstruction.[11,13,16,18] The rationale for the latter is based on the need to resect several venous collaterals for complete tumor removal, as well as the inability to predict which patients will tolerate IVC ligation without subsequent renal insufficiency or significant lower extremity edema. Our study was not designed to address this specific question. Due to the nature of our search (CPT codes), we were unable to discern whether there were additional cases in which a major vein was resected and simply ligated without being reconstructed. In general, we do not advocate venous reconstruction in cases where the venous structure is chronically occluded, the patient does not have lower extremity edema, and the existing collateral pathways (gonadal, adrenal vein, and abdominal wall collaterals for retroperitoneal tumors and greater saphenous vein for extremity tumors) are maintained during oncologic resection.

Nine (15%) of the 61 interposition graft reconstructions in our series were performed with cryopreserved cadaveric allografts, typically in the setting of a clean contaminated field. The safety and efficacy of cryopreserved allografts for aortoiliac reconstruction in the setting of infection has been recently established through a multi-institutional US study of 220 patients with a mean follow-up of 30 months, reporting low rates of aneurysm formation, recurrent infection, aortic blowout, and limb loss.[33] Our limited experience with three aortoiliac reconstructions for patients with concomitant intestinal resection has similarly shown no instances of allograft occlusion or infection. When used for venous reconstructions, however, cryopreserved allografts have been shown to have decreased patency rates: in a series of 8 patients undergoing IVC replacement with cryopreserved allografts for retroperitoneal sarcoma, graft occlusion was observed in half of the patients (three late and asymptomatic and one early and symptomatic) likely due to the susceptibility of the pliable allograft to compression from

abdominal viscera.[12] We have used cryopreserved allografts to reconstruct the IVC in two instances, one of which was complicated by early and symptomatic graft thrombosis. For this reason, we, and others,[11,18] favor IVC reconstruction with externally supported (ringed) polytetrafluoroethylene (PTFE) graft, in cases where there is no bowel contamination. We have utilized this approach in 8 patients in this study with no instances of graft infection and only one case of thrombosis in a patient who developed heparin-induced thrombocytopenia and thrombosis (HITT).

Our findings should be interpreted with caution as the relatively short follow-up in our study might have led to misclassification of certain study endpoints (death, recurrence) or under-detection of long-term vascular graft-related complications (patency, graft infection, anastomotic pseudoaneurysm). Furthermore, there are inherent selection biases submerged in any retrospective analysis that are difficult to control for. Patients in whom vascular resection was undertaken (cases) likely represent a select group with robust performance status and overall candidacy for aggressive treatment, an attribute that might have not been consistently true for controls, despite our efforts to match cases and controls on a variety of important clinicopathologic factors. Last, the lack of reliable information on cause of death for a large number of patients led us to choose overall (as opposed to disease-specific) survival as our primary endpoint. It is very likely, however, that the vast majority of the patients in this study, who died during follow-up, did indeed die of sarcoma, as this cohort includes patients with advanced disease (20% recurrent, 20% with synchronous metastasis, more than half larger than 10 cm, more than half retroperitoneal, and more than half high grade). Therefore, we feel that overall survival represents an accurate and reliable measure of treatment efficacy in this select group of sarcoma patients.

In conclusion, the need for vascular resection and reconstruction should not be a deterrent to resection for sarcoma patients, as the oncologic outcome (overall and local recurrence free survival) appears equivalent to matched cases without vascular involvement. The need for vascular reconstruction essentially doubles the morbidity of these operations, whose technical complexity spans across surgical disciplines. Meticulous multidisciplinary planning and close collaboration between surgical oncologists, orthopaedic oncologists, and vascular surgeons is critical for a successful outcome.

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**LEGENDS**

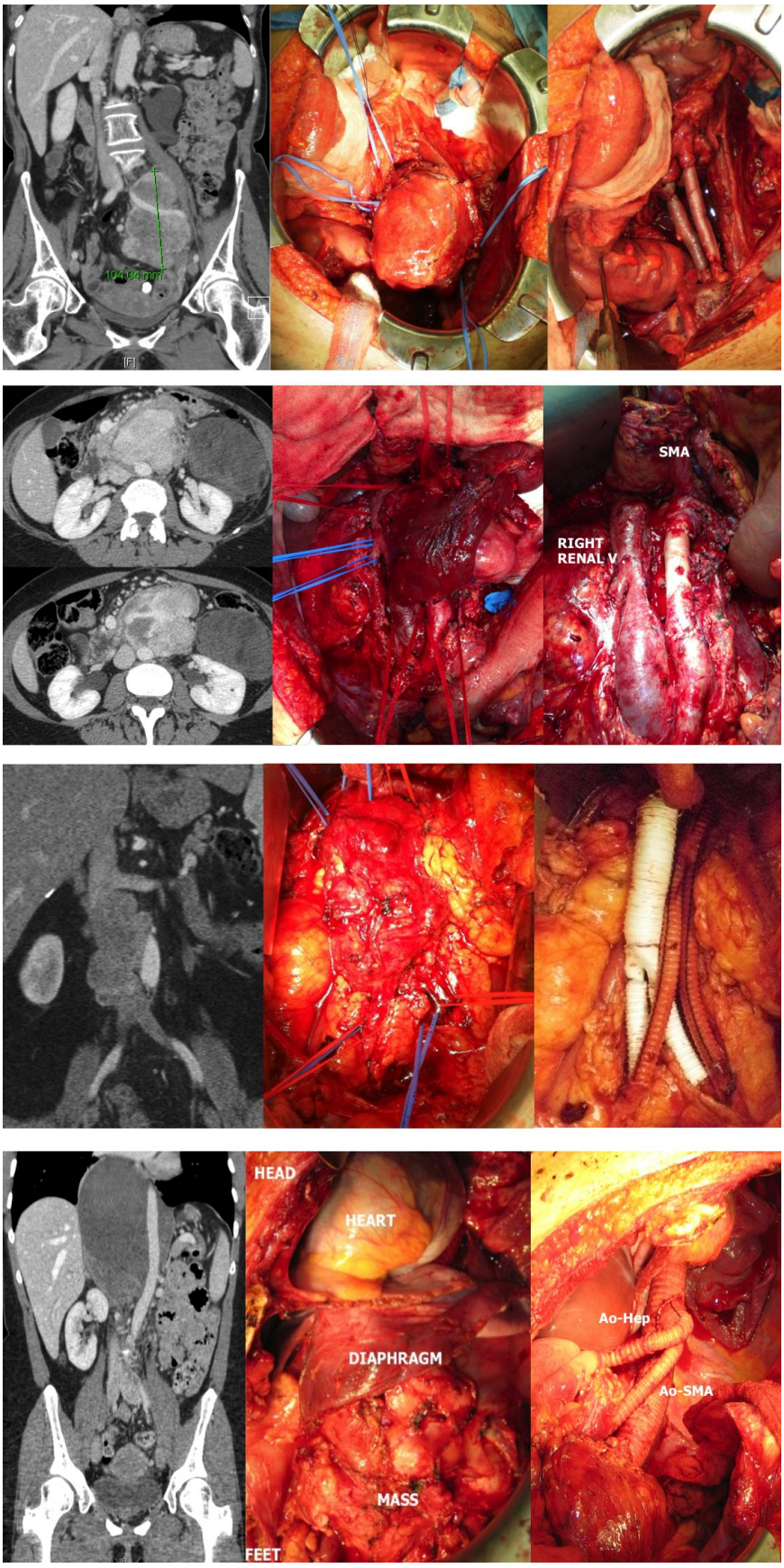
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**FIGURE 1.** Preoperative computed tomography images (left), intraoperative image of the tumor with involved vessels (middle) and of the completed vascular reconstruction (right) in four patients who underwent retroperitoneal sarcoma resection with en bloc major blood vessel resection and reconstruction. Each row represents a different patient (with the head oriented towards the top and the feet towards the bottom of the picture). **First row:** Left lower quadrant leiomyosarcoma encasing the iliac artery and vein; both vessels were reconstructed with cryopreserved iliac artery allografts given the need for sigmoid colectomy. **Second row:** Well-differentiated liposarcoma of the root of the mesentery involving the aorta (180 degrees) and the IVC (< 180 degrees). The third and fourth portions of the duodenum were resected en bloc and the pancreas and SMA have been dissected off and are retracted superiorly. The infrarenal aorta was replaced with a cryopreserved aortic allograft and the anteromedial portion of the IVC was excised and primarily repaired. **Third row:** Infrarenal IVC leiomyosarcoma encasing the aorta. The aorta was replaced with an aortoiliac Dacron (polyethylene terephthalate) graft and the IVC with an iliocaval ringed PTFE (polytetrafluoroethylene) graft. **Fourth row:** Fibromyxoid sarcoma encasing the thoracoabdominal aorta. This was replaced with a Dacron graft with additional grafts to the hepatic, SMA, and left renal arteries.

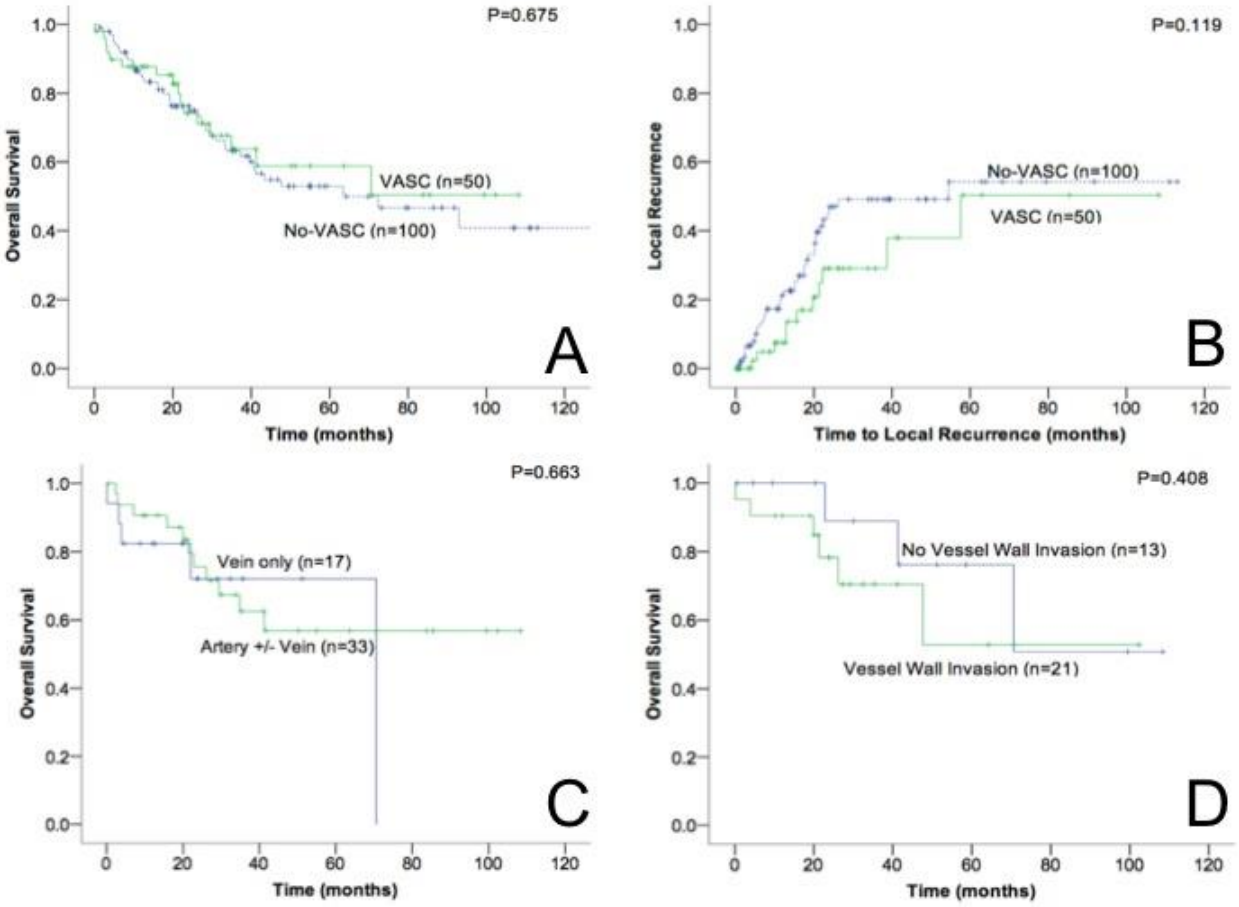


**FIGURE 2.** Comparison of overall survival (A) and time to local recurrence (B) between the VASC and NO VASC groups. Comparison of overall survival (C) based on whether vascular resection involved arterial or venous structures only (VASC patients only). Comparison of overall survival (D) based on whether the vessel removed was histologically invaded by sarcoma (VASC patients only).

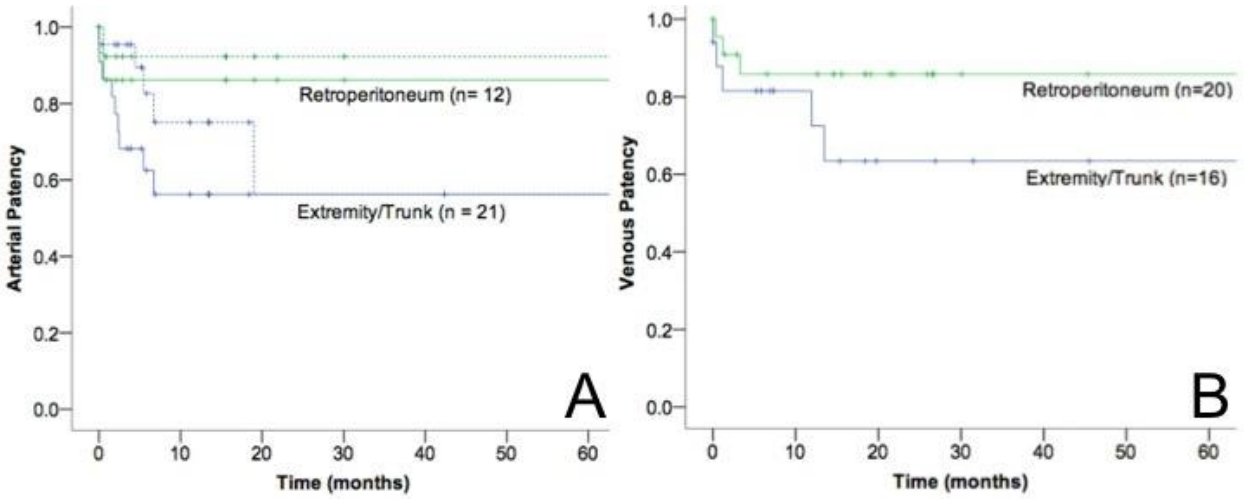


**FIGURE 3.** Patency rates (continuous line: primary patency, dashed line: assisted primary patency) of arterial (A) and venous (B) reconstructions stratified by anatomic site.

**TABLE 1.** Types of Vessels Reconstructed in 50 Sarcoma Patients

| **Artery only** (n = 14) | **Artery and Vein** (n=19) | **Vein only** (n=17) |
|---|---|---|
| Aorta (n=4)* | Aorta and IVC (n=2) | IVC (n=13)** |
| Iliac (n=2) | Iliac (n=4) | Iliac (n=1) |
| Femoral (n=3) | Femoral (n=9) | Femoral (n=1) |
| Popliteal (n=1) | Popliteal (n=3) | |
| Posterior Tibialis (n=1) | | |
| Subclavian (n=2) | | Subclavian (n=1) |
| | Brachial a. and Basilic v. (n=1) | |
| SMA (n=1) | | SMV/PV (n=1) |

*, one case with aorto-hepatic, aorto-SMA, and aorto-renal bypass

**, one case with reimplantation of the left renal vein

IVC, inferior vena cava; SMA, superior mesenteric artery; SMV, superior mesenteric vein; PV, portal vein; SVC, superior vena cava

**TABLE 2.** Types and Conduits Used for 69 Vascular Reconstructions in 50 Sarcoma Patients

| | | **Arterial Reconstructions** (n = 33) | | **Venous Reconstructions** (n = 36) | |
|---|---|---|---|---|---|
| | | Retro peritoneal (n = 12) | Extremity/ Trunk (n = 21) | Retro peritoneal (n = 20) | Extremity/ Trunk (n = 16) |
| Interposition Graft | Autologous Vein | | 18 | 1 | 13 |
| | PTFE | 3 | 2 | 9 | 1 |
| | Cryopreserved Allograft | 3 | 1 | 3 | 2 |
| | Dacron | 5 | | | |
| Patch Repair | Autologous Vein | | | 1 | |
| | Xenograft | | | 1 | |
| | Cryopreserved Allograft | 1 | | | |
| Primary Repair | | | | 5 | |

PTFE, polytetrafluoroethylene

Dacron, polyethylene terephthalate

**TABLE 3.** Clinical and Pathologic Characteristics
ASA, American Society of Anesthesiologists

| | **VASC (n = 50)** | **NO VASC (n = 100)** | **P** |
|---|---|---|---|
| Age (years) | 56 (9-90) | 57 (12-88) | 0.61 |
| Female Gender | 27 | 54 | 1 |
| Site | | | 1 |
| • Trunk | 4 | 8 | |
| • Extremity | 19 | 38 | |
| • Retroperitoneal | 27 | 54 | |
| Primary Operation (versus for recurrence) | 40 | 80 | 1 |
| Synchronous Metastasis | 11 | 20 | 0.78 |
| Histologic Type | | | 1 |
| • Leiomyosarcoma | 14 | 28 | |
| • Dedifferentiated Liposarcoma | 7 | 14 | |
| • Undifferentiated Pleomorphic Sarcoma | 5 | 10 | |
| • Synovial Sarcoma | 5 | 10 | |
| • Desmoid | 5 | 10 | |
| • Myxoid Liposarcoma | 3 | 6 | |
| • Well differentiated Liposarcoma | 2 | 4 | |
| • Endometrial Stromal Sarcoma | 2 | 4 | |
| • Fibromyxoid sarcoma | 2 | 4 | |
| • Extraskeletal Osteosarcoma | 2 | 4 | |
| • Chondrosarcoma | 1 | 2 | |
| • Angiosarcoma | 1 | 2 | |
| • Peripheral Nerve Sheath Tumor | 1 | 2 | |
| Grade | | | 0.83 |
| • Low | 14 | 28 | |
| • Intermediate | 11 | 18 | |
| • High | 25 | 54 | |
| Tumor Size (cm) | 11 (2-36) | 12 (2-36) | 0.77 |
| R1 Margins | 12 | 24 | 1 |
| Any Comorbidity | 29 | 48 | 0.25 |
| ASA Score 3 or 4 | 28 | 49 | 0.42 |
| Neoadjuvant Radiation (n=148) | 14 (27%) | 13 (13%) | **0.039** |
| Neoadjuvant Chemotherapy (n=148) | 10 (20%) | 8 (8%) | **0.037** |
| Intraoperative Radiation (n=149) | 10 (20%) | 14 (14%) | 0.360 |
| Adjuvant Chemotherapy (n=141) | 15 (32%) | 31 (33%) | 0.90 |
| Adjuvant Radiation (n=141) | 9 (19%) | 31 (33%) | 0.090 |

**TABLE 4.** Perioperative Morbidity and Mortality

| | **VASC (n = 50)** | **NO VASC (n = 100)** | **P** |
|---|---|---|---|
| Estimated Blood Loss (ml) | 850 (50-30,000) | 400 (5-14,500) | **0.0036** |
| Operating Time (minutes) | 430 (88-930) | 209 (28-900) | **<0.0001** |
| Blood Transfusion (n=141) | 33 (66%) | 30 (33%) | **<0.001** |
| Any Other Organ Resection* | 18 (67%) | 41 (76%) | 0.38 |
| Nephrectomy* | 14 (52%) | 27 (50%) | 0.87 |
| Bowel Resection* | 8 (30%) | 22 (41%) | 0.33 |
| Pancreatectomy* | 2 (7%) | 14 (26%) | 0.06 |
| Any Complication | 37 (74%) | 44 (44%) | **0.002** |
| Grade 3 or Higher Complication | 19 (38%) | 18 (18%) | **0.024** |
| Reoperation within 30 days | 9 (18%) | 9 (9%) | 0.11 |
| IR Drain for Collection | 7 (14%) | 4 (4%) | 0.06 |
| Sepsis | 4 (8%) | 5 (5%) | 0.59 |
| Reintubation | 0 (0%) | 3 (3%) | 0.55 |
| Renal Failure Requiring Dialysis | 2 (4%) | 0 (0%) | 0.13 |
| Wound Dehiscence | 5 (10%) | 7 (7%) | 0.68 |
| Wound Dehiscence (Extremity only n=57) | 3 (16%) | 7 (18%) | 0.86 |
| Discharge to Nursing Facility | 10 (20%) | 11 (11%) | 0.17 |
| Readmission within 90-days | 19 (37.3) | 22 (24.4) | 0.11 |
| 30-Day Mortality | 1 (2%) | 0 (0%) | 0.30 |
| 90-day Mortality | 3 (6%) | 2 (2%) | 0.24 |
| Length of Stay (days) | 10 (3-55) | 7 (1-63) | **0.005** |

* Among patients with retroperitoneal sarcomas (27 VASC and 54 NO VASC)
IR, Interventional Radiology

**SUPPLEMENTAL TABLE.** Univariate and Multivariate Analyses of Factors Associated with Overall Survival

| | **Univariate Analysis** | | **Multivariate Analysis** | |
|---|---|---|---|---|
| | **Hazard Ratio** (95% Confidence Interval) | **P** | **Hazard Ratio** (95% Confidence Interval) | **P** |
| Age (per year) | 1.02 (1.01-1.03) | **0.006** | 1.02 (1.00-1.04) | 0.086 |
| Female | 0.62 (0.38-1.06) | 0.081 | - | |
| Any Comorbidity | 2.08 (1.19-3.63) | **0.009** | 1.26 (0.65-2.45) | 0.497 |
| R1 Margin | 1.95 (1.12-3.38) | **0.017** | 1.76 (0.95-3.27) | 0.073 |
| Synchronous Metastasis | 2.19 (1.21-3.94) | **0.009** | 2.37 (1.26-4.47) | **0.007** |
| Vascular Reconstruction | 0.88 (0.49-1.58) | 0.675 | 0.94 (0.52-1.70) | 0.844 |
| Tumor Size (per cm) | 1.03 (0.99-1.06) | 0.069 | - | |
| Retroperitoneum vs. Extremity/Trunk | 2.01 (1.16-3.48) | **0.013** | 1.71 (0.92-3.18) | 0.092 |
| High Grade | 3.09 (1.72-5.56) | **<0.001** | 2.93 (1.60-5.35) | **<0.001** |
| Surgery for Recurrence | 1.12 (0.57-2.17) | 0.740 | - | |
| Preoperative Chemotherapy | 1.66 (0.81-3.40) | 0.165 | - | |
| Preoperative Radiation | 1.55 (1.83-2.90) | 0.167 | - | |