

Review

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Complex reconstruction of the lower extremity following sarcoma resection: a literature review

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Abstract

While amputation was traditionally the only option available for patients with sarcomas of the extremities, chemotherapy, radiation, and advances in microsurgical technique have allowed many patients to undergo limb-salvaging procedures. Given the low incidence and heterogeneity of these tumors, there is currently no standard treatment algorithm for limb reconstruction after large sarcoma resection. Thus, we systematically reviewed the various types of free tissue transfer used for the reconstruction of lower limbs after sarcoma resection. Techniques were described based on anatomic location. This literature review supports free tissue transfer as a safe and acceptable modality for reconstruction after sarcoma resection of the lower limb. It allows for the application of healthy vascularized tissue to the defect while also providing freedom of flap positioning. Flap choice is dependent on tumor and defect size, tissue type and function, as well as donor site availability.

Keywords: Lower extremity, sarcoma, reconstruction

INTRODUCTION

Soft tissue and bone sarcomas represent about 1% of all adult tumors^[1], affecting 1.8-5 out of every 100,000 people annually^[2]. The lower limb is the most common site of sarcoma occurrence, representing 29%-40% of all cases^[3,4]. Although amputation was traditionally the only option available for patients with sarcoma of the extremities, recent implementation of a multimodal treatment approach along with advancements in chemotherapy and microsurgical techniques has led to the influx of limb salvage therapy for these cancers^[5,6]. Currently, wide tumor excision combined with adjuvant and or neo-adjuvant therapy is the standard of care for the successful treatment of sarcoma of the lower limbs^[2].



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Quite often, sarcoma excision results in large anatomical soft tissue deficits with resultant exposure of vital structures such as bones, tendons, and neurovascular bundles, necessitating complex soft tissue reconstruction with vascularized soft tissue transfer thus facilitating further treatments as well as maintaining or regaining structural function and integrity of the limb in question. To this end both pedicled and free tissue transfers have become a central component of lower extremity salvage after resection and chemo-radiation therapy. Recent data has shown that these complex reconstructions have provided faster recovery with adequate soft tissue reconstruction and maintenance of functionality of the limb^[2,6-11].

Currently there is no standard treatment algorithm for limb reconstruction after large sarcoma resection. In part this due to the low incidence of these tumors as well as the heterogeneity of extremity sarcoma. This problem is further compounded by the multitude of neo-adjuvant modalities that are used to treat these tumors as well as the timing of the oncological resection. Hence a comprehensive reconstructive approach that maximizes the maintenance of function and aesthetics depends primarily on the location and size of the defects as well as the muscles, tendon, blood vessels and nerves that were extirpated. The goal of this literature review is to therefore outline various author reports published in the current literature describing the various types of free tissue transfer used for the reconstruction of the lower limbs after sarcoma resection.

METHODS

The PubMed database was used to review literature describing free tissue coverage of the lower extremity following soft tissue sarcoma resection. The entire PubMed library was used dating to 2016. The following search terms were used: “Neoplasms, Connective and Soft Tissue” [Mesh] OR (“sarcoma” [MeSH Terms] OR “sarcoma” [All Fields]) AND (“lower extremity” [MeSH Terms] OR (“lower” [All Fields] AND “extremity”[All Fields]) OR “lower extremity” [All Fields]) AND (“free tissue flaps” [MeSH Terms] OR (“free”[All Fields] AND “tissue” [All Fields] AND “flaps” [All Fields]) OR “free tissue flaps” [All Fields]. All studies published in the English language were included. Articles were excluded if they met the following criteria: exclusively pediatric patients, cadaver subjects, pathology of the pelvic girdle, exclusively pathology related to trauma, pathology related to skin neoplasms, and studies exclusively describing pedicled flaps. [Table 1](#) lists the studies included in this review. [Table 2](#) describes the types of flaps used for lower extremity reconstruction by region.

RECONSTRUCTION BASED ON TUMOR LOCATION

Thigh

Several factors must be taken into consideration when approaching reconstruction of the thigh. Primarily, malignant sarcomas of the femur are generally challenging to treat because radical resection of the tumor often requires simultaneous resection and reconstruction of the major femoral vessels. Tumor proximity to critical neurovascular structures is particularly of concern in the adductor compartment, where outcomes are generally poor, with high local recurrence rate, high complication rates and short long-term survival^[12].

The first report of reconstruction of major vessels was by Fortner *et al.*^[13] for the treatment of seven patients with sarcoma involving the iliac and femoral vessels. In their study, 3 out of 7 patients underwent vascular reconstruction with polyester or vein grafts, resulting in less postoperative complications and edema compared to the remaining 4 patients who did not undergo vascular reconstruction. In a series by Muramatsu *et al.*^[14], 12 out of 14 patients requiring arterial reconstruction underwent femoropopliteal reconstruction using a contralateral greater saphenous vein (GSV) graft ranging from 12-30 cm, while the 2 who required femoroinguinal reconstruction received expanded polytetrafluoroethylene (ePTFE). Twelve of their 15 patients additionally required venous reconstruction of the superficial vein, deep femoral vein, and greater saphenous vein, which was also done using a GSV or ePTFE graft. Of these patients, 6 had

Table 1: Studies included

Author	Year	Study describes
Abramson <i>et al.</i> ^[5]	1997	Free tissue transfer + radiotherapy
Cordeiro <i>et al.</i> ^[6]	1994	Free tissue transfer + bone reconstruction
Serletti <i>et al.</i> ^[7]	1998	Free tissue transfer
Heiner <i>et al.</i> ^[8]	1993	Free tissue transfer
Barner-Rasmussen <i>et al.</i> ^[9]	2009	Free tissue transfer
Leow <i>et al.</i> ^[10]	2005	Free tissue transfer + bone reconstruction
Momeni <i>et al.</i> ^[11]	2011	Free tissue transfer
Muramatsu <i>et al.</i> ^[14]	2011	Free tissue transfer
Ng <i>et al.</i> ^[15]	2008	Free tissue transfer
Zbucnea ^[16]	2016	Free tissue transfer
Nahabedian <i>et al.</i> ^[17]	1999	Free tissue transfer
Vaiienti <i>et al.</i> ^[18]	2013	Free tissue transfer
Cadenelli <i>et al.</i> ^[19]	2015	Free tissue transfer
Baxter <i>et al.</i> ^[20]	2007	Free tissue transfer
Miyamoto <i>et al.</i> ^[21]	2014	Free tissue transfer
Lee <i>et al.</i> ^[22]	2004	Free tissue transfer + radiotherapy
Choudry <i>et al.</i> ^[23]	2008	Free tissue transfer
Saito <i>et al.</i> ^[24]	2010	Free tissue transfer + bone reconstruction
Zweifel-Schlatter <i>et al.</i> ^[25]	2006	Free tissue transfer
Hong <i>et al.</i> ^[26]	2005	Free tissue transfer
Weichman <i>et al.</i> ^[27]	2015	Free tissue transfer
Agostini and Agostini ^[28]	2009	Free tissue transfer
Cribb <i>et al.</i> ^[29]	2010	Free tissue transfer
Brenner and Rammelt ^[30]	2002	Free tissue transfer
Medina <i>et al.</i> ^[31]	2014	Free tissue transfer
Struckmann <i>et al.</i> ^[32]	2014	Free tissue transfer
Zaretski <i>et al.</i> ^[33]	2004	Bone reconstruction
Capanna <i>et al.</i> ^[34]	1993	Bone reconstruction
Beris <i>et al.</i> ^[35]	2011	Bone reconstruction
Yajima and Tamai ^[36]	1994	Bone reconstruction
Duffy <i>et al.</i> ^[37]	2000	Bone reconstruction
Ruch and Komar ^[38]	1997	Bone reconstruction
Mastorakos <i>et al.</i> ^[39]	2002	Bone reconstruction
Enneking <i>et al.</i> ^[40]	1993	Nerve reconstruction
Doi <i>et al.</i> ^[41]	1998	Nerve reconstruction
Doi <i>et al.</i> ^[42]	1999	Nerve reconstruction
Fortner <i>et al.</i> ^[13]	1977	Vascular reconstruction
Tsukushi <i>et al.</i> ^[43]	2008	Vascular reconstruction
Nishinari <i>et al.</i> ^[44]	2015	Vascular reconstruction
Wortmann <i>et al.</i> ^[45]	2017	Vascular reconstruction
Rosenthal <i>et al.</i> ^[46]	1993	Radiotherapy
O'Sullivan <i>et al.</i> ^[47]	2004	Radiotherapy
Baldini <i>et al.</i> ^[48]	2013	Radiotherapy
Arbeit <i>et al.</i> ^[49]	1987	Radiotherapy
Shiu <i>et al.</i> ^[50]	1984	Radiotherapy
O'Sullivan <i>et al.</i> ^[51]	2002	Radiotherapy
Cheng <i>et al.</i> ^[52]	1996	Radiotherapy
Kunisada <i>et al.</i> ^[53]	2002	Radiotherapy
Davis <i>et al.</i> ^[54]	2005	Radiotherapy
Townley <i>et al.</i> ^[55]	2013	Radiotherapy
Chao <i>et al.</i> ^[56]	2012	Radiotherapy
Hidalgo <i>et al.</i> ^[57]	1992	Radiotherapy
Brennan <i>et al.</i> ^[58]	1987	Radiotherapy
Ormsby <i>et al.</i> ^[59]	1989	Radiotherapy
Hidalgo and Carrasquillo ^[60]	1992	Radiotherapy
Spierer <i>et al.</i> ^[61]	2003	Radiotherapy
Sadrian <i>et al.</i> ^[62]	2002	Radiotherapy
Pisters <i>et al.</i> ^[63]	1996	Outcomes
Popov <i>et al.</i> ^[64]	2000	Outcomes
Penna <i>et al.</i> ^[65]	2011	Outcomes
Lopez <i>et al.</i> ^[2]	2015	Outcomes

Table 2: Types of flaps used for lower extremity reconstruction based on region

Author	Year	Regions described	Flaps described		
Cordeiro <i>et al.</i> ^[6]	1994	Thigh	LD RA Fibula		
		Knee and proximal leg	LD RA Scapula		
		Mid and distal leg	RA LD Scapula Fibula		
		Foot	Radial forearm Lateral arm RA		
		Barner-Rasmussen <i>et al.</i> ^[9]	2009	Foot	LD
				Ankle	ALT
				Lower Leg	Radial forearm
				Knee	Gracilis
				Thigh	TFL
		Leow <i>et al.</i> ^[10]	2005	Inguinal	Fibula
Trochanteric	RA				
Gluteal					
Thigh	LD				
Gluteal	Fibula				
Momeni <i>et al.</i> ^[11]	2011	Knee	RA (free + pedicled)		
		Popliteal fossa			
		Middle third of the leg			
		Ankle			
		Lower leg	ALT		
Muramatsu <i>et al.</i> ^[14]	2011	Thigh	LD Pedicled RA Pedicled medial gastrocnemius TFL		
		Lateral Posterior Thigh	ALT		
		Knee	Lateral genicular artery flap		
		Knee	Advancement propeller perforator ALT		
		Knee	Gastrocnemius		
Ng <i>et al.</i> ^[15]	2008	Knee	Deep inferior epigastric artery perforator flap		
		Thigh	RA		
		Knee	Gastrocnemius		
		Leg	Gastrocnemius		
		Foot	RA		
Zbucnea <i>et al.</i> ^[16]	2016	Lower leg	Soleus		
		Lower leg	LD		
		Ankle	Composite LD + scapular bone Scapular-parascapular flap Free scapular flap ALT		
		Tibia	Lateral arm fasciocutaneous flap Scapular fasciocutaneous flap Scapular/parascapular fasciocutaneous ALT fasciocutaneous		
		Lower leg	ALT		
Cadenelli <i>et al.</i> ^[19]	2015	Knee	Adipofascial ALT		
		Knee	Radial forearm		
		Knee	LD		
		Knee	Gracilis		
		Knee	Fasciocutaneous radial forearm		
Baxter <i>et al.</i> ^[20]	2007	Lower leg	Modified radial forearm fascial flap		
		Ankle	Gracilis		
		Foot	Sural		
		Foot	Medial plantar artery ALT		
		Foot	Parascapular LD Lateral arm		
Miyamoto <i>et al.</i> ^[21]	2014	Foot			
		Foot			
		Foot			
		Foot			
		Foot			
Lee <i>et al.</i> ^[22]	2004	Thigh			
		Knee			
		Leg			
		Foot			
		Foot			
Choudry <i>et al.</i> ^[23]	2008	Lower leg			
		Lower leg			
		Ankle			
		Ankle			
		Ankle			
Saito <i>et al.</i> ^[24]	2009	Lower leg			
		Lower leg			
		Ankle			
		Ankle			
		Ankle			
Zweifel-Schlatter <i>et al.</i> ^[25]	2006	Tibia			
		Tibia			
		Tibia			
		Tibia			
		Tibia			
Hong <i>et al.</i> ^[26]	2005	Lower leg			
		Lower leg			
		Lower leg			
		Lower leg			
		Lower leg			
Weichman <i>et al.</i> ^[27]	2015	Foot			
		Foot			
		Foot			
		Foot			
		Foot			
Cribb <i>et al.</i> ^[29]	2010	Ankle			
		Ankle			
		Ankle			
		Ankle			
		Ankle			
Brenner <i>et al.</i> ^[30]	2002	Foot			
		Foot			
		Foot			
		Foot			
		Foot			
Medina <i>et al.</i> ^[31]	2014	Foot			
		Foot			
		Foot			
		Foot			
		Foot			
Struckmann <i>et al.</i> ^[32]	2014	Foot			
		Foot			
		Foot			
		Foot			
		Foot			

Zaretski <i>et al.</i> ^[33]	2004	Femur Tibia	Free vascularized fibula flap ± allograft Free double-barreled fibula
Capanna <i>et al.</i> ^[34]	1993	Femur Tibia	Free vascularized fibula flap + allograft
Beris <i>et al.</i> ^[35]	2011	Femur Tibia	Free vascularized fibula ± allograft Free double-barreled fibula
Yajima and Tamai ^[36]	1994	Femur Tibia Ankle	Twin-barrelled vascularized fibular graft
Duffy <i>et al.</i> ^[37]	2000	Femur Tibia	Free vascularized fibula
Rush and Komar ^[38]	1997	Tibia	Fibula-flexor hallucis longus osteomuscular flap
Mastorakos <i>et al.</i> ^[39]	2002	Tibia	LD RA Gastrocnemius-Soleus Gastrocnemius-RA
Doi <i>et al.</i> ^[41]	1998	Lower leg	Gracilis + motor nerve
Doi <i>et al.</i> ^[42]	1999	Thigh Lower leg	LD + motor nerve Gracilis + motor nerve

LD: latissimus dorsi; RA: rectus abdominis; ALT: anterior lateral thigh

received free latissimus dorsi flaps, while the remaining patients received pedicled flaps. In the patients who were reconstructed using free flaps, the only complications were leg edema and mild lymphedema, which the authors attributed to ischemic reperfusion or venous/lymphatic insufficiency. The use of a myocutaneous flap in combination with an autologous vein graft also results in decreased postoperative infection rates, treatment of lymphedema and fistula, and increased graft patency rates^[14].

Aesthetically, reconstruction of the thigh requires a large flap with muscle bulk that can eliminate dead space while providing adequate contour^[10]. The use of a free rectus abdominis flap has been reported to be particularly successful for this purpose^[6,10]. The latissimus dorsi flap, which is thin, large with a long vascular pedicle, ± neurotization has also been used for large defects of the thigh^[6,10]. The use of the anterior lateral thigh (ALT) flap for large thigh defects, particularly of the posterior thigh, has also been reported^[15].

Knee

Obtaining adequate soft tissue coverage of the knee remains challenging for many plastic surgeons, not only because of the biomechanics of the knee, but also due to exposure of vital structures as well as the joint space^[16-18]. Rotational muscle flaps or myocutaneous flaps such as gastrocnemius or reverse anterior lateral thigh flaps have been the mainstay for the reconstruction of tumors in this location. These flaps usually have low donor - site morbidity. However more complex defects may require the use of free tissue transfer. In these cases the deep-seated recipient popliteal vessels of the knee can make microvascular anastomosis difficult^[19], an autologous vein graft loop can be used and the distal SFA and SFV can be used as recipient vessels if there is an extended field of neoadjuvant radiation^[14].

Multiple donor sites have been successful used in free flap coverage of knee defects. These include latissimus dorsi, rectus abdominis, and scapula flaps^[6]. When there is a large contour defect in the popliteal fossa that does not require much filling of the muscular space, Leow *et al.*^[10] have also described the use of a free mini-transverse rectus abdominis (TRAM) myocutaneous flap.

In many cases where complex reconstruction of the knee region is needed, salvage of the popliteal artery, which can often be involved in the disease process, becomes critical. This has traditionally been accomplished using a combination of a local gastrocnemius flap with an interpositional vein graft^[20]. However, Miyamoto *et al.*^[21] described two cases of successful one-stage reconstruction of complex knee defects including the popliteal artery using a free flow-through ALT flap. Although the use of a deep

epigastric artery perforator flap has also been used for these situations, this flap is often too bulky and provides a less aesthetic option.

Below knee

In the distal leg, dead-space obliteration is generally not a concern and the use of bulky musculocutaneous flaps, such as TRAM flaps, can result in significant contour deformities. As a solution, several authors describe the ALT flap as a preferred method for distal lower extremity defects following sarcoma resection, given the easy ability to reshape the flap^[11,22]. In a series by Barner-Rasmussen *et al.*^[9], 73 patients with soft tissue tumors located predominantly in the distal leg received 75 free-flap procedures with a 95% flap survival rate and a 97% limb salvage rate. A majority of the flaps used were latissimus dorsi flaps (72%) and ALT flaps (12%). The rectus abdominis and latissimus dorsi flaps as well as free scapula flaps have been described for this region by Cordeiro *et al.*^[6] with an overall success rate close to 90%. Other flaps commonly used in the lower leg are the radial forearm flap, gracilis flap, tensor fascia lata flap, and fibula flap^[9].

Ankle/foot

Several factors must be taken into account when reconstructing oncologic defects of the ankle and foot. In addition to considering the need for adjuvant radiotherapy, the soft tissue of this area is very thin and must provide a smooth surface for the tendons underneath. Traditional flaps used to cover defects of the distal third of the foot have included the rectus abdominis, latissimus dorsi, gracilis, and rectus femoris flaps^[23]. Free scapular and ALT flaps have also been used with adequate results^[24]. Muscle flaps provide excellent coverage, and while they are initially quite bulky for this region, they flatten significantly with time as they atrophy. Thus fasciocutaneous flaps have been described as a successful alternative with superior contouring^[25,26].

Although the versatile ALT flap has also been used in the past, the amount of adipose deposit in this flap can be addressed by primary thinning via a supra-fascial dissection or secondary procedure using mechanical lipectomy. A third approach was described by Weichman *et al.*^[27] where they reported a series using an adipofascial ALT flap with a split thickness skin graft to cover dorsal foot defects on three patients after sarcoma resection. In addition to its superior contour, the fascial plexus of the adipofascial flap is stronger than that of the thinned ALT, and the extra fascia can be used to reconstruct local tendons^[28].

The fasciocutaneous radial forearm flap has also been reported to have good results in reconstruction of the foot and ankle, providing normal contour and durable stability^[29,30]. Unfortunately however, it can result in significant donor-site morbidity and occasional bulkiness. Thus, Medina *et al.*^[31] proposed a using a radial forearm fascial free flap for dorsal foot defects and reported its use in a patient with wound dehiscence following sarcoma resection and radiation therapy, with no resulting complications or contour defects. Another flap that can provide excellent results in the ankle if the size of the defect permits is the temporalis fascia free flap^[6].

In contrast to the dorsum of the foot, reconstruction of the weight-bearing sole of the foot requires strong soft tissue that is resistant to pressure, weight, and stress. Struckmann *et al.*^[32] covered heel defects in 12 patients with a variety of free flaps including latissimus dorsi, gracilis, lateral arm, ALT, and parascapular free flaps. They found that myofasciocutaneous flaps had the best functional results, followed by adipocutaneous and muscle flaps with split-thickness skin grafts, while fasciocutaneous flaps had the lowest outcomes. However there was no significant difference between specific flap type.

ADDITIONAL CONSIDERATIONS: COMPROMISED STRUCTURES

Bone involvement

For bone reconstruction, the flap is chosen based on specific patient needs including location of the

lesion, level of activity of the individual, need for adjuvant therapy, and growth potential. The most commonly harvested bone flap is the free fibula flap, which can be used in three major reconstructive ways: traditional vascularized fibula flap, vascularized fibula flap combined with an allograft, and vascularized double-barreled fibula^[33].

The traditional vascularized fibula flap as a bony replacement is indicated in areas that endure lighter loads or when reinforcement of weak areas is needed. The free fibula flap with an allograft, which was first described by Capanna *et al.*^[34] in 1993, involves the insertion of the vascularized fibular graft into the intramedullary canal of an allograft, which is then used to fill the bony defect. This flap provides strength and stability early on, making it ideal for anatomical locations where high forces are applied. For areas that must withstand intermediate stress loads, the free double-barreled fibula flap is typically chosen. This flap allows for twice the volume of the fibula to be substituted with the same number of microvascular anastomoses^[33]. It is generally indicated for femur and proximal tibia reconstruction as well as reconstruction of the tibia of younger patients who are physically active^[35,36]. Additionally for radiation-induced long-bone fractures, the vascularized fibula can also be osteotomized longitudinally and used as an onlay graft^[37]. The fibula can also be harvested as a combined osteocutaneous flap for composite defects of the lower extremity^[6,10].

An additional osteomuscular flap that has been reported to have good outcomes for coverage after distal tibial osteosarcoma resection is the fibula-flexor hallucis longus osteomuscular flap^[38]. Saito *et al.*^[24] also describe adequate aesthetic and functional outcomes with the use of a free composite graft of latissimus dorsi and scapular bone as well as a free osteocutaneous scapular-parascapular flap. Finally, in cases of allograft bone reconstruction of the lower extremities, soft tissue flap coverage using latissimus dorsi and rectus abdominis flaps has been shown to maximize limb salvage^[39].

Nerve reconstruction

Radical sarcoma resection often leads not only to extensive soft tissue defects, but also suboptimal degrees of functionality secondary to damage to surrounding nerves. Functional outcomes following conventional limb-sparing procedures reported in the literature have been close to 75%^[40].

Reinnervated muscle transfer, which has been extremely valuable in a number of reconstructive procedures, may also become necessary in patients with sarcoma resection. Doi *et al.*^[41] describe a patient with synovial sarcoma of the anterior compartment of the lower leg who received a gracilis flap to cover the defect. The motor nerve of the gracilis was sutured to the motor branch of the tibialis anterior muscle from the peroneal nerve, resulting in gradual increase in power and range of toe and ankle extension postoperatively. In a second series by Doi *et al.*^[42], reinnervated latissimus dorsi transfer was used to improve or supplement knee flexion or extension by connecting to the sciatic or femoral nerve at the time of reconstruction.

Vascular reconstruction

While arterial reconstruction is always indicated after limb-sparing surgery to prevent ischemia, the need for venous reconstruction is not as well-established, as venous ligation compromise the limb. Studies showing high occlusion rates have led to debates regarding the benefits of venous revascularization^[43]. Additionally, there have been reports of symptoms of severe venous insufficiency such as edema, claudication, and hyperpigmentation after reconstruction^[44].

A large series of lower limb soft tissue sarcoma resection with arterial and venous reconstruction was conducted by Nishinari *et al.*^[44] in 25 patients. Graft occlusion rates were found to be significantly greater in patients who received synthetic grafts vs. those who received saphenous vein grafts ($P = 0.02$), which is consistent with the results of other studies^[14]. However occlusion rates were not different between

arterial and venous reconstruction and there was no association between prior radiotherapy and graft occlusion^[44]. Wortman *et al.*^[45] reported one-year patency rates of venous bypass grafts to be 65%, with high numbers of overall bypass-related complications including thrombosis and emboli as well as infections. Common wound complications that occur are wound healing difficulties, infections, and lymphatic fistulas.

NEOADJUVANT AND ADJUVANT THERAPY

Surgery with wide margins alone can be implemented to treat sarcoma of the extremities that is subcutaneous or intramuscular, small in size, or low in grade. However, if the resected margin is close, or if there is extramuscular involvement, surgery must be combined with adjuvant radiotherapy. For those that are high-grade or large in size, neoadjuvant chemotherapy must also be considered^[46]. The need for additional therapy is often a determining factor in flap selection, as wound-healing difficulties can delay the onset of adjuvant therapy and negatively affect long-term survival.

Radiotherapy may be administered either pre- or postoperatively with similar local control and overall survival rates^[47]. The concern with radiation therapy is the complications it causes with wound healing. Reported complications have ranged from 33%-44% in the past, with severe morbidity in 22%-27% of patients^[48-50]. Abramson *et al.*^[5] however only reported a 12.5% wound complication rate, including a patient who developed radiation necrosis and required a second free tissue transfer months after his initial treatment.

While preoperative radiotherapy results in higher rates of wound complications^[51-53], patients treated with postoperative radiotherapy experience more long-term fibrosis, edema and joint stiffness^[54]. The National Cancer Institute of Canada (NCI Canada) conducted a randomized control trial comparing wound complications in patients who received preoperative vs. those postoperative radiotherapy and found that 35% of those in the preoperative group had major wound complications compared to 17% of those in the postoperative group^[51]. O'Sullivan *et al.*^[51] found higher rates of wound complications and reoperations in patients who received preoperative radiation. However a larger percentage of patients with wound complications in the postoperative radiation group required other invasive procedures.

Townley *et al.*^[55] compared patients with preoperative irradiation to a control group who received no radiation and found similar microvascular complication rates such as those requiring intra-operative revision or flap reexploration or loss. Though wound healing complications were more common in the group who received radiation, the ultimate outcomes were similar between both groups. Some factors associated with wound complications in sarcoma patients who receive preoperative radiation are tumor size > 10 cm, tumor proximity to skin surface < 3 mm, and current smoking status^[48].

Chao and associates compared complication rates between patients receiving neoadjuvant and adjuvant irradiation and found no significant difference in perioperative complication rates or rates of salvaged pedicle thrombosis between the two groups. However, the rate of total free flap loss was lower in patients receiving neoadjuvant radiation, suggesting that the introduction of new, well-vascularized tissue counteracts the effects of the radiation. The authors also attributed this finding to the fact that higher doses and larger fields of irradiation are involved with adjuvant therapy, and with neoadjuvant therapy, irradiated tissue may be excised during tumor resection. Additionally, they found that late recipient-site complications (occurring > 30 days after surgery) occurred more frequently in patients who received adjuvant radiation (26.1% vs. 6.8%, $P = 0.0006$), although the reoperation rate following these complications was similar between the groups^[56]. Because wound complications are generally treatable without resulting in permanent damage, preoperative radiotherapy is preferred by many practitioners^[48].

Brachytherapy, another form of adjuvant therapy, is a method of administering radioisotopes directly into a surgical wound to treat residual tumor^[57]. Addition of brachytherapy to surgical excision has been shown to reduce tumor recurrence rates from 14% to 4%^[58]. Brachytherapy was initially administered during the immediate postoperative period and resulted in high rates of wound complications^[49]. Waiting until at least the 5th postoperative day is associated with significantly lower rates^[59]. In a study by Lee *et al.*^[22], brachytherapy was initiated about 7 days after free tissue transfer and resulted in a 29% complication rate, including partial-thickness skin necrosis, venous thrombosis necessitating flap exploration, kinking of the brachytherapy catheters, and partial flap skin loss. Hidalgo *et al.*^[60] described 3 patients who were treated with adjuvant brachytherapy 7-10 days postoperatively with no wound-healing complications. Although considered typically safe, the number of wound complications requiring reoperation has been shown to be higher with brachytherapy than with external beam radiation therapy^[61]. Preoperative intraarterial chemotherapy is another option and has been shown to have no effect on free flap results^[62].

OUTCOMES AND RECURRENCE

Because of the prolonged surgical time and extensive periods of bed rest combined with immunosuppressive therapy following sarcoma resection, surgical treatment of these tumors is generally associated with high numbers of postoperative complications. Lopez *et al.*^[2] found that patients who received combined pedicled + free flaps after sarcoma resection had significantly higher wound complications rates compared to patients who received just one, although systemic complications were distributed equally between all groups.

Recurrence rates are generally high following flap reconstruction after resection of advanced, high-grade sarcomas^[63]. Popov *et al.*^[64] found a statistically significant correlation between recurrence and extracompartmental tumor location ($P < 0.01$) and large tumor size (> 4 cm) ($P < 0.01$). Postoperative wound complications can also lead to amputation following tumor resection and flap reconstruction.

CONCLUSION

As wide local excision has become the most commonly accepted approach to the surgical treatment of sarcomas, reconstructive surgical techniques become crucial to the success of this line of therapy. Although pedicled flaps have been traditionally preferred for oncologic resections, their use is sometimes precluded by the use of neoadjuvant radiation as well as the size of the defect left after the resection. The need to re-establish function also makes the use of a pedicle/local flap less optimal. Several recent studies have reported successful functional and aesthetic results using free tissue transfer as the main modality for reconstruction after sarcoma resection of the limb^[6,7,56]. Free tissue transfer allows for the application of healthy vascularized tissue to the defect while also providing freedom of flap positioning as well as avoidance of stretching or kinking of the vasculature^[2]. Studies of sarcoma resection and free tissue reconstruction have reported high success rates, with complication rates ranging between 2%-22%^[7,64,65] and limb salvage rates close to 100%^[6,57,64,65]. Flap choice is dependent on tumor and defect size, tissue type and function, as well as donor site availability, thus resulting in numerous different treatment options. Given the low incidence and prevalence of lower extremity sarcomas as well as the heterogeneity of the sarcomas and their respective neo-adjuvant treatments, there are currently no clear treatment guidelines or specific algorithms for the reconstruction of soft tissue defects following oncologic resection. The lack of significant case volume makes it difficult for any single institution to conduct a study comparing the success rates of various flaps, and although a systematic review would be helpful, the innate nature of the pathology also leads to a paucity of literature consisting largely of studies describing small numbers of isolated cases. This descriptive review however attempts to provide an overview of the various reconstructive options that are available, as well as the considerations that must be taken into account when treating patients with soft tissue defects of the lower limb following sarcoma resection.

DECLARATIONS

Authors' contributions

Performed the literature search and reviewed the articles: Azadgoli B, Perrault DP

Drafted the manuscript: Azadgoli B

Revised the manuscript: Carre AL, Wong AK

Reviewed the manuscript and approved its final version: all authors

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There are no conflicts of interest.

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Not applicable.

Ethics approval

Not applicable.

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