*Indian Journal of Public Health Research & Development*
*Volume 13 | Issue 4 | October-December 2022*

# Surgical and Oncological Outcomes of Extremity soft Tissue Sarcoma following en bloc Resection of the Neurovascular Bundle

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**How to cite this article:** Haitham Fekry Othman, Reham Saied Oreaba, Marawan Yousry, Assem Ahmed Elbrashy et al Surgical and Oncological Outcomes of Extremity soft Tissue Sarcoma following en bloc Resection of the Neurovascular Bundle. Volume 13 | Issue 4 | October-December 2022

**Abstract**

**Purpose:** Vascular involvement is a major limitation in attaining limb salvage with negative margins for managing soft tissue sarcomas (STS). The study evaluated surgical and oncological outcomes of vascular resection and reconstruction during the management of extremities STS.

**Methods:** The study involved 60 patients with STS treated with limb-sparing surgery divided into two groups; the Reconstruction Group (n=30) needed vascular reconstruction (VR) due to vascular involvement, and the Non-reconstruction Group (n=30) did not require vascular resection. All patients were followed up for at least one year to compare surgical and oncological outcomes.

**Results:** Vascular reconstruction involved a major artery and vein (n=16), a major artery alone (n=13), or a major vein alone (n=1). Most patients (n = 22) had VR with a saphenous vein graft. An artificial Gore-Tex graft was used in the other cases. A primary vascular repair was possible for the femoral artery in 3 more patients. Major wound complications, DVT, and persistent severe edema were more frequent in the Reconstruction Group (p = 0.004 0.015, and 0.001, respectively). Amputation was eventually required in 17% of the reconstruction group and a single patient in the non-reconstruction group. The overall survival (OS) at 18 months was apparently higher in the Reconstruction group (85.9%) than the non-reconstruction group (64.7%, p = 0.063). On multivariate analysis, age at diagnosis and surgical margin were the independent factors affecting OS. The functional outcome of both groups was similar (p= 0.676).

**Conclusion:** En-bloc resection of major vascular structures with the tumor and reconstruction has proven to be a feasible option in limb-salvage surgery. Vascular resection en bloc with limb sarcoma in locally advanced disease increases the safety of the surgical margins and gives comparable life expectancy and RFS to limb sarcoma patients with early disease who were treated with resection without vascular involvement. However, it keeps the advantage of having preserved functioning limb.

**Keywords:** soft tissue sarcoma, vascular resection, negative margin

## Introduction

Soft tissue sarcomas (STSs) can arise anywhere in the body, but extremities are the most common primary sites accounting for 60% of the cases[1].

Traditionally, STSs of the extremities were treated with amputation, especially for tumors close to the vascular bundle[2]. In nearly all patients, surgery is the primary local therapy. The therapeutic goals in treating extremity STS are survival and prevention

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of local recurrence with minimal morbidity and maintaining function[3]. Limb salvage surgery was proved feasible with adequate free margins in most patients with STS of the limbs[4] with better functional outcomes[5]. However, vascular [2]involvement is a major limitation in attaining limb salvage with negative margins. Therefore, vascular resection and reconstruction became a critical element of surgical removal of STSs infiltrating or enclosing a major vessel [6].

Few studies are available in the literature reporting the outcome of limb salvage surgery with vessel reconstruction in cases of STS. This study aimed to evaluate the surgical and oncological outcomes of vascular resection and reconstruction during the management of extremities STS.

## Patients and Methods

A prospectively collected database of 60 patients treated at National Cancer Institute, Cairo University for a primary or locally recurrent STS of the extremity. All patients were treated with limb-sparing surgery and were divided into two groups. The first group, Reconstruction Group (n=30), needed vascular reconstruction due to vascular involvement. Vessel resection was necessary to obtain adequate oncological surgical margins. The Non-reconstruction Group (n=30) did not require vascular. All patients were followed up for at least one year or to the time of death.

Comparison for Surgical and Oncological Outcome

The two groups were compared regarding demographic criteria, tumor characteristics, treatment modalities, surgical outcome, and oncological outcome.

The functional outcome of surgery was evaluated by the Toronto Extremity Salvage Score (TESS)[7].

## Results

The tumor size was larger in the Reconstruction Group but not statistically significant (p=0.055). Most tumors were histologically graded 2 or 3. Malignant fibrous histiocytoma and synovial sarcoma were the most common histological diagnoses.

In the Reconstruction Group, 16 patients had both a major artery and vein resected together en bloc with the tumor, 13 had a major artery removed, and one required excision of only a major vein with the tumor. Vessels resected and reconstructed were the common femoral (n = 14), superficial femoral (n = 8), popliteal (n = 4), axillary (n = 2) and brachial (n =1). Most patients (n = 22) had vascular reconstruction with a saphenous vein graft for both the artery and vein (n = 9) or the artery alone (n = 9). In four cases, the artery was reconstructed with an artificial Gore-Tex graft, and the vein was replaced with a saphenous vein graft. The artery alone was replaced with a Gore-Tex graft in another four patients. A primary vascular repair was possible for the femoral artery in 3 more patients. At the same time, associated femoral veins were ligated without reconstruction. Also, another patient had the femoral vein resected only without reconstruction, and these patients developed DVT and severe edema, which resolved with therapeutic anticoagulation. In addition to the vascular resections, four patients required resection of major motor nerves (Table 1).

Table 1 shows a comparison of surgical and oncological outcomes in the two groups. Persistent severe or very severe postoperative limb edema was more frequent in the Reconstruction group (p = 0.001).

**Table 1: Treatment outcomes in the two studied groups**

| | Reconstruction Group (n = 30) | Non-reconstruction Group (n = 30) | p value |
|---|---|---|---|
| Margin | | | 0.115 |
| R0 > 1 cm | 18 (60.0%) | 10 (33.3%) | |
| R0 < 1 cm | 8 (26.7%) | 14 (46.7%) | |
| R1 | 4 (13.3%) | 6 (20.0%) | |
| Muscle transfer | 13 (43.3%) | 5 (16.7%) | 0.024 |
| Motor nerve resection | 4 (13.3%) | 0 (0.0%) | 0.112 |
| Deep Vein Thrombosis | 11 (36.7%) | 3 (10.0%) | 0.015 |
| Significant edema | 26 (86.7%) | 6 (20.0%) | < 0.001 |
| Wound complications | 20 (66.7%) | 9 (30.0%) | 0.004 |
| Hospital stay (days) | | | 0.067 |
| ≤ 7 | 14 (46.7%) | 21 (70.0%) | |
| < 7 | 16 (53.3%) | 9 (30.0%) | |

*Data are presented as number (%)*

The limb salvage rate of the Reconstruction Group was 83%, as five patients ultimately underwent amputation. All of them received preoperative radiation. Two patients experienced severe wound

infection despite initial local flap coverage in the distal thigh. This led to osteomyelitis and compromised function of the GSV grafts for arterial replacement and required an above-knee amputation. Two patients experienced a rupture of the iliofemoral vascular repair after repeated wound complications. The last patient had a compartment syndrome developed peri-operatively, likely because the saphenous vein graft used for reconstruction was too small in diameter compared with the size of the autogenous common femoral vein, thus essentially creating a relative outflow obstruction and, finally, breakdown of the vascular anastomoses that necessitated a hip disarticulation. A single patient in the Non-reconstruction group needed amputation due to local recurrence fixed to the bone.

## Survival and effect of different prognostic factors

The median follow-up period was 17 months (range: 2-28 months). The overall survival (OS) at 18 months was higher in the Reconstruction group (85.9%) than the Non-reconstruction group (64.7%), but the difference was not statistically significant (p = 0.063). On multivariate analysis, age at diagnosis and surgical margin were the independent factors affecting overall survival (Table 3).

**Table 2: Factors affecting overall survival of the whole studied group (n=60)**

| Prognostic factor | | n | No. Died | OS at 18 m (%) | p - value |
|---|---|---|---|---|---|
| Treatment type | Reconstruction | 30 | 3 | 85.9 | 0.063 |
| | No Reconstruction | 30 | 10 | 64.7 | |
| Age (years) | > 50 | 23 | 8 | 63.2 | 0.056 |
| | ≤ 50 | 37 | 5 | 90.0 | |
| Sex | Female | 27 | 6 | 74.3 | 0.878 |
| | Male | 33 | 7 | 78.9 | |
| Size (cm) | ≤ 10 | 27 | 3 | 91.7 | 0.017 |
| | > 10 | 33 | 10 | 67.8 | |
| Location | Thigh | 28 | 5 | 83.1 | 0.572 |
| | Others | 32 | 8 | 77.3 | |
| Pathological type | MFH | 22 | 8 | 71.0 | 0.120 |
| | Synovial | 16 | 2 | 81.8 | |
| | Other | 22 | 3 | 87.8 | |
| Grade | Grade 1-2 | 29 | 3 | 88.2 | 0.026 |
| | Grade 3-4 | 31 | 10 | 70.4 | |
| Previous unplanned excision | Yes | 16 | 5 | 64.2 | 0.190 |
| | No | 44 | 8 | 84.5 | |
| RTH | Postoperative | 42 | 6 | 88.4 | 0.006 |
| | Preoperative | 15 | 7 | 52.5 | |
| Margin | R0 > 1 cm | 28 | 1 | 96.4 | 0.006 |
| | R0 < 1 cm | 22 | 7 | 79.5 | |
| | R1 | 10 | 5 | 33.8 | |
| Muscle flap | Yes | 18 | 5 | 60.9 | 0.202 |
| | No | 42 | 8 | 86.0 | |
| Limb Fate | Limp salvage | 54 | 11 | 82.8 | 0.475 |
| | Amputation | 6 | 2 | 50.0 | |

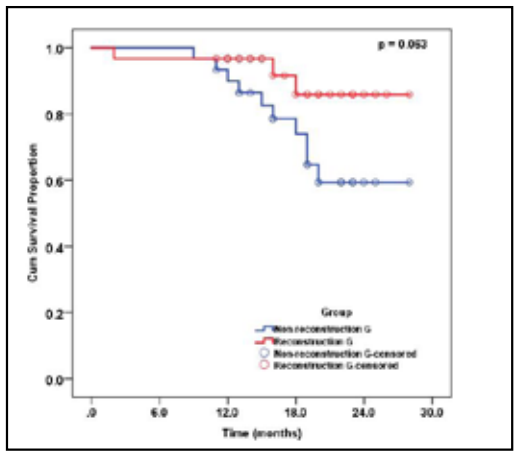
OS: Overall survival, MFH: malignant fibrous histiocytoma, RTH: Radiotherapy

**Table 3: Multivariate analysis of factors affecting overall survival**

| | B | p-value | HR | 95%CI |
|---|---|---|---|---|
| Age | 1.293 | 0.026 | 3.65 | 1.16-11.41 |
| Margin | | 0.018 | | |
| Margin (R0 < vs. R0 > 1 cm) | 2.473 | 0.021 | 11.86 | 1.45-97.20 |
| Margin (R0 < vs. R1) | 3.156 | 0.005 | 23.47 | 2.62-210.34 |

B: regression coefficient, HR: Hazard ratio, CI: Confidence Interval

**Figure 1: Overall survival of Reconstruction and Non-reconstruction groups**




The RFS of the two groups were slightly different but without statistical significance (p = 0.155). Large tumor size, advanced grade, previous unplanned surgery, preoperative radiotherapy, positive surgical margin, and muscle flaps were associated with worse RFS (Table 4). Multivariate analysis was invalid due to the small number of events in some subgroups.

**Table 4: Factors affecting recurrence-free survival of the whole studied group (n=60)**

| Prognostic factor | | n | No. Recurrences | RFS at 18 m (%) | p-value |
|---|---|---|---|---|---|
| Treatment type | Reconstruction | 30 | 5 | 83.0 | 0.155 |
| | No Reconstruction | 30 | 10 | 71.0 | |
| Age (years) | > 50 | 23 | 7 | 73.8 | 0.445 |
| | ≤ 50 | 37 | 8 | 79.0 | |
| Sex | Female | 27 | 7 | 78.8 | 0.795 |
| | Male | 33 | 8 | 75.4 | |
| Size (cm) | ≤ 10 | 27 | 4 | 87.7 | 0.045 |
| | > 10 | 33 | 11 | 67.8 | |
| Location | Thigh | 28 | 6 | 78.7 | 0.454 |
| | Others | 32 | 9 | 75.8 | |
| Pathological type | MFH | 22 | 5 | 79.2 | 0.856 |
| | Synovial | 16 | 5 | 78.8 | |
| | Other | 22 | 5 | 73.6 | |
| Grade | Grade 1-2 | 29 | 3 | 87.8 | 0.005 |
| | Grade 3-4 | 31 | 12 | 67.0 | |
| Previous unplanned excision | Yes | 16 | 9 | 43.9 | < 0.001 |
| | No | 44 | 6 | 89.5 | |
| RTH | Postoperative | 42 | 6 | 86.5 | < 0.001 |
| | Preoperative | 15 | 9 | 45.7 | |
| Margin | R0 > 1 cm | 28 | 1 | 95.0 | < 0.001 |
| | R0 < 1 cm | 22 | 4 | 95.2 | |
| | R1 | 10 | 10 | 0.0 | |
| Muscle flap | Yes | 18 | 8 | 52.5 | 0.010 |
| | No | 42 | 7 | 86.7 | |
| Limb Fate | Limp salvage | 54 | 12 | 79.6 | 0.202 |
| | Amputation | 6 | 3 | 53.3 | |

*RFS: Recurrence-free survival, MFH: malignant fibrous histiocytoma, RTH: Radiotherapy*

The functional outcome of both groups was similar. The median postoperative TESS score range was 65 (range: 35-100) in the Reconstruction Group compared to 59 (range: 40-100) in the Non-reconstruction Group (p= 0.676).

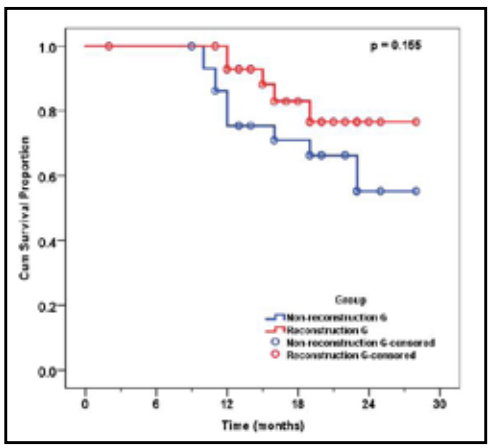



**Figure 2: Recurrence-free survival of Reconstruction and Non-reconstruction groups**

## Discussion:

The treatment goals of extremities STSs are long-term survival, avoiding recurrence, and maintaining function. Thus, limb-sparing surgery plus radiotherapy is the optimal choice. Invasion of large vascular structures creates a major challenge in managing these cases to assure safe excision with adequate surgical margins while maintaining a sufficient vascular supply of the limb. In this study, the amputation rate was higher in patients requiring vascular resection and reconstruction. This higher risk of amputation was associated with a significantly higher rate of wound complications. Two-thirds of the reconstruction group had major wound complications compared to 30% of the control group. Furthermore, resection of major vessels leads to loss of collateral vessels and interruption of lymphatic vessels. This causes further impairment of wound perfusion and increases postoperative edema [8]. Meta-analysis has shown that wound complication rates varied from

17.6% to 48%[9]. In one series, wound complications were recorded in 43.3%. It was more common in cases of vascular reconstruction (34.5% vs 15.3%; p = 0.05) [10].

Deep venous thrombosis was significantly more common in the reconstruction group (p=0.015). This complication may be another factor contributing to the higher rate of amputation. It has been shown that patients undergoing vascular surgery are at a higher risk of developing perioperative DVT[11]. Patients with STSs may be at increased risk of DVT due to malignancy and poor functional independence. [12]

It is crucial to note that all five patients who fated to have an amputation received preoperative radiotherapy. Major wound complications were a common precipitating factor in four cases. It is believed that radio- and chemotherapy may inhibit wound healing by preventing collagen synthesis[13]. It is known that previous radiotherapy in flap procedures may affect vascular availability[14]. Preoperative radiotherapy is often associated with higher rates of wound complications when surgery is done after the standard dose of 50 Gy[15]. In a multicenter randomized trial, major wound complications were recorded in 35% of patients treated with preoperative RT[16]. This risk is increased in lower extremities sarcomas adjacent to major neurovascular structures[17].

Yet, the current study has shown a relative survival advantage in the vascular reconstruction group. Thus, we believe that limb-salvage surgery followed by reconstruction of the vascular defect is the best alternative in cases involving vascular structures. The guidelines of this type of surgery need to be standardized. In a trial for guiding surgical management of STSs, Schwarzbach et al. [18] suggested their classification of vascular involvement pattern. They proposed arterial and venous reconstruction in type I involving both major arteries and veins if collateral venous drainage was impaired. Arterial reconstruction will be enough with adequate venous drainage. In the current study, 16 patients were classified as Type I, while 13 were Type II.

It was found that venous resection without reconstruction leads to limb edema and discoloration[19,20]. However, venous reconstruction did not reduce limb edema in other studies [21,22]. In the current series, we have performed venous reconstruction in 13 patients with a saphenous vein graft. Many reports support this approach of attempting venous reconstruction in all cases, especially when the collateral flow is unclear [23,24]. The rate of postoperative edema may correlate with the degree of disruption of venous collaterals at the time of resection[25].

An important limitation of this study is that it is not a typical comparative one as randomization is not possible. The patients in the non-reconstruction group did not require any type of vascular manipulation. However, we supposed that a comparative group is a better way to show the impact of vascular resection and reconstruction on outcome of treatment of STSs. In conclusion, limb-salvage surgery of extremities STSs is an effective treatment option achieving negative margins in most cases. Vascular resection and reconstruction were associated with more postoperative wound complications, DVT, and severe limb edema. Also, amputation was more frequent after vascular reconstruction. Overall survival was better after reconstruction but with no statistically significant difference.

**Ethical clearance:** taken from the NCI, Egypt ethical committee

**Source of funding:** self-funding

**Conflict of interest:** nil

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