

Limb-Sparing Surgery with Vascular Reconstruction in Lower Extremity Soft Tissue Sarcoma: Promising Results

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Abstract

It is not certain in the revised literature as to consider major vessel infiltration in extremity soft tissue sarcomas, constitutes an indication for amputation. This prospective study included fifteen patients with lower limb soft tissue sarcomas with main vessels invasion. They underwent radical resection and restoration of blood flow as the cornerstone step of limb preservation.

Purpose: To review the impact of vascular graft replacement following "radical" resection of Soft Tissue Sarcoma (STS) invading major lower limb vasculature on short term outcomes as regard limb-salvage rate.

Methods: Between December 2014 and January 2018, 22 consecutive patients with STS of the lower limb with vascular invasion were investigated, operated and followed up in the Vascular Surgery Department, Mansoura University Hospitals and were followed up for a period that ranged from 3-36 months with mean of 13 months, and a life table analysis was constructed for patency of arterial grafts and for the limb salvage rate.

Results: Out of the total (n=22), only 15 patients (12 males and 3 females) aged between 16-57 years had vascular replacement grafts (11 ePTFE, 2 saphenous vein grafts) for arterial reconstruction and 3 replacement grafts (2 ePTFE, 1 saphenous vein graft) for venous reconstruction. Life table analysis for arterial reconstruction showed primary patency rate of 73.85% at 10 months and 64.6% at the end of study with limb salvage rate of 86.7% at last follow up visit.

Conclusion: Malignant vascular infiltration should not be a barrier for radical resection for STS patients despite malignant vascular invasion and patients can avoid amputation after careful selection of patients.

Keywords Soft tissue sarcoma; Vascular reconstruction; Limb-sparing

Introduction

Limb salvage surgery, combining radical resection and radiotherapy, is the standard treatment of soft tissue sarcoma of the lower extremity. In the only randomized study comparing amputation with limb perseveration, Rosengerg et al. demonstrated that despite slightly higher local recurrence rates, limb salvage was not detrimental to patient survival [1], this is in keeping with data from other institutions, where the rates of initial amputation have decreased from 40% to approximately 5% as more effective surgical and oncological strategies evolved [2]. With this improvement in the extended surgical procedures, many surgeons have extended the indications for resection of locally advanced tumors to include those with invasion of major vessels that requires concomitant vascular reconstruction [3,4]. Local tumor control depends mainly on the type of resection and the neoadjuvant therapy which plays a key role in the local control of the tumor [5].

Major vascular reconstruction has allowed extending the limits of resection from local to radical, If Soft Tissue Sarcoma (STS) of primary vascular origin, then vascular resection is inevitable. Furthermore, if

STS infiltrate major vessels, then the vessels must also be resected to meet the established procedural standards, therefore it was proposed that whenever it is impossible to achieve wide resection margin without vascular resection, so vascular resection is indicated [6,7]. Incomplete resection of soft tissue sarcoma results in poor outcome and high rate of locoregional recurrence [8].

However, little is known as regard late morbidity of vascular reconstructions performed with tumor resection, including the incidence of occlusion of vascular grafts as well as associated limb amputation or mortality due to such vascular procedures.

The objective of this study was to highlight our experience in limb-sparing surgery in soft tissue sarcoma of lower limb with vascular invasion and to review the impact of such procedures as regard limb-survival.

Patients and Methods

This prospective study was conducted at Mansoura University Hospital between December 2014 and January 2018 in the vascular surgery department for Patients with soft tissue sarcoma who required a concomitant resection of a major vascular structure and vascular reconstruction in an attempt to achieve complete tumor radical resection (n=15). Patients were diagnosed as STS with vascular infiltration and encasement by:

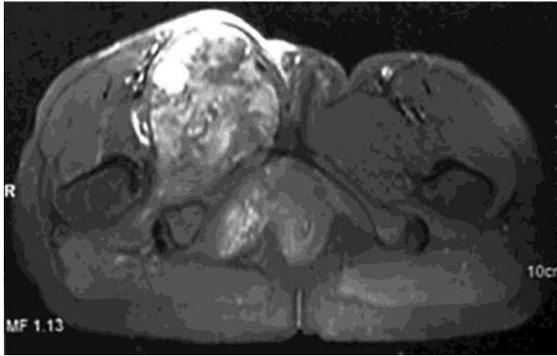


Figure 1: MRI of the upper thigh and groin showing STS involving the iliofemoral artery.



Figure 2: MRI of STS of the popliteal region compressing the popliteal artery.



Figure 3: MR angiography showing invasion of the iliofemoral artery.

CT and MRI scan (Figures 1 and 2), colour duplex sonography and MR angiography of the lower extremity (Figure 3) were done in all patients candidates for elective surgery. All patients had a preoperative baseline CT chest, abdominal ultrasound, bone survey.

Exclusion criteria

In locally recurrent STS after unplanned prior surgery and advanced stage of STS with distant metastasis. Tumours that were dissected easily along the major vessel adventitial layer that did not affect safety of excision were also excluded from the study (n=7).

Our study was approved by the regional ethical committee, after obtaining the Institutional Research Board (IRB) under number R. 18.04.164. All patients gave informed consent. Vascular "resection and reconstruction" was done in fifteen patients and all tumors were not of primary vascular origin.

The decision for vascular resection and replacement was done preoperatively in 22 patients, 7 patients were excluded on the basis of intraoperative findings. These procedures took place in a non-irradiated field and primary tumor site in 15 patients (100%).

In this study vascular involvement by the tumor were classified into:

- Arterial and venous involvement (group 1) (n=3)
- Arterial involvement only (group II) (n=10)
- Venous involvement only (group III) (n=2) (popliteal vein)
- Non-involved major vascular structure (group IV) (n=7)

The tumor location, size, pathology and histological grade were also assessed (Table 1).

Characteristics	No. (n=15)	%
Male	12	80%
Female	3	20%
Tumor origin:	15	100%
Non vascular origin	0	0%
Vascular origin		
Histological diagnosis:	7	46.66%
Fibrosarcoma	3	20%
Synovial sarcoma	3	20%
Liposarcoma	2	13.33%
Neurogenic sarcoma		
Tumor location:	12	80%
Thigh	2	13.33%
Popliteal fossa	1	6.66%
Groin		
Histological grade:	6	40%
High grade	6	40%
Intermediate grade	3	20%
Low grade		

Vessel infiltration:	10	66.66%
Artery alone	2	13.13%
Vein alone	3	20%
Artery, Vein	7*	
No vessel infiltration		
*excluded from the results		

Table 1: Clinical and pathological factors in patients with STS of lower extremity involving major blood vessels.

Surgical technique

An elliptical incision is made around the previous biopsy incision or needle biopsy site. Flaps are developed to nearly the palpable extent of the tumor. Proximal and distal entry in the compartment helps to determine the width of the flaps more accurately to avoid unnecessary wide flaps and when the course of major blood vessels is close to sarcoma location, vessel loops and vascular clamps are applied then dissection is continued far to the vessel sheath which was removed with the tumor with 3 cm of uninvolved structure. Neural structures were included in the resected specimen if they were encased or infiltrated by the tumor.

For sarcoma of the groin (Case No. 1) that was clearly located below the inguinal ligament a vertical abdomino-inguinal incision (Figure 4) with division of inguinal ligament was done to gain entry to retroperitoneal space and allows control of external iliac artery.



Figure 4: Abdomino-inguinal incision and division of inguinal ligament for groin sarcoma.

When resecting sarcoma of the thigh, the incision, centering over the middle of the mass is parallel to course of femoral vessels for exposure of proximal superficial femoral artery with division of the hiatus tendineus is made for exposure of distal superficial femoral artery and popliteal artery (Figure 5) and for sarcoma of the popliteal region and medial aspect of the knee, a longitudinal medial incision is made which allows exposure of distal SFA and popliteal artery.

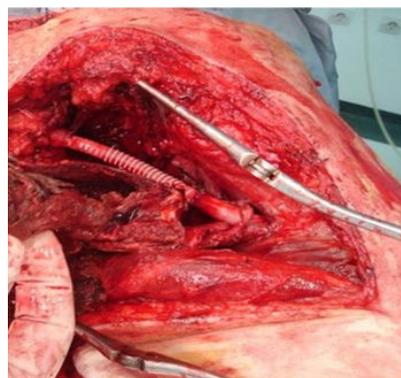


Figure 5: Above knee femoro-popliteal ePTFE graft.

Reconstruction then takes place and finally when adjacent muscles are detached at one of their two ends and are rotated to cover the grafts.

Arterial and deep venous flow was restored anatomically according to the resection site, the length of the vascular defect and, diameter of the involved vessel. Arteries were reconstructed by ring-enforced synthetic graft (expanded polytetrafluoroethylene (ePTFE 8 mm) and by (reversed great saphenous vein). In group I patients superficial femoral veins were reconstructed by ring-sustained ePTFE (6 mm) prostheses (n=2) or autologous vein grafts (non-reversed GSV) (n=1). If the GSV had not been removed previously and was patent (duplex details) venous replacement was not performed. Anatomic repair (end to end anastomosis) was the preferred reconstruction, and the contralateral GSV was the preferred autologous graft for arterial and venous reconstructive procedures (Figure 6).



Figure 6: Postoperative angiography after reconstruction of proximal superficial femoral artery showing patent vascular graft.

At operation, arterial and venous involvement group 1 soft tissue sarcoma (n=3) were assessed and all arteries (superficial femoral artery) (n=3) were resected and replaced by ePTFE (8 mm) graft and 3 superficial femoral veins were resected and replaced by non reversed saphenous vein graft from the other limb in one patient and 2 short segment (6 mm) ePTFE for other two veins and venous reconstruction was done due to thrombosis & fibrosis of ipsilateral great saphenous vein (n=3).

Routinely, patients received intravenous prophylactic antibiotic, 3rd generation cephalosporin 1gm before surgery and drains were placed. Perioperatively, a low-dose regimen of low molecular weight heparin (enoxaparin sodium) was given subcutaneously and 5000 unit unfractionated heparin with clampig.of the artery before resection. After discharge, oral anticoagulation therapy was administered restrictively only in below-knee reconstructions. All our patients received postoperative radiotherapy including field size and operative scar, (n=15).

Medical records included the operative procedure details, vascular graft used, pathology of the tumor, and perioperative and postoperative complications. Late survival and tumor recurrence were determined and characterized by review of clinical records and pathology reports. Patency of the grafts were determined by clinical examination, review of follow-up duplex sonogram, the main outcome measures were early (<30 days) morbidity and mortality, late (>30 days) vascular morbidity and mortality. Graft thrombosis, locoregional tumor recurrence was determined as end point of the study. Primary patency of the vascular reconstruction grafts and limb salvage rate were assessed.

Follow up

Patients were seen regularly during the observation period in vascular outpatient clinic. The standard follow up was weekly for the first month, and every month after surgery. Patients were questioned about symptoms suggestive of graft thrombosis, including pain and swelling. Clinical examinations were usually combined with duplex sonography and CT angiography (post-operative) for selected cases to delineate distal runoff circulation in cases of postoperative thrombosed graft with symptomatic peripheral arterial insufficiency. In addition, patients were also seen according to the routine oncologic follow-up schedule using CT chest and MRI of the primary & bone scan if needed.

Statistical analysis

Clinical data were collected from the patients' clinical records, then the data was analyzed using SPSS (Statistical Package for Social Sciences) version 20. Kaplan-Meier method was used to estimate the patency rate for the group.

Results

Fifteen patients (12 male, 3 females) with ages ranging from 16 to 57 years (mean age, 36 years) underwent radical resection with vascular reconstruction (16 vascular replacement grafts).

Medical comorbid conditions included hypertension in 6 patients (40%), diabetes mellitus in 6 patients (40%) and known coronary artery disease in one patient (6.66%).

Tumor size ranges from (5.5 cm-15 cm); with average 10.9 cm and 80% of the tumors were in the thigh.

Pathological examination of the resected specimen revealed complete tumor resection with negative margin in 100%. 46.66% were fibrosarcoma and 13.33% were neurogenic sarcoma, 20% of the tumors were of low histological grade (Table 1).

The operative procedure was the initial surgical procedure for tumor resection in all patients (100%).

Vessels which were involved and resected were the ileofemoral artery (external iliac and proximal part of common femoral artery (n=1), proximal superficial femoral artery (n=6), distal superficial femoral artery (n=4), popliteal artery (n=2) and superficial femoral vein (n=3) and 2 popliteal veins were resected and not replaced because they were already thrombosed.

Thirteen arterial reconstructive procedures included ileofemoral ePTFE graft replacement in 1 case (7.69%), 6 femoro-femoral (46.15%), 4 femoro-popliteal above knee (30.76%), 2 femoro-popliteal below knee (15.38%). Three reconstructive procedures for venous involvement, they were all in SFV (100%). The resected veins were replaced in 2 patients by short segment ePTFE graft and one contralateral saphenous vein graft (Table 2).

Vessels affected	Reconstructive procedure and graft used	%
Ileofemoral artery	Resection+ileofemoral replacement ePTFE graft (8 mm) (n=1)	6.25 %
Proximal superficial femoral artery	Resection+femoro-femoral replacement ePTFE graft (8 mm) (n=6)	37.5 %
Distal superficial femoral artery	Resection+femoro-popliteal above knee ePTFE graft (8 mm) (n=4)	25%
Popliteal artery	Resection+femoro-popliteal below knee (graft saphenous graft) (n=2)	12.5 %
Superficial femoral vein (SFV)	Resection+femoro-femoral non-reversed saphenous graft (n=1), and ePTFE (6 mm) (n=2)	18.7 5%
Resection type:	N=15	100 %
CR with -ve margin	N=0	0%
CR with +ve margin	N=15	100 %
Surgery +ERT		100 %
CR=Complete resection, ePTFE=Expanded polytetrafluoroethylene, ERT=External radiotherapy		

Table 2: Treatment and reconstructive procedures in STS lower extremity patients.

The length of graft used ranged from 5 cm-19 cm (average of 12.5 cm). Thirteen ePTFE (81.25%) were used (8 mm, n=11) and (6 mm, n=2) and 3 great saphenous vein interposition graft (2 reversed for arterial, and one non-reversed for venous cases (18.75%) were used in this series.

Follow up period ranged from 3-36 months with mean of 13 months. Early postoperative morbidity (<30 days) showed soft tissue and skin necrosis in 3 patients (20%), these patients needed debridement and secondary closure in the 2nd week of postoperative period in 2 patients, one patient showed gaped wound and graft exposure that was left to granulate and healed satisfactory. Twelve cases (80%) showed leg swelling in the operated leg that was easily controlled by elevation, elastic support in all cases. Two patients developed hematoma (13.33%) and one patient needed re-exploration and re-fashioning of distal anastomosis due to expanding hematoma and the other needed evacuation. Two patients developed compartmental syndrome that needed fasciotomy (n=2) and one developed peronei paresis due to residual peroneal nerve palsy in early postoperative course (Table 3).

Variable	No.	%
Early morbidity <30 days:	12	80%
Leg swelling	3	20%
Soft tissue, skin necrosis	2	13.33%
Wound revision (secondary closure)	2	13.33%
Haematoma	1	6.66%
Infection	1	6.25%
Refashioning of distal anastomosis	1	6.66%
Peronei paresis	1	6.25%
Graft thrombosis		
Late morbidity >30 days:	6	37.5%
Graft thrombosis (2 venous, 4 arterial)	1	6.25%
Excision of graft and obturator bypass	0	0%
Revision of bypass	2	13.33%
Severe lymphatic obstruction	2	13.33%
Above knee amputation	2	13.33%
Distant metastasis	1	6.66%
Local recurrence of STS		
Function:	2	13.33%
Excellent	10	66.66%
Fair	3	20%
Poor		
Status:	12	80%
ANED	0	0%
DOD	3	20%
AWED		
ANED=Alive with no evidence of disease, DOD=Dead of disease, AWED=Alive with evidence of disease MST, SCORE: Musculoskeletal, Tumor score.		

Table 3: Postoperative complications and functional outcome of the current series.

All venous replacement grafts (18.75%) of this series were thrombosed by 2 weeks, 10 and 12 months of the study and those patients complained of variable degrees of oedema and it was managed conservatively.

Two patients developed severe lymphatic obstruction (13.33%) in the late postoperative period in group I patients after reconstruction of both superficial femoral artery and vein. These patients were managed in a conservative manner.

The 1st patient in this series showed a groin, upper thigh STS that necessitated resection of ileofemoral artery with ePTFE (8 mm) ileofemoral replacement, unfortunately she developed staphylococcal infection, secondary hemorrhage 2 weeks postoperatively that necessitated excision of the graft and control of infection for 2 weeks by IV antibiotic administration on the basis of bacterial sensitivity test and later on, an obturator bypass was performed but eventually it was thrombosed with detachment of distal anastomotic suture line (Figure 7) and the patients experienced irreversible ischaemia that necessitated high above knee amputation.

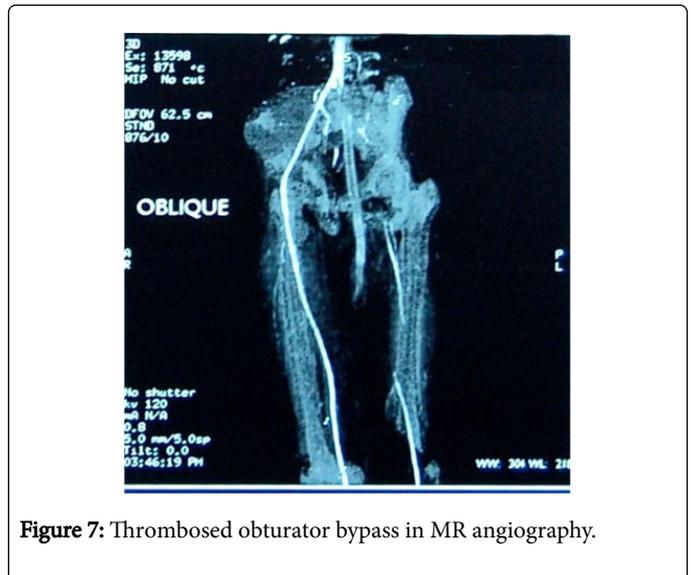


Figure 7: Thrombosed obturator bypass in MR angiography.

Clinical examination, colour duplex sonography (n=15) and CT angiography in 3 patients were performed in postoperative follow up period to document vascular graft patency.

The primary patency rate for arterial reconstruction grafts showed patency rate of 73.85% at 10 months and 64.6% at the end of study (Figure 8).

Limb salvage rate was (86.7%) at the end of the study (Figure 9) and functional results were assessed as good in 12 patients (80%) and poor in 3 cases (20%) due to nerve injury at fasciotomy in one patient and severe lymphatic obstruction in 2 cases. Locoregional recurrence of the resected neoplasm occurred in one patient (6.66%) during follow up period and this patient underwent high above knee amputation. Distant pulmonary metastasis in 2 patients (13.33%).

There was no perioperative or postoperative mortality in the studied group and fifteen patients were alive at the end of study and 12 of them (80%) were alive with no evidence of disease and 3 patients were alive with evidence of disease (20%).

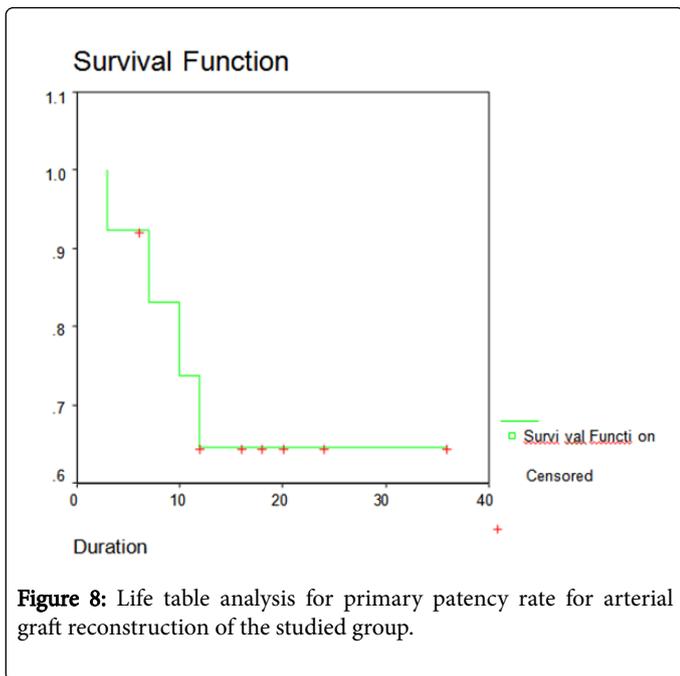


Figure 8: Life table analysis for primary patency rate for arterial graft reconstruction of the studied group.

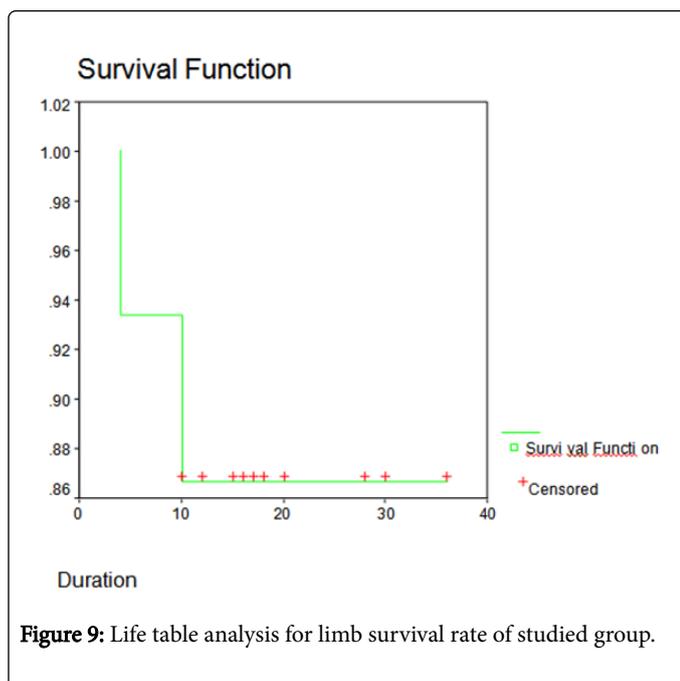


Figure 9: Life table analysis for limb survival rate of studied group.

Discussion

Current advances in vascular techniques, conduit technology permit reconstruction of all vessels with a high degree of durability [9]. Despite the recognized success of vascular reconstructions, particularly for major abdominal and thoracic vessels, many surgeons still consider tumor invasion of critical vascular structures a relative contraindication to tumor removal [10]. Our study was performed to highlight on our experience in that frequently encountered vascular interference procedures.

Koperna et al. found that morbidity rate associated with vascular procedures was 21% in 13 patients who underwent resections of lower extremity sarcomas [11]. However, late graft complications were few and limb salvage was possible in patients who otherwise would have required amputation. In contrast, to these favorable reports, Bianchi et al. found morbidity and mortality to be significant and substantially increased in patients undergoing a variety of oncologic and concomitant vascular procedures at their institution [12].

When performing a vascular reconstructive procedure as part of an oncologic surgery, the additional late morbidity that may occur with failure of the reconstruction (graft thrombosis) can be reviewed by constructing a life table where limb loss or failure of a vascular reconstruction is a primary end point. Another potential concern of any vascular reconstruction is late failure with compromise to vital structures or limb loss. In this study, late vascular morbidity did occur with failure of 4 arterial reconstructions grafts within the period of follow up and in spite of this failure there was no limb loss and those patients had good, distal runoff circulation and were managed in a conservative therapy.

A major complication in these extensive tumor operations is wound infection, which is reinforced by the prolonged surgery and postoperative large cavities filled with fluid from interrupted lymphatics. Matthias et al. reported incidence of infection 9.52% and it was managed successfully in all cases [13]. Davis et al. reported 12 additional procedures to achieve wound healing in 9 vascular reconstruction procedures with mean time for wound healing was significantly higher ($p < 0.002$) [14]. However, in the present study surgical infection developed in one patient (6.66%) and wound necrosis in 3 patients but eventually all were healed at last follow up.

The value of venous reconstruction in extremity tumor surgery has not yet been established. However, interruption of the venous outflow added to the interruption of the lymphatic outflow that was entailed by the extensive soft tissue resection may cause severe edema. Some authors concluded that venous reconstruction is not essential, either to avoid intractable edema or to ensure patency of the arterial system [15]. In this series, a varying of degree of oedema occurred (80%) and 2 cases developed severe lymphatic obstruction after reconstruction of superficial femoral A, veins and all were managed in a conservative way. In fact our results showed that the all grafts used for venous reconstruction clot fairly promptly and had no impact on limb survival.

Bergan et al. and Yeager et al. reported that the patency of autogenous saphenous vein grafts was significantly better than that of polytetrafluoroethylene grafts in infrapopliteal vascular reconstructions [16,17]. But, they also stated that there was no significant difference between the patency or saphenous vein grafts and polytetrafluoroethylene grafts in the femoro-popliteal regions and the autogenous saphenous vein graft is considered safer than the synthetic graft in vascular reconstruction after resection of major vessel of the extremities, but the synthetic grafts have the advantages of shortening the operation time, the availability of grafts with size and length matching the resected vessels. In the present series, 2 saphenous vein grafts and 11 of ePTFE for arterial reconstructions were used where ePTFE grafts were used for replacement of ileofemoral and femoro-popliteal arteries and saphenous vein grafts were used for arterial reconstruction below knee and one saphenous vein graft was patent at last follow up visit.

Costanzo et al. reported a primary patency rate of 93% and 90% at 12 and 24 months respectively, and in this study the primary patency rate for arterial reconstruction was 73.85% and 64.6% at 10 months and at the end of the study [18].

In reports by Koperna et al. and Karakousis et al. local recurrence rates of lower extremity sarcomas were found to be 6% and 0%, respectively [11,19]. Nishinari et al. conducted a prospective study for 25 STS patients with 15 died of cancer, 3 alive with recurrence 7 alive without recurrence and one patient had disarticulation of hip due to local recurrence [20]. Of the fifteen lower extremity sarcomas resected, in this series no patients died of distant metastatic disease at last follow up visit and only one cases (6.66%) recurred in this series and this patient had a high above knee amputation later on.

In a study done by Robert E et al. they reported 10% amputation rate that was related to arterial occlusion, infection and tumor recurrence and 50% of studied patients were alive with no evidence of disease and satisfactory function (81.25%) was possible even with the additional sacrifice of a single major peripheral nerve and in this series, 2 cases (13.33%) needed amputation due to infection (6.66%) in one patient and local recurrence of the tumor in the other (6.66%) [21].

Davis et al. evaluated the functional status using a validated tool, the musculoskeletal, tumor score [14]. (MSTS) and there was no significant difference between limb sparing alone and limb sparing with vascular reconstruction. In our study, the functional outcome of the studied patients followed the older functional ratings contained simple terms such as excellent, fair and poor. These data were included in the analysis but were not amenable to more sophisticated analyses. Functional status was rated as excellent in 2 patients (13.33%), fair in 10 patients (66.66%), and poor in 3 patients (20%) due to nerve injury at fasciotomy in one patient and in 2 patients with severe lymphedema.

limb functional status was evaluated using the MSTS score for lower extremity that include walking ability, gait and use of supports in addition to pain and emotional acceptance, and finally we had fair outcome in 10 patients (66.66%).

In conclusion, invasion of major vascular structures has been considered by some a barrier to the removal of large neoplasms. Our results are in support of the fact-that the need for resection and reconstruction of a main artery should not prohibit the resection of any given tumor. This study demonstrates that most arterial reconstructions performed in this setting have a high degree of success, do not appreciably increase overall early morbidity and mortality, and have little influence on short-term outcome. Although late graft occlusion has occurred, most could be managed successfully due to development of good collateral circulation and did not result in limb loss.

Although a study involving a larger patient population is needed, results from the current series and data gathered from similar reports in the literature clearly indicate that patients can avoid amputation, despite malignant involvement of major vessels to their extremities.

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