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Vascular resection en-bloc with tumor removal and graft reconstruction is safe and effective in soft tissue sarcoma (STS) of the extremities and retroperitoneum

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ABSTRACT

Background: To analyze the outcome of a series of patients who underwent vascular resection as part of an excision of a soft tissue sarcoma (STS).
Study design: All consecutive patients affected by localized STS of an extremity or retroperitoneum treated between January 2000 and December 2013 with surgery including vascular resection were considered. Overall survival (OS), crude cumulative incidence (CCI) of local recurrence (LR) and distant metastases (DM) were estimated by Kaplan-Meier. Long-term vascular graft patency rate was assessed.
Results: 2692 patients received an operation for localized disease with 105 (3.9%) cases undergoing vascular resection. Median FU was 32 months. 5-year OS, CCI of LR and DM were 62%, 12% and 58% respectively. Vascular reconstructions consisted of 52 arterial and 16 venous grafts in extremities; 12 arterial and 33 venous grafts in the retroperitoneum. Graft thrombosis occurred in 16 patients (7/64 arterial and 9/49 venous reconstructions). Arterial occlusions occurred at a median of 36 months after surgery and were treated by prosthesis replacement (3), Fogarty catheter embolectomy (2), percutaneous angioplasty (1) and observation (1). One patient eventually required amputation. Venous occlusions occurred at a median of 4 months post surgery and were all treated conservatively. Overall arterial and venous reconstruction patency rates were 89% and 82% respectively.
Conclusions: Vascular resection to facilitate resection of STS has an acceptable long term patency rate. However it was associated to a high risk of distant spread. Although the encasement of the vascular bundle does not represent a contraindication to surgery there is an association with a high metastatic risk by virtue of the locally advanced nature of the disease and this should be considered when planning treatment.

Abbreviations: STS, soft tissue sarcoma; OS, overall survival; CCI, crude cumulative incidence; LR, local recurrence; DM, distant metastasis; FU, follow up; FNCLCC, fédération nationale des centres de lutte contre le cancer; R0, microscopic negative surgical margins; R1, microscopic positive surgical margins; R2, macroscopic positive surgical margins; Gy, Gray; Preop, preoperative; Post-op, postoperative; IQ, interquartile; IVC, inferior vena cava; PTFE, polytetrafluoroethylene; LMWH, low molecular weight heparin; HR, hazard ratio; CI, confidence interval; LRFS, local recurrence free survival; DMFS, distant metastasis free survival; NR, not reported; A, artery; V, vein; DFS, disease free survival; Aex, extremities artery; Arp, retroperitoneal artery; Vex, extremities vein; Vrp, retroperitoneal vein.

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1. Introduction

Soft tissue sarcomas (STS) are rare tumors with an expected incidence of 5 new cases per 100,000 population per year. Although they can occur anywhere in the body, they predominantly affect limbs, girdles and retroperitoneum [1,2].

Surgery is the mainstay of treatment and it is aimed at obtaining a macroscopically complete resection along with negative microscopic surgical margins, as the risk of local recurrence predominantly relates to the status of the surgical margins after excision [3–8]. Indeed, sarcomas usually respect anatomical boundaries with local anatomy able to influence tumor growth by setting a natural barrier to their extension. In general, sarcomas follow the path of least anatomical resistance and initially grow within the anatomical compartment in which they arise [9–12]. Nevertheless, major vessels may sometimes be involved or even give rise to STS. In these cases, a comprehensive surgical procedure should encompass vascular resection and reconstruction. To date, data regarding long term graft patency rates and oncological outcomes after concomitant STS surgery and vascular resection are limited [13–22].

The aim of this study was to analyze the outcome of a consecutive series of patients from our institution undergoing vascular resection and/or reconstruction as part of surgery for STS.

2. Patients and methods

All consecutive patients with a localized STS of the extremity or retroperitoneum who underwent en-bloc vascular resection with the tumor between January 2000 and December 2013 were included (Table 1).

Clinical data were extracted from a prospectively maintained database of all adult patients with soft tissue sarcoma surgically treated at our institution. Data recorded included gender, age at diagnosis, site, size, depth, histology, tumor grade, margin status, vessels resected, type of reconstruction, adjuvant treatments, dates of disease specific events, death or last follow up.

The FNCLCC grading system was applied to the untreated primary tumor.

Surgical excision was considered macroscopically complete in the absence of gross residual disease and macroscopically incomplete resections were classified as R2. All macroscopically complete resections were classified microscopically according to the closest surgical margin: positive (R1) - tumor within 1 mm of the inked surface or negative (R0) - absence of tumor 1 mm from the inked surface.

Criteria for vascular resection included encasement of the vessels by the tumor (Fig. 1-panel A) as well as invasion of the side wall when pushed at the periphery of the lesion (Fig. 1-panel B).

The indication for pre/post-operative radiation therapy was assessed by both the operating surgeon and the radiation oncologist and delivered when a high risk of local relapse was deemed to exist on clinical grounds. However, no definitive selection criteria for those receiving radiation were prospectively recorded. Where delivered, external beam radiation was used with doses ranging from 45 Gy to 70 Gy (median 60 Gy).

Pre/post-operative chemotherapy was given at the discretion of the multidisciplinary institutional sarcoma board or as part of ongoing clinical trials. Anthracycline-based regimens were used and in most of the cases, combined with Ifosfamide.

Patients were followed up postoperatively with clinical and radiological assessment every 4 months for the first two years, then six-monthly until the fifth postoperative year and annually thereafter.

Table 1
Demographic, clinical and pathological characteristics of the study population.

	N	%
Total	105	
Patient's age, years		
Median (IQR)	55 (44–64)	
Gender		
Female	45	43
Male	60	57
Tumor size, cm		
Median (IQR)	9 (6–14)	
FNCLCC		
I	13	12
II	32	31
III	60	57
Site		
Upper extremities	12	11
Lower extremities	50	48
Retroperitoneum	43	41
Histological subtype		
Leiomyosarcoma	48	45
Liposarcoma	15	14
Synovial sarcoma	9	8
RCML	7	7
MPNST	6	6
Sarcoma NOS	5	5
UPS	4	4
EMC	4	4
Myxofibrosarcoma	2	2
Ewing Sarcoma	2	2
Epithelioid Angiosarcoma	2	2
SFT	1	1
Chemotherapy		
Done (preop/postop/pre-postop)	65 (45/16/4)	62
Not done	40	38
Radiation therapy		
Done (preop/postop)	59 (32/27)	56
Not done	46	44

IQR: interquartile range; **FNCLCC:** Fédération Nationale des Centres de Lutte Contre Le Cancer; **RCML:** round cell myxoid liposarcoma; **MPNST:** malignant peripheral nerve sheath tumor; **NOS:** not otherwise specified; **UPS:**undifferentiated pleomorphic sarcoma; **EMC:**extraskeletal myxoid chondrosarcoma; **SFT:** solitary fibrous tumor; **preop**: preoperative; **postop**: postoperative.

2.1. Statistical methods

The study endpoints were graft patency rate, overall survival (OS), incidence of local recurrence (LR) and distant metastasis (DM).

In the statistical analysis, cases of LR occurring concomitantly with DM were included in the estimation of CCI (Crude Cumulative Incidence) curves as DM.

Study variables (age [≤50 years/>50 years], gender, tumor histology [leiomyosarcoma vs others], tumor grade, main tumor diameter [<9 cm/≥9 cm], surgical margins, perioperative chemotherapy and/or radiation therapy) were subject to univariate analysis followed by multivariate analysis of significant variables.

Survival and disease free outcomes were compared using Kaplan-Meier plots and Log-Rank tests. All analyses were performed using IBM SPSS 19 (IBM Corp. Armonk, NY), with $p < 0.05$ deemed to be indicative of statistical significance.

3. Results

In the study period 2692 patients affected by localized STS of the extremity or retroperitoneum underwent surgery with curative intent. Among them 105 (3.9%) underwent vascular resection as part of the procedure to remove the tumor and were included for analysis. In 50 (48%) patients the vascular bundle had a 360° degrees involvement. 103 (98%) patients underwent a macroscopic