Selected Techniques

Use of Cryopreserved Arterial Allografts as a Reconstruction Strategy in Peripheral Sarcoma Surgery

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Background: Complete resection of lower limb soft tissue sarcoma may require vascular resection and reconstruction. While prosthetic grafts and autologous saphenous veins are commonly employed, superior patency has been described for autologous veins. However, their use implies harvesting, mostly on the contralateral limb. Limited data exist on the use of cryopreserved arterial allografts for such vascular replacement.

Methods: We report a retrospective series of 11 patients with locally aggressive extremity sarcomas undergoing 20 vascular resections and reconstructions with cryopreserved arterial allografts over a 5-year period. A total of 10 arteries and 10 veins were reconstructed. The mean tumor length on resected specimen was 15.4 cm, with the thigh being the most frequent site of resection. Six patients required additional osseous reconstruction with mega-implants or bone allograft.

Results: Limb salvage was achieved in 91% of patients. One amputation was necessary because of untreatable infection following fracture of a bone allograft in an irradiated area. The 1-year secondary arterial patency was 78%, with one graft requiring revision due to a mechanical friction on a mega-implant. The 1-year venous patency was 69%.

Conclusion: Our series represents the first homogeneous cohort treated with cryopreserved arterial allografts for vascular reconstruction in sarcoma surgery, showing favorable outcomes despite extensive resection characteristics. Their use avoids contralateral limb morbidity and offers promising patency and limb-salvage outcomes.

INTRODUCTION

Nowadays, limb-sparing surgery is the standard approach for treating lower limb soft tissue sarcomas.[1] Prognostic varies significantly based on factors such as diagnostic stage, histologic subtype, tumor grade, size and location, as well as patient age and treatment response. In localized soft tissue sarcomas, the 5-year survival rate is about 81%.[2] In 3—10% of cases, tumors invade major vascular

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Ann Vasc Surg 2026; 122: 536–542
https://doi.org/10.1016/j.avsg.2025.08.004

Manuscript received: June 22, 2025; manuscript accepted: August 6, 2025; published online: 26 August 2025

structures, requiring extended resection and subsequent vascular reconstruction.[3,4] Previous series have assessed the outcomes of limb-sparing surgeries involving vascular replacement with prosthetic grafts, autologous saphenous veins, or far less frequently arterial allografts.[4–6] Patency outcomes of arterial and venous reconstructions vary significantly primarily based on the type of substitute conduit used. Among those, autologous veins generally demonstrate superior patency, but their harvest adds morbidity, particularly to the contralateral limb.[5,6] Cryopreserved arterial allografts are recognized as a viable alternative for vascular reconstruction, particularly when prosthetics are contraindicated (e.g., infected fields) or when autologous veins are unavailable. Literature supports their use, demonstrating at least noninferiority in primary patency, especially in complex clinical scenarios involving infection and arterial disease.[7–9]

In this study, we present a homogeneous series of patients undergoing vascular reconstruction with cryopreserved arterial allografts during limb sarcoma resection, with a focus on the clinical outcomes and patency rates associated with these grafts.

Table I. Patients' demographics and tumor characteristics

Characteristics	No. ($N = 11$) (%)
Age, mean 46	
''Young'' population subgroup, range 13–45, mean age 22	6
''Older'' population subgroup, range 68–84, mean age 76	5
Sex	
Male	3 (27%)
Female	8 (73%)
Tumor histology type	
Osteosarcoma	4 (36%)
Liposarcoma	2 (18%)
PEComa	2 (18%)
Ewing sarcoma	1 (9%)
Myxofibrosarcoma	1 (9%)
Leiomyosarcoma	1 (9%)

PEComa, perivascular epithelioid cell tumor.

METHODS

We retrospectively reviewed a series of 11 patients treated between 2018 and 2023 for locally aggressive limb sarcomas that required vascular resection and reconstruction. A total of 20 vascular reconstructions (10 arterial and 10 venous) was performed with cryopreserved arterial allografts.

Patients were evaluated with preoperative computed tomography (CT) or magnetic resonance imaging for vascular involvement. We planned to replace either one or both vessels based on the degree of vascular contact between the tumor and the superficial femoral vessels, as observed in these imaging studies, with the ultimate goal of achieving a microscopically complete tumor resection. Superficial femoral arterial allografts were selected based on the best diameter match with the native vessel and the minimal length required for replacement in order to achieve the best anastomotic fit and optimal hemodynamics by reducing risk of kinking or tension. The allografts were obtained from the European Homograft Bank, where vascular grafts harvested from cadaveric donors are first screened for infectious diseases and assessed for tissue quality before sterilization. They are stored in a cryoprotective solution (dimethyl sulfoxide) to prevent ice-crystal formation and tissue damage, at temperatures ranging from −80°C to −130°C in liquid nitrogen, hence preserving their structural integrity for several years. Following processing, the vascular allografts were rendered acellular, minimizing immunogenicity. As a result, ABO or Human Leukocyte Antigen matching is unnecessary, and immunosuppression is not required. En bloc resection of the tumor, including the involved vascular pedicles, was performed with immediate vascular reconstruction under intravenous heparin, the cryopreserved arterial allografts having been previously prepared by ligating collateral branches. After completion of the anastomosis and immediately after the complete surgical reconstruction, distal pedal flow were monitored by continuous-wave Doppler. Postoperative antithrombotic medication consisted in low–molecular-weight heparin for 1 month and lifelong antiplatelet therapy. Continuous-wave Doppler monitoring was performed daily during the in-hospital stay.

Summary statistics were reported as mean (range) and incidence (percentage) for continuous and categorical parameters, respectively. Patency duration was defined as the time spanning from the surgery date to the date at which loss of patency is observed. Patients who died prior to the event of interest and those without loss of patency were censored at their last visit. Overall survival (OS) was defined as the time from the date of surgery to

Table II. Operative and reconstructive characteristics

Operative characteristics	No. ($N = 11$) (%)
R0 resection	11 (100%)
Site of vascular resection	
Inguinal	1 (9%)
Thigh	9 (82%)
Popliteal	1 (9%)
Vascular reconstruction	
Both arterial and venous	9 (82%)
Single arterial	1 (9%)
Single venous	1 (9%)
Associated mega implant	5 (45%)
Associated bone allograft	1 (9%)

the date of death. Patients who did not meet the event were censored at their last visit date. Median Kaplan–Meier estimates and 95% confidence interval were reported, along with the corresponding curves to estimate OS and graft patency rates. Statistical analysis was performed using Statistical Analysis System software (Version 9.4; SAS Institute Inc, Cary, NC, USA). The study received approval from the institutional ethics committee, ''Comité d'éthique hospitalo-facultaire, Université catholique de Louvain'' with references B403201523492.

RESULTS

Patients characteristics are summarized in Table I. Although there were 2 distinct age groups related to different tumor histology types, the overall mean age was 46 years old (range, 13–84). There were 3 males (27%) and 8 females (73%).

Main operative characteristics are described in Table II. The mean tumor length on resected specimen was 15.4 cm. Most tumors were located in the thigh (82% of cases), with osteosarcoma being the most common histology (36% of cases). Reconstruction included both artery and vein in 9 patients, artery only in 1, and vein only in another. The vascular reconstruction technique employed was a termino-terminal interposition. Six patients required additional osseous reconstruction with mega-implants or bone allograft (Fig. 1). Complete microscopic resection was achieved in all cases. Clinical and duplex ultrasound follow-up was conducted biannually, with a mean follow-up of

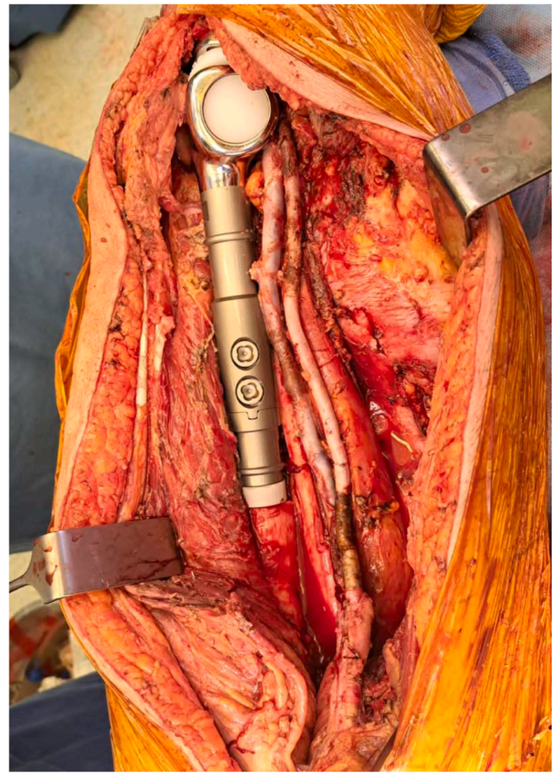

Fig. 1. Preoperative view of superficial femoral artery and vein reconstruction with arterial allografts and an associated megaimplant.

32.5 months. In case of complication, a CT angiography was performed to control patency of the reconstruction. Two early deaths (18%) occurred among the older patients, in the third and fifth month post-surgery, due to disease progression.

Limb salvage was achieved in 91% of patients. We deplored one amputation that was performed 16 months postoperatively in a patient of 70 years old, due to a nonhealing infection after a bone allograft fracture in an irradiated territory. The 1-year secondary arterial patency rate was 78% (Fig. 2). Three arterial occlusions were observed. One graft ruptured 7 months after initial surgery due to a friction mechanism on a mega-implant (Compress device, Zimmer Biomet). The patient presented with acute lower limb pain and a large knee hematoma. An urgent CT angiography revealed that the bypass was compressed by the hematoma, indicating an acute hemorrhage leading to bypass compression and resulting in acute limb ischemia. An urgent thrombectomy of the allograft was performed with patch insertion to restore secondary patency. In addition, a fascia lata patch was placed between the graft and the mega-implant to prevent direct mechanical stress on the vascular graft. A below-

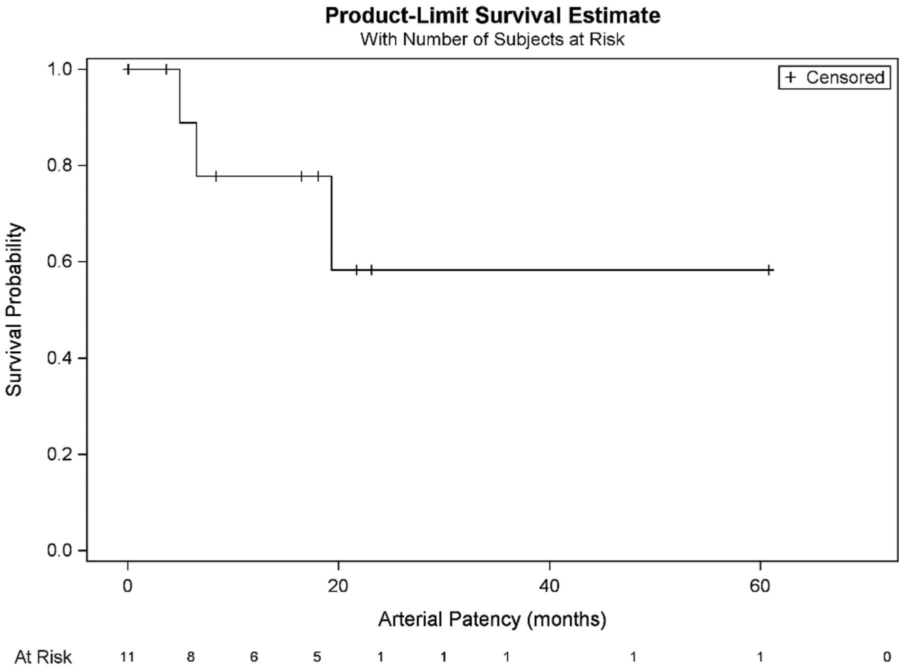

Fig. 2. Kaplan—Meier curve for secondary arterial patency. Kaplan—Meier survival analysis showing secondary arterial graft patency over time. The 1-year secondary patency rate was 78%.

knee bypass was found to be occluded on routine duplex ultrasound and confirmed by CT angiography at 19 postoperative months in a patient aged 19 years old. The occlusion showed few symptoms and more than likely resulted from a diameter mismatch between the allograft and the native vessel. It did not require any complementary treatment. Another arterial thrombosis, entirely asymptomatic, was detected after the completion of postoperative radiotherapy at 6 postoperative months during routine duplex ultrasound follow-up in an 18 years old patient. The last arterial occlusion, which was associated with venous graft thrombosis, occurred secondary to a wound dehiscence, complicating mobilization for knee flexion contracture in an 84 years old patient. It required complementary CT angiography investigation but no additional revascularization. The 1-year venous patency rate was 69% (Fig. 3). Three venous occlusions occurred and were discovered at the systematic duplex follow-up: two following radiotherapy and 1 due to a wound dehiscence. All venous thromboses were managed conservatively and remained clinically well tolerated. The overall complication rate was 54%. The most common complications were healing disorder, seroma, and surgical site infection (45%). Bone allograft fracture was noticed in 9% of cases. Functional outcomes were satisfactory across the cohort.

Median OS and both artery and veinous patency durations were not estimable due to insufficient events, mainly due to the small size of the cohort and the short follow-up period. The 1-year OS rate was 81.8 .

DISCUSSION

Limb salvage surgery is nowadays considered the standard treatment for resection of soft tissue sarcomas infiltrating major blood vessels, as it has showed better functional outcomes and quality of life.[10,11] The procedure involves vascular resection and reconstruction, with vascular substitutes mainly consisting of autologous venous or prosthetic grafts. Arterial reconstruction generally demonstrates more favorable patency rates compared to venous reconstruction. Arterial patency outcomes are primarily influenced by the location (above/below-knee) and length of the reconstruction, as well as the type of conduit used. Commonly, below-knee bypasses and more extensive reconstructions are associated with lower patency rate.[12–14] In reconstructive procedures during soft tissue sarcoma resection, autologous saphenous

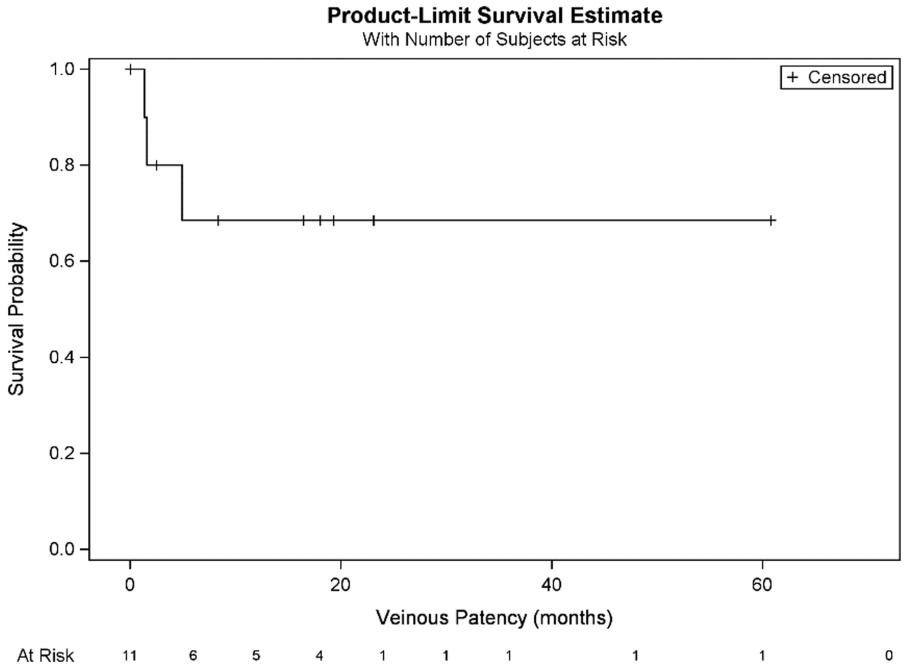

Fig. 3. Kaplan−Meier curve for venous patency. Kaplan−Meier analysis demonstrating venous graft patency. The 1-year patency rate was 69%.

vein grafts have demonstrated significantly higher patency rates compared to synthetic grafts. Park et al. reported a 2-year arterial and venous graft patency rate of 83.3% for autologous vein grafts versus 14.3% for prosthetic grafts ($P < 0.001$), with 52.9% of the procedures involving femoral bypasses.[15] Schwarzbach et al. reported a secondary 2-year patency rate of 78.3% for arterial reconstructions, including 7 iliofemoral or femoral bypasses, 10 femoropopliteal bypasses, and 2 below-knee bypasses. Among these, 40% of the reconstructions used vein grafts, while 60% involved prosthetic material.[5] Cetinkaya et al. described a 2-year arterial patency rate of 84.6%, with 91% of reconstructions performed using autologous veins. The majority of tumors were located in the thigh (61.5%), with a mean tumor size of 9.1 cm.[16] A recent series by Kang et al. involving 43 patients reported 1-year primary patency rates of 82.5% for arterial and 56.3% for venous reconstructions. The conduits used included autologous saphenous veins in 56.2%, artificial grafts in 26.3%, and cryopreserved allografts in 15.8%.[17] The necessity of venous reconstruction after resection remains debated[17]; however, most surgeons favor venous reconstruction due to the risk of severe venous congestion and leg edema. Tsukushi et al. compared outcomes between 12 cases of arterial reconstruction only and 13 cases of combined arterial and venous reconstructions, reporting similar rates of leg edema and functional outcomes in both groups, suggesting venous reconstruction was not necessary.[18] Davis et al. also reported that venous reconstruction was not performed in 9 vascular reconstructions during operations on 154 soft tissue sarcoma cases.[19] Schwarzbach et al. reported a 2-year primary venous patency rate of 54.9%, with no patients requiring operative or interventional treatment; venous thrombosis was either clinically asymptomatic or associated with well-tolerated edema.[5]

Table III summarizes patency and clinical results of our series and those of key studies in similar oncologic settings. Table IV summarizes the comparative advantages and disadvantages of potential vascular substitutes.

Our study is limited by the relatively small number of patients included and the short follow-up period, impacting on the estimates of survival and patency rates being at 1 year.

CONCLUSIONS

We present a first homogenous series of cryopreserved arterial allografts used for vascular reconstruction in limb-salvage soft tissue sarcoma

Table III. Patency and clinical results: comparing our results with key reports in similar oncologic settings

Studies	Total number and type of vascular reconstructions	Conduits characteristics	Arterial and venous patency	Limb salvage rate	Complications rates	Tumor length resection
Our present series	20 10 arterial 10 venous	Arterial allografts	Arterial: 78% at 1 year Venous: 67% at 1 year	91%	54%	15.4 cm
Kang et al. 2023	64	17 synthetic	Arterial: 82.5% at 1 year	97.4% at 1 year, 95.1% at 2 years	53%	NA
	43 arterial	36 Autologous vein	Venous: 56.3% at 1 year	89.4% at 3 years		
	21 venous	11 arterial allografts				
Cetinkaya et al. 2019	24	23 autologous vein	Arterial: 84.6% at 2 years	100%	69,2%	9.1 cm
	22 arterial	1 synthetic graft	Venous: 75.2% at 2 years			
	22 venous					
Park et al. 2018	27	6 synthetic	Arterial: 73% at 2 years	88%	NA	10.2 cm
	14 arterial	21 autologous vein	Venous: 61% at 2 years			
	13 venous					
Schwarzbach et al. 2005	32	22 synthetic dacron/ePTFE 10 autologous vein	Arterial: 78.3% at 2 years	94% at 2 years	57,2%	10.5 cm
	20 arterial		Venous: 54.9% at 2 years			
	12 venous					

Table IV. Evaluating vascular conduits: comparative characteristics

Type of vascular conduits	Pro	Con
Synthetic grafts	Widely available[12,13]	High infection risk[3] Less compliant[13] Poor long-term patency, especially in below-knee bypass[14]
Autologous saphenous vein	Superior long-term patency[15]	Requires contralateral vein harvesting[17] Potential limitation in diameter and length[17] Caliber mismatch when reversed[14]
Cryopreserved arterial allografts	Optimal biomechanical properties[6,9] Resistant in infected or high-risk surgical fields[1,7,8]	Limited availability[9] Risk of late degeneration (e.g., aneurysm)[6]

surgery, demonstrating favorable clinical outcomes despite significant extensive resection characteristics (length of tumoral resection, required concomitant bone allograft or substitutes). Despite their relative availability, cryopreserved arterial allografts theorically represent optimal substitutes for arterial replacement from a mechanical perspective. They have also shown resistance in infected or high-risk surgical fields. These allografts can be especially considered for large vascular resection, avoiding the need for vein harvesting from the contralateral limb and mitigating concerns about length, diameter limitations, or caliber mismatch (e.g., reversed vein). Duplex ultrasound surveillance of implanted cryopreserved arterial allografts is essential to monitor for potential degenerative changes. Larger patient series are needed to further validate these findings.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Valérie Lacroix: Writing – review & editing, Writing – original draft. **Pierre-Louis Docquier:** Data curation. **Xavier Banse:** Methodology. **Robin Evrard:** Methodology. **Arnaud Colle:** Methodology. **Maxime Elens:** Methodology. **Thomas Schubert:** Writing – review & editing, Methodology.

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