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Original Article

Early and Mid-Term Outcomes after Vascular Reconstruction for Patients with Lower-Extremity Soft-Tissue Malignant Tumors

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Objective: To evaluate limb-salvage surgery including vascular resection for lower-extremity soft-tissue sarcomas and carcinomas for adult patients.

Materials and Methods: Eight consecutive patients (median age, 59 years) who underwent vascular replacement during surgery for malignant tumors in the lower limbs between November 2006 and March 2018 were evaluated. Patient data were retrospectively obtained in a computerized database. Arterial and venous reconstructions were performed for seven patients, with one additional patient receiving venous reconstruction only. Autologous-vein (n=6) and synthetic bypasses were used for arterial repairs, whereas only autologous veins were implanted for venous repairs.

Results: Morbidity was 62.5%, and in-hospital mortality was 12.5%. At a median follow-up of 24 months, the primary patency rates of arterial and venous reconstructions were 85.7% and 62.5%, respectively. Limb salvage was achieved in all cases.

Conclusion: Early and mid-term bypass patency rates, the high percentage of limb salvage, and the oncologic outcome underline the efficacy of en bloc resection of soft-tissue tumors involving major vessels of the lower limbs. The anticipated need for vascular resection and reconstruction should not be a contraindication to sarcoma and carcinoma resections. However, efforts to achieve better control over systemic spread are required for long-term survival.

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Introduction

Malignant soft-tissue tumors frequently occur in the lower limbs, and three quarters of soft-tissue sarcomas are histologically classified as malignant fibrous histiocytoma, liposarcoma, leiomyosarcoma, synovial sarcoma, and malignant peripheral nerve-sheath tumors.[1)] The first choice of treatment is surgical resection, and, to prevent recurrence, it is important to obtain adequate surgical margins. In general, it is important to perform an extensive resection that is separated by 3 cm or more,[2)] but, in cases involving vascular invasion, resection of the blood vessels that is accompanied by revascularization is necessary for a radical cure. In this study, we examined resected cases of lower-extremity malignant soft-tissue tumors that included vascular resections that were performed at our facility, and we report the utility of the revascularization method.

Patients and Methods

From 2006 to 2018, a total of eight patients with primary soft-tissue tumors of the lower extremities underwent en bloc resection of the tumor that involved the arteries and veins. This study included six males and two females, with a mean patient age of 59 years (range, 16–88 years). The average tumor size was 9.0 cm (range, 4–24 cm). Diagnoses included liposarcoma (3), myxofibrosarcoma (2), synovial sarcoma (1), leiomyosarcoma (1), and squamous cell carcinoma (1). Tumor locations were in the thigh or inguinal regions. Arterial and venous reconstructions were performed for all patients, except for one patient who received venous reconstruction only. Autologous-vein (n=6) and synthetic (expanded polytetrafluoroethylene [ePTFE]; n=1) bypasses were used for the arterial repairs, whereas only autologous veins were implanted for venous repairs. Patient characteristics are given in

Table 1 Patient characteristics

Case	Age/sex	Site	Histology	Vessels involved	Tumor size (cm)	Preoperative treatment
1	66/F	Thigh	Leiomyosarcoma	SFA, DFA CFV, FV, DFV	7.4	—
2	38/M	Thigh	Myxofibrosarcoma	CFA, SFA, DFA CFV, FV, DFV	5.0	—
3	16/F	Thigh	Synovial sarcoma	CFA, SFA, DFA CFV, FV, DFV	9.5	—
4	61/M	Thigh	Myxofibrosarcoma	CFA, SFA, DFA CFV, FV, DFV	24.0	—
5	68/M	Groin	Squamous cell carcinoma	CFA, SFA, DFA CFV, FV, DFV	4.0	CRT
6	57/M	Groin	Liposarcoma	EIA, CFA, SFA, DFA CFV, FV, DFV	7.9	—
7	88/M	Thigh	Liposarcoma	CFV	5.3	—
8	81/M	Thigh	Liposarcoma	SFA, FV	9.0	—

CFA: common femoral artery; CFV: common femoral vein; CRT: chemoradiotherapy; DFA: deep femoral artery; DFV: deep femoral vein; EIA: external iliac artery; FV: femoral vein; SFA: superficial femoral artery

Fig. 1 Preoperative computed-tomography images of a patient with synovial sarcoma (case 3). The superficial femoral artery (SFA) and femoral vein (FV, arrow) are immediately adjacent to the mass and are displaced laterally, with no evidence of a tissue plane between them and the lesion.

Table 1. The presence or absence of vascular invasion was assessed by preoperative computed tomography (CT) (**Fig. 1**) and magnetic resonance imaging, and, ultimately, the indication of revascularization was determined by the intraoperative findings. Surgery was first performed by an orthopedic surgeon to expose the tumor. A cardiovascular surgeon then performed vein grafting and vascular anastomosis, after determining the indication of resection of each vessel, combined with the planned resection site of the vessel. Afterwards, the orthopedic surgeon closed the wound and, if necessary, a plastic surgeon carried out additional treatments, such as muscle flap grafting. Approval for this study was obtained from the Kumamoto University Institutional Review Board.

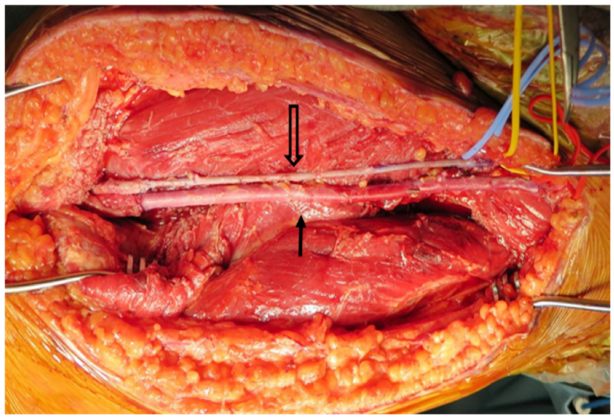

Fig. 2 Resection of the left superficial femoral vessels and replacement with saphenous vein grafts. The black arrow is the artery; the white arrow is the vein.

Arterial Reconstruction

In all patients undergoing arterial reconstruction, an anatomical iliofemoral repair was performed: one repair used an ePTFE prosthesis (Gore-Tex, W. L. Gore & Associates, Inc., Flagstaff, AZ, USA), and six repairs used autologous vein grafts (**Fig. 2**). Autologous grafts consisted of the contralateral great saphenous vein (GSV) (n = 6). The GSV was implanted in the reverse direction. In all patients but one, the deep femoral artery was ligated. Vascular reconstruction was performed first from the arterial anastomosis. In principle, an end-to-end anastomosis by-over and-over continuous suturing was performed, but, in the case of a size mismatch, the arterial proximal side was closed and an end-to-side anastomosis was performed.

Venous Reconstruction

The venous reconstructions comprised eight iliofemoral

reconstructions. All repairs consisted of autologous vein grafts of either the contralateral GSV (n = 7) or ipsilateral GSV (n = 1). The GSV was implanted in the non-reverse direction. In six patients, the deep femoral vein was ligated. Postoperative graft assessment was performed with a duplex ultrasound scan or a CT scan (**Fig. 3**).

Results

One patient died in hospital as a result of bone and lung metastases. Therefore, the in-hospital mortality rate was 12.5%. Morbidity was 62.5%, including wound infection (3), hematoma (1), pneumonia (1), deep vein thrombosis and pulmonary thromboembolism (1), and leakage of lymphatic fluid (1). Limb salvage was achieved in all cases. At a median follow-up of 24 months, the primary patency rates of arterial and venous reconstructions were 85.7% and 62.5%, respectively. There were no cases that led to amputation, and the edema of the affected limbs was within the allowable range. Postoperative ankle brachial index (ABI) measurements were performed in four cases, and the measured values were within the normal range.

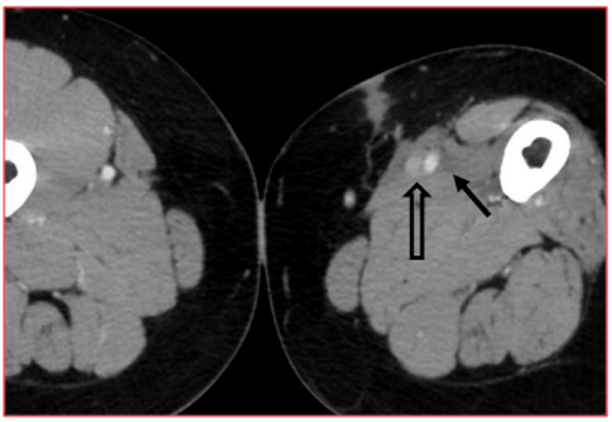

Fig. 3 Postoperative CT image showing that the reconstructed artery (black arrow) and vein (white arrow) are patent.

During the observation period, two patients died because of distant metastasis (one case of in-hospital death, and one case of death occurring 37 months after operation), while each of the other six patients remained alive without recurrence and could walk without assistance or using an orthosis or crutches (**Table 2**).

Discussion

The majority of soft-tissue tumors are benign and are associated with a very high cure rate after their surgical excision. Malignant mesenchymal neoplasms amount to less than 1% of the overall human burden of malignant tumors; however, they are life-threatening and may pose a significant diagnostic and therapeutic challenge, since there are more than 50 histological subtypes of soft-tissue tumors, which are often associated with unique clinical, prognostic, and therapeutic features.[1] The annual clinical incidence of benign soft-tissue tumors has been estimated to be up to 3,000/million population, whereas the annual incidence of soft-tissue sarcoma is around 30/million, i.e., less than 1% of all malignant tumors. Soft-tissue sarcomas may occur anywhere, but three quarters are located in the extremities (most commonly in the thigh) and 10% each in the trunk wall and retroperitoneum. There is a slight male predominance for soft-tissue sarcomas. Like almost all other malignancies, soft-tissue sarcomas become more common with increasing age; the median age is 65 years. Approximately 10,980 cases of soft-tissue tumors occur annually in the United States, but such cases occur much less frequently than for lung cancer (221,130 cases) and for colon cancer (141,210 cases).[3]

The incidence of malignant soft-tissue tumors in Japan is about 20/million population, and, according to the registration of national bone and soft tumors (2006–2009), the occurrence frequency by tissue type is liposarcoma (36.0%), malignant fibrous histiocytic tumor (23.1%), leiomyosarcoma (7.9%), synovial sarcoma (5.5%), myxofibrosarcoma (5.5%), and malignant peripheral nerve-

Table 2 Perioperative morbidity and mortality

Case	Arterial graft	Venous graft	Complications	Arterial patency	Venous patency	Limb salvage	Postoperative ABI (R/L)	Current status
1	ePTFE	SVG	—	Occluded	Occluded	Yes	—	DOD
2	SVG	SVG	Wound infection	Patent	Patent	Yes	1.20/1.29	ANED
3	SVG	SVG	—	Patent	Patent	Yes	1.03/0.98	ANED
4	SVG	SVG	Hematoma, wound infection	Patent	Occluded	Yes	1.03/1.12	ANED
5	SVG	SVG	Pneumonia, wound infection	Patent	Patent	Yes	0.95/1.17	ANED
6	SVG	SVG	DVT, PTE	Patent	Occluded	Yes	—	DOD
7	—	SVG	Leakage of lymphatic fluid	—	Patent	Yes	—	ANED
8	SVG	SVG	—	No evaluation	No evaluation	Yes	—	ANED

ABI: ankle brachial index (underlined on the side of reconstruction); ANED: alive with no evidence of disease; DOD: dead of disease; DVT: deep vein thrombosis; ePTFE: expanded polytetrafluoroethylene; PTE: pulmonary thromboembolism; SVG: saphenous vein graft

sheath tumor (4.9%).[4] Although surgery remains the principal therapeutic modality for soft-tissue sarcomas, the extent of surgery required, along with the optimum combination of radiotherapy and chemotherapy, remains controversial. A properly executed surgical resection remains the most important part of overall treatment. In general, the scope of the excision is dictated by the size of the tumor, its anatomical relation to normal structures (e.g., major neurovascular bundles), and the degree of function that would be lost after the operation. Tumor removal within the same compartment where a lesion exists should be done using a margin greater than 3 cm distant from the lesion.[2] However, depending on the extent of tumor infiltration, it may be inevitable that the major blood vessels must be resected to obtain an appropriate resection margin, in which case revascularization is required for the achievement of limb salvage. Several reports have been made about malignant soft-tissue tumor surgeries including vascular replacement. Poultsides et al. reported that vascular resection and reconstruction during sarcoma resection significantly increases perioperative morbidity.[5] However, the oncologic outcome appears equivalent to that of cases without major vascular involvement. Regarding the reconstruction graft and the prognosis of limbs, there is one report that showed that the secondary patency rate of the arterial graft was 78% at 34 months, while the patency rate of the venous graft was 54% and the limb salvage rate 94%.[6] Arterial reconstruction is absolutely necessary to achieve limb salvage, but it is controversial as to whether or not venous reconstruction is necessary. While there are reports stating that there is no difference in edema of the lower extremities that is related to the presence or absence of venous reconstruction, Matsushita et al. argue that severe chronic venous disease was observed in 30% of patients who did not receive venous reconstruction.[7] The indication for venous reconstruction may also be based on the presence or absence of other sources of venous outflow, particularly deep veins. The deep femoral vein may be a source of collateralization. Therefore, venous reconstruction may be beneficial in reducing or preventing leg edema in the absence of other sources of collateralization, such as the deep femoral vein.[7] In our series, the deep femoral vein was involved with the tumor in six out of eight cases. For this reason, we hypothesize that reconstruction of both the arteries and the veins is necessary for optimal outcomes. As a result, no severe lower-extremity swelling after surgery was observed for the cases in this study. For the arterial graft, an ePTFE prosthesis was used for the first case of the series, but all subsequent cases involved a saphenous vein graft (SVG). The reason for using an ePTFE graft for the first case was not recorded, and the details are unknown, but the diameter difference between the SVG and the femoral artery may be one cause. If the tumor is close to the inguinal region, the proximal anastomosis site becomes the common femoral artery or the distal external iliac artery, and the diameter may exceed 10 mm in some cases. In fact, we also experienced cases in which the proximal anastomosis of the SVG was forced to the end-to-side, because of differences in diameter. All cases were patent, except for the first case's ePTFE graft, which was occluded within 7 months after the operation. For all cases, SVGs were used for venous reconstruction. Three out of seven cases were obstructed at an early time point postoperatively, but the edema of the affected limb was not serious. It is difficult to discuss the effect of venous reconstruction on edema, because of the lymphedema associated with extensive resection, but, as reported by Matsushita et al., there is a possibility that lower-limb function can be greatly affected.[7] It seems a reasonable strategy to perform reconstruction for all cases, to improve outcomes.

Although there are many reports where the graft selection was for the SVG, some studies used synthetic grafts for nearly half of their cases.[8] The greatest advantage of a SVG is reduced infection rates, and a SVG is generally considered to be better than a synthetic graft. Conversely, the disadvantages are that harvesting takes time and a sufficient diameter may not be obtained. As a result, we experienced cases for which an end-to-end anastomosis could not be performed. The superiority of the synthetic graft relates to the characteristics of the time required for harvest being negligible and a graft of sufficient size being able to be prepared. Not only for the proximal anastomosis but also for the distal anastomosis, there are few cases where the SVG-diameter difference becomes a problem. Conversely, the most serious problem is infection of the synthetic graft. Since extensive exfoliation is necessary for tumor resection, the rate of postoperative wound infection is high. Three out of eight cases in our study suffered wound infection. Reoperations resulting from reconstructed synthetic-graft infections have been reported; therefore, we will continue to use the SVG for reconstructions in the future.

This study was limited by the size of the patient cohort (only eight cases). Malignant soft-tissue tumors account for less than 1% of all malignant tumors,[9] and only 5%–10% of those tumors require vascular reconstruction[5,6,10]; therefore, it seems that there is limited scope to develop treatment strategies. However, as described above, survival rates, including local recurrence, are not inferior to those of cases without major vascular involvement, even for cases requiring vascular reconstruction, so the anticipated need for vascular resection and reconstruction should not be a contraindication to sarcoma resection. As with other carcinomas, distant metastasis is also a major problem of malignant soft-tissue tumors. Even though

local recurrence can be controlled with extensive resection, death resulting from distant metastasis still occurs. Surgery still remains the most successful treatment for soft-tissue tumors, as no effective adjuvant therapy exists; however, further research into new treatments such as antibody therapy,[11] carbon-ion radiotherapy,[12] and proton-beam radiation therapy[13] will improve patient outcomes.

Conclusion

Mid-term arterial bypass patency rates, the high percentage of limb salvage, and the oncologic outcome underline the efficacy of en bloc resection of soft-tissue tumors involving major vessels of the lower limbs. Vascular replacement enables a limb-sparing resection to be performed, resulting in acceptable local tumor control and preservation of limb function. Disease-specific morbidity must be anticipated; however, the limitation for long-term disease-free survival is the occurrence of distant metastases. Therefore, new systemic therapies must be developed to control disseminated tumor growth.

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Disclosure Statement

There is no conflict of interest to be disclosed with respect to this article.

Author Contributions

Study conception: TF
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

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