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Objective: **This study analyzed the outcomes of a series of consecutive patients diagnosed with a retroperitoneal soft tissue sarcoma (RSTS) with vascular involvement and who underwent a multidisciplinary operation.**
Methods: **Between 2000 and 2013, 126 patients were referred for oncovascular surgery in our institution. Among these, 31 consecutive patients underwent operations for RSTS with vascular involvement. A vascular/oncologic team determined the surgical strategy preoperatively.**
Results: **Median follow-up was 34.4 months (interquartile range, 48.1 months). Twenty patients (65%) were referred for primary RSTS and 11 (35%) for local recurrence. The most common histologic diagnosis was liposarcoma (54.8%), mainly high-grade and intermediate-grade RSTS. Prosthetic grafts were usually used for vascular reconstruction. Median hospital stay was 17 days (interquartile range, 14.5; range, 7-190 days). The grade 3 and 4 morbidity rate was 19.3%. Each resection was macroscopically complete (R0-R1). Median progression-free survival was 10 months, and median overall survival was not reached. Overall survival rates were 77.4% at 1 year and 61.3% at 3 years.**
Conclusions: **Vascular resection and reconstruction are safe and feasible in case of RSTS. The morbidity rate was acceptable, and there were no perioperative deaths. Despite recurrence rates that remain high, oncovascular resection enhances resection margins and allows encouraging survival results for patients often considered as nonresectable.**

Retroperitoneal soft tissue sarcomas (RSTSs) are rare and often difficult to manage.[1] Surgical resection is the cornerstone of their treatment, and the capacity to achieve an R0 resection during the primary resection attempt is essential for any chance of potential cure or long-term survival.[2-4]

The standard treatment of these lesions is compartmental resection and an en bloc resection of the tumor mass and of the adjacent organs and tissues.[3,5,6] In a subset of patients, RSTSs involve major blood vessels, either being in contact with the vessel tissue or encasing it. In such patients, compartmental resection including resection of the major blood vessel concerned, and often its reconstruction, must be discussed.

Data concerning the significance of blood vessels involvement in RSTSs are lacking. The correct way to manage such patients is still unclear because vascular involvement might be considered as an indicator of nonresectability. Curative surgery in a variety of tumor locations can be achieved even in this complex subset of patients thanks to a detailed preoperative planning that includes vascular and surgical oncology specialists.[7]

Scant data exist regarding the outcomes of patients undergoing compartmental resection for RSTSs associated with an en bloc resection of the major blood vessels.[8] The aim of our study was to analyze the surgical and oncologic outcomes of a consecutive series of patients who were diagnosed a RSTS with vascular involvement and who underwent a multidisciplinary operation and follow-up.

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METHODS

The local Ethics Committee Review Board approved the protocol for this study and waived the requirement for informed consent because of its retrospective character. The study was conducted according to the Declaration of Helsinki and European Good Clinical Practice. Patients were informed that their clinical and scientific data could be used for scientific purposes before their care in our institution.

Patients and diagnosis

Between January 2000 and December 2013, 126 patients underwent multidisciplinary oncovascular surgery in our institution; among these, 31 RSTSs were included in the study (Fig 1). Our deliberate policy is to perform joint interventions for patients with planned oncovascular

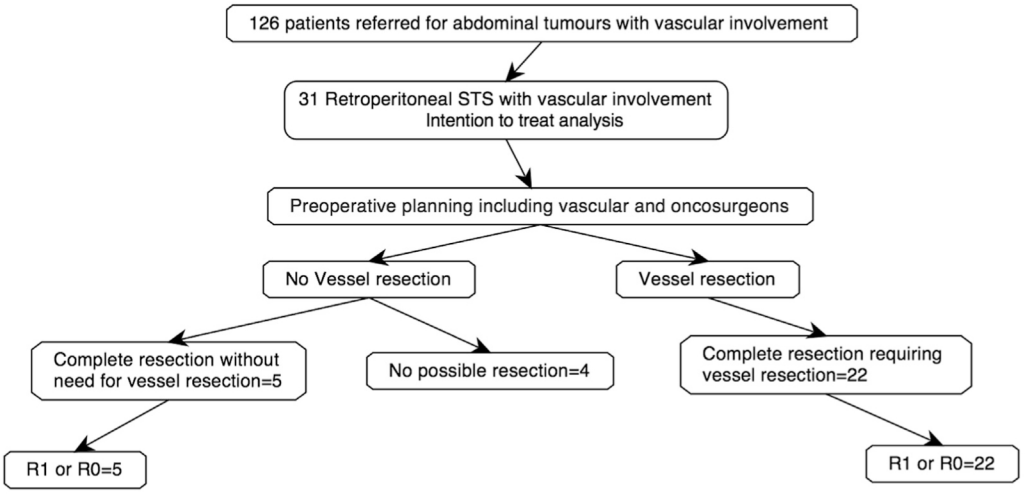

Fig 1. Flowchart of the study. *STS,* Soft tissue sarcomas.

resection. The decision-making algorithm depends on the grade determined on the preoperative biopsy specimen and on the type of vascular involvement contact versus the extent of invasion.

All patients had preoperative magnetic resonance imaging or computed tomography (CT) imaging and underwent preoperative image-guided core needle biopsy with a 14- or 16-gauge coaxial needle. The RSTS grade was determined by the degree of cellularity, differentiation, pleomorphism, necrosis, and mitotic activity and categorized in FNCLCC (Fédération Nationale des Centres de Lutte Contre le Cancer) grades. An expert pathologist established the histologic diagnosis according to the World Health Organization classification.

Surgical intervention

Each patient was first evaluated in a multidisciplinary oncologic board as recommended in the field. Patients for whom the therapeutic strategy included surgery were then discussed in a second staff meeting gathering of vascular and oncologic surgeons. The operative strategy was determined according to the RSTS subtype, grade, and findings on preoperative imaging. All patients with grade 2 and 3 sarcomas underwent compartmental resection, including systematic resection of uninvolved contiguous organs to obtain free margins and containment. This often involved kidney, psoas muscle, and when necessary, distal pancreatectomy, splenectomy, or intestinal resections. The completeness of surgical resection was defined using the International Union for Cancer Control (UICC) classification (R0, cure or complete resection with no residual tumor; R1, microscopic residual tumor; R2, macroscopic residual tumor).

Vascular involvement

Involvement of major vessels was confirmed on preoperative imaging when it did not show a rim of normal tissue in the tumor-to-vessel interface. The multidisciplinary team in these cases consisted of oncologic and vascular surgery experts, and the strategy was determined based on the supposed vessels involved and the extent of their involvement.

Reconstruction strategy

Reconstructions were performed using three types of prosthetics: standard (polytetrafluoroethylene [PTFE] or Dacron [DuPont, Wilmington, Del]), externally supported (PTFE) for reconstructions of large veins, or silver-coated to minimize the risk of infection in case of concomitant digestive anastomosis.

Arterial reconstruction. Except for internal iliac arteries, major arteries were always reconstructed. Primary anastomoses, reinsertion, or synthetic prostheses were used depending on the length of the resected vessel. Autologous venous grafts were not used.

Venous reconstruction. Reconstruction of involved and patent veins with no evidence of thrombosis on the preoperative scan was always performed with synthetic prostheses (except for the internal iliac vein, which was not reconstructed when involved). Conversely, when venous thrombosis was observed, with establishment of a collateral circulation, no reconstruction was performed to avoid any risk of postoperative embolism (Fig 2).

Contralateral renal vessels management. When the tumor was in contact with the inferior vena cava or with the juxtarenal aorta, the contralateral renal vessels were reconstructed to preserve renal function. The left renal vein was reconstructed as often as possible, even if a functional renal-azygos-lumbar arch was detected on preoperative imaging, to increase the flow in the inferior vena cava and enable a second resection of the pedicle in case of local recurrence (Fig 2).

Adjuvant therapy

For patients with high-grade RSTS, adjuvant chemotherapy was discussed in oncologic postoperative board,

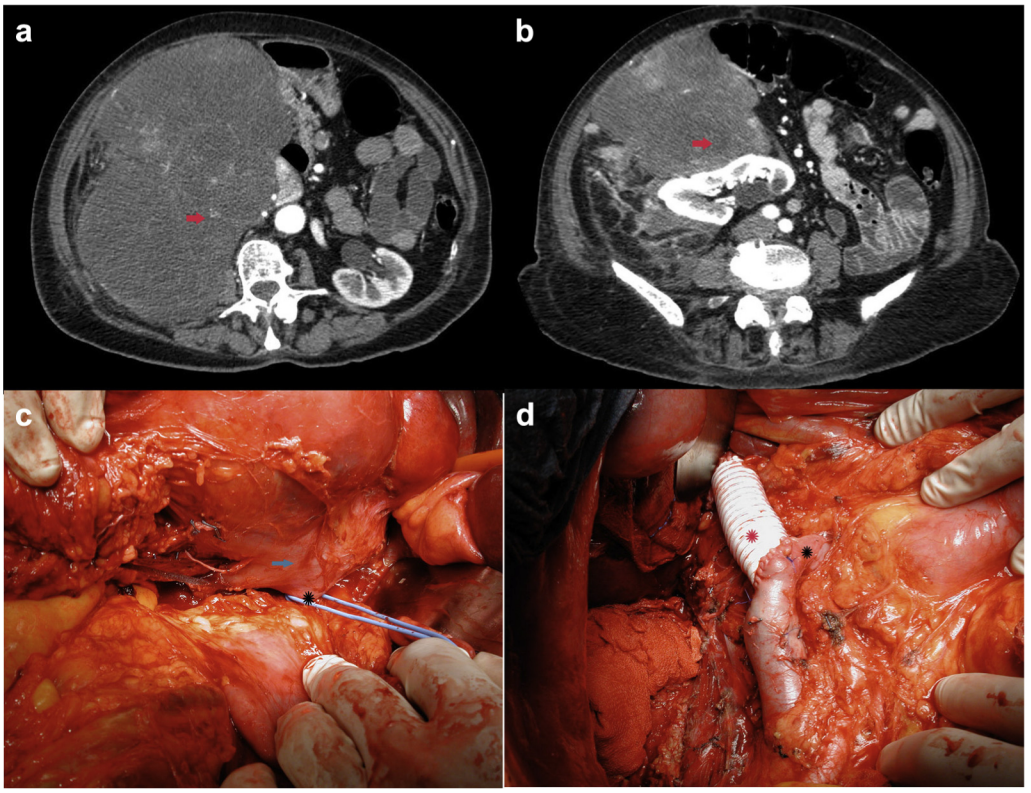

Fig 2. **a** and **b,** Abdominal computed tomography (CT) scan shows a voluminous retroperitoneal soft tissue sarcoma (RSTS; *red arrow*) located in the right compartment encasing the inferior vena cava. **c,** Intraoperative view shows the large RSTS encasing the inferior vena cava (*green arrow*). **d,** Intraoperative view shows the resected inferior vena cava replaced by a prosthetic graft (*red star*) and the preservation of the left renal vein (*black star*).

considering anatomopathologic results and surgical margins. For patients with large tumors, indication for adjuvant therapy was determined by the tumor grade, the estimated histologic aggressiveness of the tumor, and the surgical margins. Patients who underwent a R1 resection were administered radiotherapy or chemotherapy, or both, in the adjuvant setting.

Follow-up

Patients were seen every 4 months for the first 2 years and every 6 months afterwards. To check for recurrences, patients underwent a clinical examination and CT angiography or magnetic resonance imaging. CT scans were used to determined the patency of the arterial and venous reconstructions.

Statistical analysis

Analyses were performed in intention-to-treat including the 31 patients with a planned oncovascular resection. Quantitative variables are described with medians and interquartile ranges (IQRs) when relevant and qualitative variables with percentages. Overall survival (OS) and progression-free survival (PFS) were calculated using the Kaplan-Meier method. The log-rank test was performed to compare survival time distributions between curves regarding histologic margins, sarcoma subtypes, and grades. Two-sided P values were computed, and an effect was considered statistically significant at $P \leq .05$. Data were analyzed using SPSS 22 software (IBM Corp, Armonk, NY).

RESULTS

Patient characteristics

Among the 126 patients who underwent multidisciplinary oncovascular operations in our institution between 2000 and 2013, 31 patients, 17 men (54.8%) and 14 women (45.2%), presented with a RSTS for which a vascular resection was planned (Fig 1). The median age at diagnosis was 62.1 years (range, 25-80 years), the median tumor size was 12 cm (range, 4-32 cm), and median follow-up was 34.4 months (IQR, 48.1 months).

Referral was for a primary RSTS in 28 patients (65%) and for local recurrence in 11 (35%), of whom eight patients were diagnosed with the first local recurrence and three with the second local recurrence. Concomitant disseminated disease was discovered in the operative room in four patients (12.9%), including two with single hepatic metastasis and two with limited peritoneal sarcomatosis.

Table I. Clinical and pathologic factors in 31 patients with retroperitoneal soft tissue sarcomas (RSTSs) involving major blood vessels

Characteristics	*No. (%) (N = 31)*
Presentation status	
Primary tumor	20 (64.52)
Local recurrence	11 (35.48)
Metastasis at diagnosis	4 (12.90)
Histologic subtype	
Leiomyosarcoma	10 (32.26)
Liposarcoma	17 (54.84)
Dedifferentiated liposarcoma	14 (45.1)
Well-differentiated liposarcoma	3 (9.7)
Undifferentiated sarcoma	3 (9.68)
Synovial sarcoma	1 (3.23)
Tumor size, cm	
<5	2 (6.45)
5-10	13 (41.94)
>10	16 (51.61)
Tumor grade	
Grade 1	2 (6.45)
Grade 2	13 (41.94)
Grade 3	13 (41.94)

The most common histologic diagnoses were liposarcoma (54.84%) and leiomyosarcoma (32.26%). RSTS tumors were high grade (grade 3) in 42%, intermediate grade (grade 2) in 42%, low-grade (grade 1) in 6.5%, and one tumor could not be classified (Table I).

Twenty patients were treatment-naïve at baseline. Eleven patients with high-grade RSTSs received neoadjuvant therapy, consisting of chemotherapy (n = 5) in case of limited resectability aiming at achieving tumor shrinkage, or radiotherapy (n = 6) for a few patients included in the STRASS (Surgery With or Without Radiation Therapy in Treating Patients With Previously Untreated Nonmetastatic Retroperitoneal Soft Tissue Sarcoma) clinical trial (NCT01344018).

Surgical procedure

Resected organs and vessels. Among the 31 patients with planned vascular resection, tumor resection was not possible in 4 patients, comprising 2 patients with metastatic disease discovered at laparotomy, 1 with an important vascular involved considered too large to be resected (aortocaval plus celiac axis and superior mesenteric artery involvement), and 1 with an iliofemoral recurrence considered unresectable.

The most frequently resected organs were kidney (48.4%), small bowel (16.1%), pancreas (13.0%), and duodenum (9.7%). In the patients with local recurrence, nephrectomy had already been performed during the first operation. As implied by compartmental surgery, multivisceral resection was often necessary (Table II).

Among the 27 patients who had tumor resection, 5 patients (16.1%) with planned oncovascular surgery did not undergo vascular resection: 1 aged patient with poor general status, 2 with metastatic disease that

Table II. Resected organs during compartmental resection in 31 patients with retroperitoneal soft tissue sarcomas (RSTSs)

Resected organs	*No. (%) (N = 31)*
Kidney	15 (48.4)
Duodenum	3 (9.7)
Small bowel	5 (16.1)
Left colon	2 (6.5)
Right colon	2 (6.5)
Liver	2 (6.5)
Pancreas	4 (12.9)
Ureter	1 (3.2)
Stomach	2 (6.5)

was too extensive, 1 patient with a small bowel adenocarcinoma revealed during surgery, and 1 patient for whom vascular resection was considered not necessary and whose vessels were preserved.

One vessel was resected in 22.6% of patients, 2 in 29.0%, 3 in 32.3%, and 4 in 3.2%. The most commonly resected vessel was the inferior vena cava (42%), followed by the right external iliac artery (12.9%), the left renal vein (12.9%), the right external iliac vein (9.7%), and the common iliac arteries on either side (6.5% each; Table III).

Resectability limits. Setting resectability and nonresectability criteria is very difficult, especially in those difficult cases, and because it is surgeon dependent. Nevertheless, tumors that crossed the midline or invaded the liver were, in our study, not a priori considered a contraindication. Major technical difficulties that could be assessed by preoperative imaging included invasion of the mesenteric superior and the celiac axis, invasion of the vena cava above the hepatic veins, and invasion of the root of the mesentery. Setting up a venous extracorporeal circulation and resecting the root of the mesentery reconstructed with direct anastomosis in case of proximal tumors were techniques used to overcome these limits.

Vascular reconstruction. Of 44 vessels resected in 22 patients, 31 vessels were reconstructed using synthetic grafts, 7 were reimplanted, 3 required direct sutures in case of direct anastomosis without tension, and 3 vascular resections did not require any reconstruction (Table III).

Morbidity and mortality

The median hospital stay was 17 days (IQR, 14.5; range, 7-190 days). No patients died postoperatively. Grade 3 and 4 (Clavien-Dindo[9]) early postoperative morbidity rate was 19.3% (Table IV). Early thrombosis of the inferior vena cava prosthesis developed in one patient, and a repeat operation was required to remove the thrombus, without adverse consequences. Five patients showed long-term morbidity: diaphragmatic palsy was reported in 3 patients, lymphedema of the lower limb in 1, and chronic diarrhea due to malabsorption in 1.

Table III. Resected vessels and reconstruction method

Variable	*No. (%) (N = 31)*
Resected vessels	
Left external iliac vein	1 (3.2)
Right external iliac artery	4 (12.9)
Right external iliac vein	3 (9.7)
Right internal iliac pedicle	1 (3.2)
Left internal iliac pedicle	1 (3.2)
Right femoral vein	1 (3.2)
Right femoral artery	1 (3.2)
Right primitive iliac artery	2 (6.5)
Left common iliac artery	2 (6.5)
Left common iliac vein	2 (6.5)
Right common iliac vein	3 (9.7)
Infra renal aorta	2 (6.5)
Superior mesenteric artery	1 (3.2)
Ileocolic artery	1 (3.2)
Superior mesenteric vein	1 (3.2)
Vena cava	13 (42)
Retrohepatic vena cava	3 (9.7)
Infrahepatic vena cava	10 (32.3)
Left renal vein	4 (12.9)
Right renal vein	1 (3.2)
Resected vessels per patient, No.	
None	9 (29.0)
One	7 (22.6)
Two	9 (29.0)
Three	5 (16.1)
Four	1 (3.2)
Reconstruction method	
No reconstruction	3 (7.0)
Direct suture	3 (7.0)
Prosthetic graft	31 (72.1)
Reimplantation	7 (16.3)

Table IV. Early postoperative morbidity in the entire population and in the patients with a vascular resection

Early morbidity	*Total population (n = 31), No. (%)*	*Vascular resection (n = 22), No. (%)*
No morbidity	19 (61.3)	14 (63.6)
Overall morbidity	12 (38.7)	8 (36.4)
Clavien-Dindo		
I	3 (9.6)	2 (9.1)
II	3 (9.6)	2 (9.1)
III	6 (19.3)	4 (18.2)
IIIa	1 (3.2)	1 (4.6)
IIIb	5 (16.1)	3 (13.6)
IV/V	0 (0)	0 (0)
Prosthesis infection	1 (3.2)	1 (4.6)
Prosthesis thrombosis	1 (3.2)	1 (4.6)
Deep collection	1 (3.2)	1 (4.6)
Postoperative hemorrhage	3 (9.7)	3 (13.6)
Phlebitis/pulmonary embolism	3 (9.7)	1 (4.6)
Gastrointestinal fistula	5 (16.1)	3 (13.6)
Reintervention	5 (16.1)	3 (13.6)
Nonsurgical morbidity	4 (12.9)	2 (9.1)
Pancreatitis	1 (3.2)	0 (0)
Urinary infection	2 (6.4)	1 (4.6)
Catheter infection	1 (3.2)	1 (4.6)

Oncologic results and histology

As detailed before, among the 31 patients who underwent surgery for RSTS, tumor resection was not possible in four patients (12.9%); thus, 27 had a complete compartmental surgery. Five of these 27 patients did not undergo vascular resection but only underwent a macroscopically complete surgical resection of the tumor. Complete microscopic resection (R0) was achieved in 18 patients (58.1%) and R1 resection in nine (29.0%). There was no R2 resection.

Vascular resection was performed in 22 patients: vascular invasion was histologically confirmed in 16, and six had no real invasion but an encasement. Six patients had a primary leiomyosarcoma of the vena cava involving neighboring organs, and in four patients this was associated with a tumor thrombus.

Recurrence patterns. Recurrent disease was reported during follow-up in 22 of the 31 patients (70.9%). Distant metastases were found in 13 patients (41.9%), isolated local recurrence in 5 (16.1%), and both local and distant metastases in 4 (12.9%). Considering the 22 patients who underwent oncovascular resection, metastatic disease was present in 10 (45.5%), local recurrence in 3 (13.6%), and local and metastatic recurrence in 2 (9.1%). Among the four patients who initially had a metastatic disease, two presented local and distant recurrences and two presented only distant metastases during follow-up. Most frequent metastases were hepatic (n = 7) or pulmonary (n = 5), and eight patients presented with a peritoneal sarcomatosis. Treatment of recurrent disease consisted of chemotherapy in 8 patients, radiotherapy in 2, and surgical intervention in 7.

PFS. After a median follow-up of 34.4 months (IQR, 48.1 months), the median PFS was 10 months (95% confidence interval [CI], 5.8-13.9). The median PFS was 11.2, 22.6, and 0.9 months for R0, R1 and unresectable patients, respectively, which was statistically different between R0-R1 and no tumor resection ($P = .009$; Fig 3).

Considering the 22 patients who underwent oncovascular resection, the median PFS was 18.7 months (95% CI, 5.9-32.6 months). For the 16 patients with histologically proven vascular invasion, PFS was 11.2 months (95% CI, 7.1-25.1 months), which was not significantly different ($P = .68$) from the PFS of 18.7 months (95% CI, 0-37.7 months) for simple encasement. The Pearson correlation test found no statistical correlation between vascular invasion and local recurrence.

OS. Thirteen patients died during the follow-up period. Median OS time was not reached. Overall 1-year and 3-year survival rates were 77.4% and 61.3%, respectively.

At the last follow-up, 50.0%, 71.4%, and 50% patients with tumors of grades 1, 2, and 3, respectively, were alive. When correlated to the resection margins, the median OS was not reached for R0, R1, and was 6.1 months when no tumor resection was performed (Fig 4).

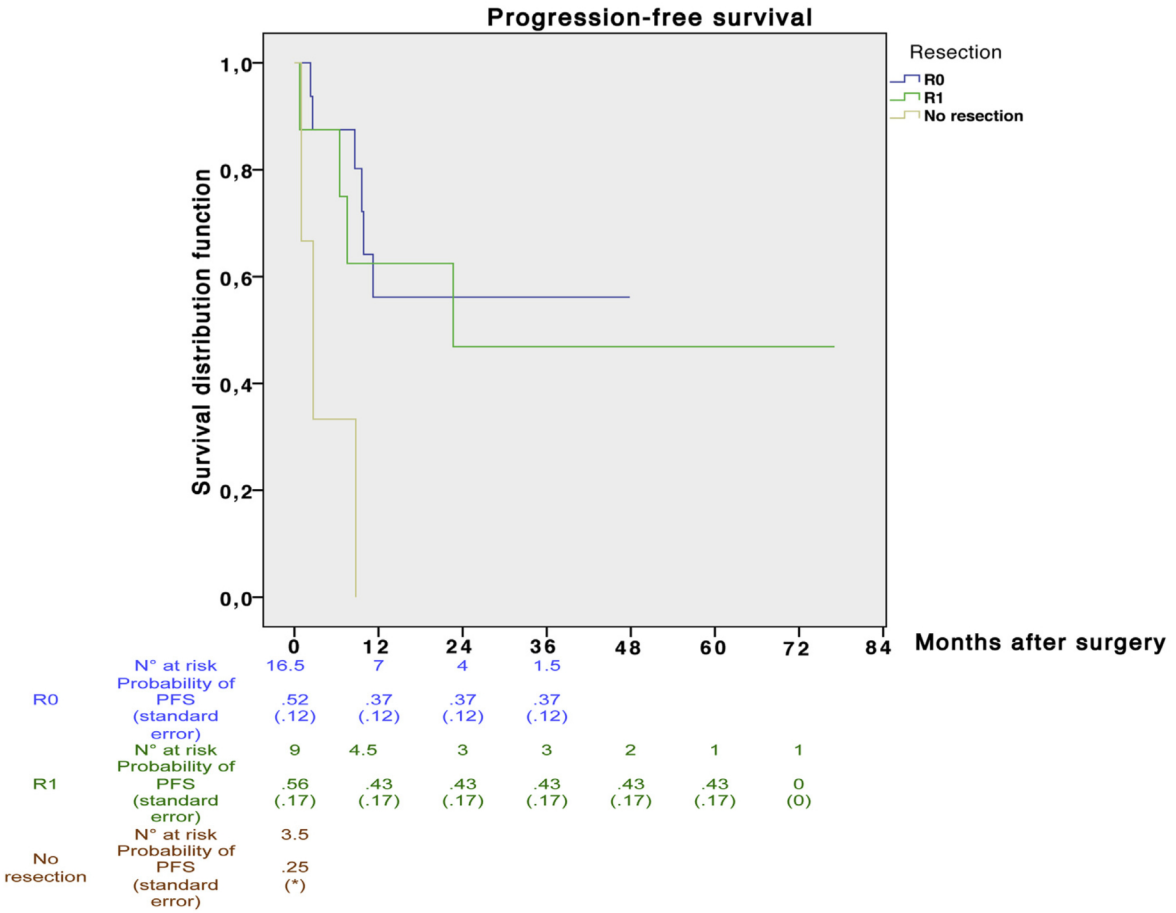

Fig 3. Progression-free survival (*PFS*) of all patients after resection of retroperitoneal soft tissue sarcoma (RSTS) with blood vessel involvement, with specific PFS depending on the completeness of resection (R0 and R1). *Not calculable.

Patency of reconstructed vessels. No late thrombosis occurred during follow-up. All of the reconstructed vessels appeared to remain functional.

DISCUSSION

In case of RSTS, quality and completeness of surgical resection are critically important. Unlike epithelial tumors, RSTS can abut onto surrounding organs even at an early stage.

The recent development of aggressive multidisciplinary strategies has led to a significant drop in local recurrence rates.[3,6,10-12] The concept of compartmental surgery includes en bloc resection of the surrounding organs to ensure a macroscopically and microscopically free margin. This approach, being technically demanding, requires the operation to be performed in high-volume centers by trained surgeons with specific sarcoma expertise. Vascular invasion has often been considered a contraindication to surgical resection. This may be due to technical feasibility of the procedure, high morbidity rate in low-volume series, and lack of survival data in this subgroup of patients. Enhanced resectability and lower local recurrence rates, thanks to planned vascular resections, have already been described in patients with limb sarcomas.[13,14]

Our deliberate policy of performing joint interventions and the high-volume of patients referred to our institution led us to develop a systematic approach to oncovascular resection. Compartmental resection with vascular resection was always performed for each patient, except in case of grade 1 sarcoma with vascular contact and without invasion.

In case of high-grade RSTS, a resection of the concerned vessels was always done irrespective of whether the vessel was invaded or only in contact with the tumor. In case of complete thrombosis of the vein or involvement of the internal iliac pedicle, no reconstruction was performed, as previously detailed.

When a right-sided RSTS abutted on the duodenum, a pancreatoduodenectomy could be considered to enhance the margins. In case of simple contact, we did not systematically perform a pancreatoduodenectomy. This strategy is justified by the high morbidity rate of the procedure and particularly by the risk of pancreatic fistula in this subset of patients with a normal soft pancreas and in whom a vascular graft may have been necessary.[15] Our study shows

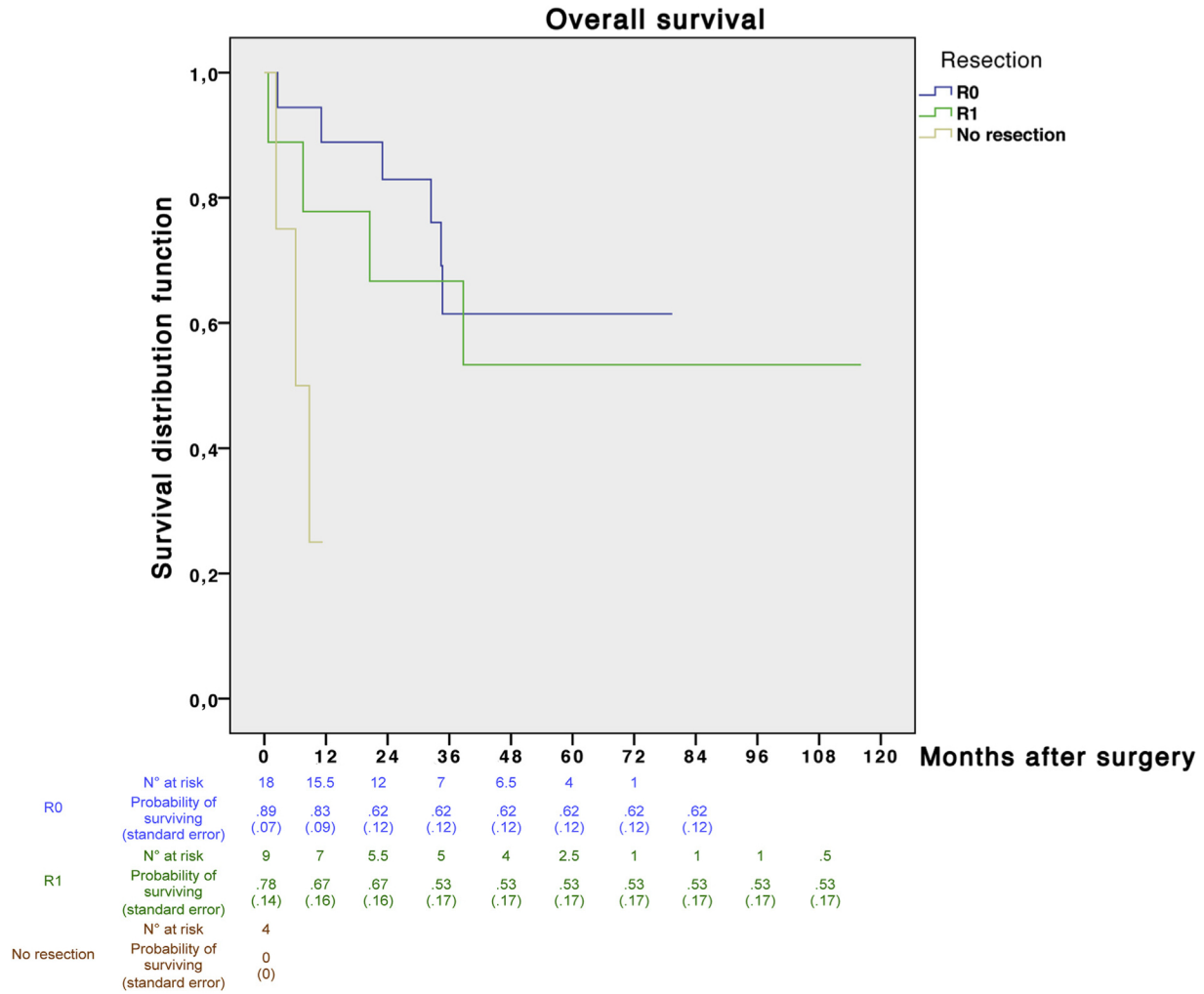

Fig 4. Overall survival (OS) of all patients after resection of retroperitoneal soft tissue sarcoma (RSTS) with blood vessel involvement, with specific OS depending on the completeness of resection (R0, R1, and no resection).

it is acceptable to take into account the complication rate of vascular replacement in our systematic strategy. Moreover, an R0/R1 resection rate of 87% emphasizes the importance of preoperative surgical planning and of the collaboration between surgical oncology and vascular specialties.

Including in our study six patients presenting with primitive leiomyosarcoma of the vena cava may be questionable. We did not wish to separate these patients in our report discussing the collaboration between vascular and oncologic surgeons in the management of RSTS. Indeed, the problem is the same, even though the other way round: oncologic surgeons do need the presence of a vascular surgeon in the operating room for sarcomas just as vascular surgeons may need an oncologic surgeon for leiomyosarcomas in which free margins can be achieved by resecting the surrounding viscera.

A systematic management strategy for vascular reconstruction was adopted to optimize our results. Synthetic grafts were used to reconstruct 31 vessels in our study, with infection and thrombosis occurring only in one patient each. Vascular reconstruction should thus be performed systematically for major arteries (except internal iliac arteries) and for major veins when not occluded preoperatively. Inferior vena cava or external iliac vein ligation without reconstruction results in major edema and may increase the risk of renal insufficiency. Some authors share this opinion,[8,16,17] whereas others routinely perform inferior vena cava resection without reconstruction.[18] In case of massive tumor invasion of a major vein, a collateral circulation is usually developed at the time of resection, with little or no long-term sequelae of the resection without reconstruction.[19] When performed without establishing collateral circulation, a resection without reconstruction may have significant consequences on the quality of life of these patients.

The morbidity rate we reported was similar to the rate described by Schwarzbach et al.[8] In this study, the reintervention rate was 16%, comparable with the rate reported in

a larger series without vessel resection.[6] This suggests that synchronous vascular resections did not increase the complication rates, although these procedures are considered potentially more complex. The absence of postoperative deaths and a relatively low postoperative complication rate, considering these demanding operations, may be explained by the presence of vascular and oncologic senior surgeons working together in a "four-hand" procedure, which is probably an effective way of increasing operative safety.

The survival data presented here are comparable to those shown by Schwarzbach et al[8] in a series of 25 patients with sarcomas with vascular involvement. In our study, 29% of the patients presented a local recurrence, which is slightly higher than that reported by Bonvalot et al[3,6] and Gronchi et al[20] for retroperitoneal tumors after compartmental surgery without vascular resection. This high recurrence rate might be explained by the specific population in our study, in which 35% of patients are referred to our institution for local recurrence. In our selected patients with a relatively slow evolution of their disease, the relatively low PFS value contrasting with encouraging OS figures can be explained by the high frequency of distant metastasis reported rather than local recurrence.

The results obtained with oncovascular resection in our study are similar to those recently presented by Poultsides et al.[21] They confirm the need of a vascular surgeon before, during, and after surgery to manage such difficult cases. Interestingly, microscopically confirmed vascular invasion did not increase local recurrence, probably because of the margin enhancement obtained by vessel resection. The question thus was whether vessel resection decreased the recurrence rate. Only a randomized clinical trial could answer this point.

Adjuvant treatments have not yet shown a demonstrable survival benefit in the treatment of RSTS,[22-24] which advocates in favor of optimized and aggressive surgical strategies, including vascular resection or regional hyperthermia and chemotherapy.[25] Neoadjuvant radiotherapy is not yet considered a standard of care, although a study suggests it reduces the risk of local reccurrences.[26] In our institution, radiotherapy was administered only for patients included in the STRASS clinical trial. The current trend is toward more aggressive surgery in RSTS to lower local recurrence rate.[27]

Despite a small number of patients, our study demonstrates that low morbidity and encouraging survival results can be obtained in case of vascular involvement, thanks to a close collaboration between oncology and vascular surgeons. In the absence of other treatment options, as neither radiotherapy[28] nor chemotherapy[22] improves OS, this aggressive approach seems to be justified in selected patients.

CONCLUSIONS

Vascular resection and reconstruction are safe and feasible in case of RSTS. This strategy did not increase morbidity but is a way to improve the resection margins. It allows encouraging survival figures for patients who were often considered nonresectable, although recurrence rates remain high. In case of patent vascular invasion, removing vessels and grafting replacement would be the best option and would no longer be considered a contraindication. In case of simple contact, only multi-institutional prospective studies performed in high-volume centers may validate this aggressive approach.

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AUTHOR CONTRIBUTIONS

Conception and design: MB, SC, FQ
Analysis and interpretation: MB, SC, PA, FQ
Data collection: LD, PR, LC, PA, FQ
Writing the article: MB, FQ
Critical revision of the article: MB, SM, PA, FQ
Final approval of the article: MB, SC, LD, SM, PR, LC, PA, FQ
Statistical analysis: MB
Obtained funding: Not applicable
Overall responsibility: FQ

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