Free Tissue Transfer for Limb Salvage in High-Risk Patients: Worth the Risk

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Significance: Microsurgical free tissue transfer is a powerful tool in the arsenal of reconstructive surgeons, oftentimes as the final option in limb salvage before amputation. Patients presenting for limb salvage frequently carry with them multiple co-morbidities such as diabetes mellitus, end-stage renal disease, and peripheral vascular disease. Surgeons are oftentimes hesitant to attempt free tissue transfer in these medically complex individuals due to beliefs that the patient would not tolerate prolonged anesthesia, the surgery is doomed to fail, or the patient would be better off with an amputation. Because amputees actually demonstrate higher mortality rates, the decision to not to proceed with limb salvage should be made with great care.

Recent Advances: By reviewing the success rates with free tissue transfer for limb salvage in high-risk patients, the target articles have shown that this option is indeed viable even in this patient population. Specifically, reasonable success rates are presented for limb salvage using free tissue transfer in patients with end-stage renal disease, a single-vessel leg and critical limb ischemia.

Critical Issues: The articles reviewed demonstrate that free tissue transfer for limb salvage in properly selected patients with end-stage renal disease or severe peripheral vascular disease is worth attempting. Before surgery, these patients must undergo a complete cardiac work-up regardless of previous cardiac history.

Future Directions: When necessary, free tissue transfer should be pursued by the reconstructive surgeon even in high-risk medically complex patients.

SCOPE

WOUNDS OF THE LOWER EXTREMITY with exposed bone, tendon, artery, or nerve often require coverage with well-vascularized tissues to go on to heal and to stay healed despite the continued stress of ambulation. Simple grafting, including split- and full-thickness skin grafts, with or without revascularized neodermis, is often insufficient and may not succeed on these wounds. Local flaps are useful around the ankle although their reach is often limited by donor-site morbidity and/or the quality of

blood supply at the base of the flap. Pedicled flaps, including gastrocnemius muscle, anterior tibial muscle, soleus muscle, and saphenous artery flaps, are useful for coverage of vital structures in the upper two-third of the lower leg. In the lower one-third of the leg, however, few local and pedicled flaps exist that provide adequate bulk to cover the larger of these typically complex wounds. When a larger wound of the distal one-third of the leg is encountered, the reconstructive surgeon classically turns to microsurgical free

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tissue transfer for limb salvage. While more complex to perform, a free flap has as high a success rate and lower complication rate than any other mode of reconstruction.¹

Frequently, patients presenting for limb salvage have wounds related to long-standing medical conditions such as diabetes mellitus, hypertension, and peripheral vascular disease. Elevated glucose levels and local areas of ischemia have been shown to be responsible for the delayed wound healing seen in these patients. When present, end-stage renal disease further complicates wound healing potential. In addition to their contribution to wound formation and impediment to wound healing, these co-morbidities are also thought to contribute to increased difficulty and rates of failure with free tissue transfer.

TARGET ARTICLES

1. Chien SH, Huang CC, Hsu H, Chiu CH, Lin CM, and Tsai JP: Free tissue transfers for limb salvage in patients with end-stage renal disease on dialysis. *Plast Reconstr Surg* 2011; **127**: 122.

2. Ducic I, Rao SS, and Attinger CE: Outcomes of microvascular reconstruction of single-vessel lower extremities: limb salvage versus amputation. *J Reconstr Microsurg* 2009; **25**: 475.

3. Randon C, Jacobs B, De Ryck F, Van Landuyt K, and Vermassen F: A 15-year experience with combined vascular reconstruction and free flap transfer for limb salvage. *Eur J Vasc Endovasc Surg* 2009; **38**: 338.

CLINICAL RELEVANCE

The decision of whether or not to proceed with microsurgical reconstruction of the lower extremity versus settling for amputation is not always clear for the reconstructive surgeon. Just as the field of microsurgery in limb salvage has evolved rapidly since its advent in the 1960s the distinct indications and contraindications for pursuing such therapy are evolving as well. Without the possibility of a successful functional outcome, microsurgery becomes less and amputation more of an attractive option. Therefore, a realistic evaluation of the eventual functionality of the reconstructed limb must be made before considering microsurgery.

For successful microvascular tissue transfer to take place, a patient must have adequate lower

extremity recipient vessels and be able to withstand prolonged time under anesthesia. Although the presence of conditions that affect the integrity of the recipient vessels, such as atherosclerosis, can complicate the surgeon's ability to perform an anastomosis, successful tissue transfer is indeed possible in this patient population.^{2,3} In some patients, however, atherosclerosis has led to occlusion of two of the three main vessels supplying the leg. In patients with only a single-vessel leg, microsurgical free tissue transfer is either omitted as an option or approached with caution as the procedure itself can theoretically put at risk the only remaining blood supply to the extremity. Patients even further along in their disease course can present with large soft tissue defects in combination with critical limb ischemia due to the lack of vessel run off. In these patients, the ability to both revascularize the extremity and heal the wound is so fraught with risk that amputation is often the only solution sought.

Before contemplating surgery, the reconstructive surgeon must look at the patient as a whole and take into account their general health when deciding whether or not to attempt free tissue transfer. Microsurgery is associated with prolonged operative times ranging from 5 to 20 h, subjecting patients to extended anesthesia with increased risks of deep venous thrombosis, pulmonary embolism, and myocardial infarction. While the safety of microsurgery in patients over the age of 70 has been demonstrated in the literature, individuals with multiple co-morbidities, as assessed by the American Society of Anesthesiology classification scheme, have been shown to have increased postoperative complications.⁴ Patients with end-stage renal disease have multiple co-morbidities and are at particular risk for postoperative complications. Indeed, many have suggested that these patients with multiple co-morbidities should get cardiac clearance before considering microsurgery as a reconstructive option.

TRANSLATIONAL RELEVANCE

When approaching a wound, the reconstructive surgeon utilizes one of several methodologies for deciding on the best treatment strategy. The traditional reconstructive ladder starts with closure by secondary intention, followed by direct closure, skin grafting, local flaps, distant flaps, and finally microsurgical free tissue transfer. Classical teaching was that a surgeon should attempt to climb the ladder when trying to achieve closure,

utilizing the simplest method possible to succeed.⁵ More recent teachings, however, suggest that although some wounds could be solved by simpler methods, more complex methods of reconstruction are at times preferred for optimal outcomes. One modification to the reconstructive ladder, the reconstructive elevator, acknowledges the concept of increasing levels of complexity while allowing the reconstructive surgeon to ascend directly to the appropriate level.⁶ This modification is particularly important in the lower extremity where function is paramount. This has given the reconstructive surgeons the ability to go to microsurgical free transfer for lower extremity wounds when it is most appropriate.

Peripheral vascular disease is characterized by the accumulation of atherosclerotic plaque in vessels leading to stiff vessel walls with turbulent and diminished blood flow. When allowed to progress, total occlusion of vessels is the final result. Although possible in the upper extremities, peripheral vascular disease preferentially affects the lower extremity. In microsurgery, the calcified vessel walls can make the vascular anastomosis more challenging, possibly explaining the higher rates of free flap failure seen in lower extremity reconstruction as compared with those performed on other regions of the body.^{7,8}

Patients with end-stage renal disease are another group that suffers from increased rates of microsurgical flap failure.^{3,9,10} Possible reasons for this increased rate of flap failure seen include the presence of calcified vessels, a general diminished capacity for wound healing, and an increased risk for both thromboembolic events as well as bleeding and hematoma formation from anticoagulation used at dialysis.^{11,12}

EXPERIMENTAL MODEL OR MATERIAL: ADVANTAGES AND LIMITATIONS

Outcomes studies are performed in either a prospective or retrospective manner. In the patient populations being studied, decisions are made to attempt limb salvage at the bequest of the patient and agreement of the reconstructive surgeon. As such, these patients cannot be randomized in a prospective manner to either receive microsurgical reconstruction or not given the ethical dilemma such an experimental design would pose. The surgeon scientist is frequently forced to analyze the data based on previous experiences through retrospective chart review. To lend power to any retrospective chart review, large patient numbers (*n*) and long follow-up are necessary. In addition, a

thorough analysis of possibly confounding variables, including demographics, co-morbidities, type of reconstruction attempted, possible variability between operating surgeons, treatment protocols, complications, and outcomes is necessary to draw meaningful conclusions.

DISCUSSION OF FINDINGS AND RELEVANT LITERATURE

In patients requiring microsurgical free tissue transfer for limb salvage, the decision to proceed with surgery must be weighed against the chance of successful surgery, achieving a functional result, as well as the patient's ability to tolerate such surgery. In addition to the anesthetic risk, the consequences of flap failure in these individuals are great, as they will not only face major amputation but also have donor-site wounds with the potential complications of donor-site infection, seroma, hematoma, dehiscence, and damage to surrounding structures during flap elevation. Given these risk factors, certain patients are thought to be too high risk for microsurgery. If the labeling of patient's high risk is inaccurate, it can lead to early major amputation in an attempt to ensure survival. Unfortunately, major amputation does not necessarily lead to improved survival, as demonstrated by the 50% to 70% mortality rate at 5 years in diabetics.¹³

Previously, the presence of peripheral vascular disease was thought to be a negative predictor of successful microsurgical free flap reconstruction, making them high risk for not only flap failure but also perioperative morbidity. Numerous studies have shown, however, that patients with peripheral vascular disease are not necessarily poor candidates for microsurgical free tissue transfer for limb salvage.^{8,10,13-16} This type of reconstruction has been successful in patients at the time of vascular bypass, after vascular bypass and without bypass. In patients where bypass is not possible but are dependent on a single artery for blood supply, free tissue transfer has frequently been omitted as an option over fears of inciting critical limb ischemia if an occlusion were to occur distal to the anastomosis. Despite these fears microsurgical free tissue transfer does still seem warranted with success rates as high as 100% seen for flap survival.¹⁶

When necessary, free tissue transfer combined with vascular reconstruction during the same operative setting has yielded success rates as high as 93% for limb salvage at 1 year and 77% at 5 years. Beyond the benefits of decreased trips to

the operating room and earlier wound coverage, combining the two procedures may in fact lead to increased success of vascular reconstruction. Lorenzetti *et al.* has shown that the transferred tissue provides a low-resistance outflow bed to the vascular graft. The low resistance bed created by adding the flap can increase graft flow by up to 50%.¹⁷ In addition, the transferred tissue can provide coverage of the distal anastomosis site, thus protecting the distal bypass site, which is often poorly covered. The caveat is that the covered wound should be free of infection before considering wound coverage.

Although peripheral vascular disease does not appear to put patients at undue risk for flap failure, one condition has stood out as a negative predictor for success reaching statistical significance in multiple studies. That factor is end-stage renal disease requiring hemodialysis. Some authors have even recommended immediate amputation in these patients when combined with lower limb ischemia.^{18–20} Despite this discouraging data, some still believe that free tissue transfer in patients with end-stage renal disease can be performed provided that certain factors are controlled for before surgery. Chief among these conditions is the need for a formal cardiologic evaluation to ensure that the patient can safely undergo a major operation. In addition, the surgery is performed the day after dialysis and if possible under epidural anesthesia. Lastly, in those patients with prior vascular reconstruction, there appears to be a higher risk of ultimate failure and need for amputation. Therefore, when facing patients with end-stage renal disease on hemodialysis who have undergone vascular reconstruction, the physician must initiate a very frank discussion placing emphasis on the increased risk for flap failure and perioperative complications after free tissue transfer for limb salvage.

INNOVATION

In the articles reviewed the authors analyzed their success with free tissue transfer for limb salvage in patients at high risk for failure or perioperative complications. Despite their high risk, these patients enjoyed limb salvage rates ranging from 80% to 90% at 1 year. These encouraging re-

TAKE-HOME MESSAGE

Basic science advances

- When approaching a complex wound, reconstructive surgeons should utilize the most appropriate method of reconstruction for obtaining functional results even if a simpler method is available.

Clinical science advances

- In patients presenting with critical limb ischemia and large open wounds, combined revascularization and free tissue transfer procedures are possible and may even improve graft patency rates due to improved outflow and protection of anastomosis sites.
- Patients with single-vessel runoff to their legs successfully underwent free tissue transfer for limb salvage without increasing their risk of critical limb ischemia.
- Acceptable rates of limb salvage utilizing free tissue transfer and perioperative morbidity are possible in patients with end-stage renal disease requiring hemodialysis.

Relevance to clinical care

- In patients with a reasonable prognosis for restoration of function following successful limb salvage, microsurgical free tissue transfer should be considered for reconstruction even in the face of severe peripheral vascular disease and end-stage renal disease.
- A thorough cardiac work-up is necessary in these high-risk patients before attempting free tissue transfer even in patients without a history of cardiovascular disease.
- Attempts to perform free tissue transfer should only be made by surgeons trained and skilled in the art of microsurgery, especially in these technically demanding patients.

sults suggest that in patients with a single-vessel leg, free tissue transfer has been and can be performed with acceptable success rates. In those patients already suffering from critical limb ischemia and large open wounds, combining vascular reconstruction with free flap transfer provides excellent coverage and may even improve bypass outcomes. Lastly, in patients with end-stage renal disease, free tissue transfer can be attempted in many patients but should probably be avoided in those who have undergone previous vascular reconstruction.

CAUTION, CRITICAL REMARKS, AND RECOMMENDATIONS

Function is the key in evaluating a limb with an open wound. Depending on the activity of the patient, the amount of restored function necessary for acceptable quality of life varies greatly. It is different for a world-class athlete, a blue-collar worker, a sedentary person, a young athletic person, and a person living in a nursing home. The existence of a reconstructive elevator that forces

the surgeon to consider all options while allowing him or her the freedom to go directly to the solution that leads to the most appropriate reconstruction for the patient means that microsurgery should always be seriously considered. The three target articles show that even with the most complex of patients, it remains a viable solutions: those patients with single-vessel legs, those with renal failure, and those who require immediate coverage of the bypass. Of course, for microsurgery to be an option, the surgeon must be very skilled in the art as these are the most difficult of all microsurgical procedures. If the surgeon is gifted and the patient is an appropriate candidate, microsurgery can restore function in limbs that would otherwise have been poorly reconstructed and difficult to use or the patient would have undergone a major amputation.

SUMMARY ILLUSTRATION

General algorithm for the reconstructive surgeon approaching high-risk patients in need of free tissue transfer for limb salvage.

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