Review

Tackling bone loss of the lower extremity: vascularized bone grafting

Christine V. Schaeffer, John T. Stranix

Department of Plastic and Reconstructive Surgery, The University of Virginia, Charlottesville, VA 22903, USA.

Correspondence to: Dr. John T. Stranix. Department of Plastic and Reconstructive Surgery, The University of Virginia, PO Box 800376, Charlottesville, VA 22903, USA. E-mail: jts3v@virginia.edu

Abstract

Post-traumatic lower extremity bone loss in the setting of high-energy trauma can occur acutely as a result of an open fracture and surgical debridement, or secondarily as a result of nonunion or infection. Several techniques have been described in the literature for the management of these bony defects, including non-vascularized bone grafts, vascularized bone grafts and distraction osteogenesis. Herein, the authors review the role of vascularized bone grafts in the management of post-traumatic bone loss in the lower extremity.

Keywords: Lower extremity, vascularized bone, segmental defect

INTRODUCTION

The first step in the management of patients with high energy trauma resulting in open fractures of the lower extremity includes early and aggressive debridement of devitalized and contaminated soft tissue and bone. Multiple operative debridements are often required before bony reconstruction can be considered[1,2]. Bone defects following lower extremity trauma occur acutely in the setting of significant fracture comminution, open fractures, and following aggressive debridement and secondarily in the setting of aseptic or septic nonunion. Temporary external fixators are used to stabilize the extremity and maintain length[3]. The goal of bony reconstruction is to provide stability and reestablish limb length.

The first successful free vascularized bone graft was performed and described by Taylor *et al.*[4] in 1978 for a post-traumatic intercalary bone defect - a free fibula flap was used to reconstruct a 12.5 cm defect of the tibia. Subsequently, the vascularized rib (Buncke *et al.*[5], 1977) and vascularized iliac crest (Taylor and Watson[6], 1978) bone grafts were successfully performed and described in the literature for lower extremity bony reconstruction. The medial femoral condyle flap was first described in 1990 by Hayashi and Maruyama, and applied to lower extremity reconstruction by Doi and Sakai[7] in 1994. Since the 1970s, the vascularized free fibula flap has remained the workhorse flap for post-traumatic lower extremity bony reconstruction, followed by the less commonly utilized iliac crest, medial femoral condyle and rib donor sites[8,9].

INDICATIONS FOR VASCULARIZED BONE GRAFTS

Several classification systems have been created in attempts to uniformly describe the degree of lower extremity trauma. The Gustilo and Anderson[10] classification is well known and categorizes open fractures based on the degree of soft tissue injury. Unlike the Gustilo system, the extent of bony defects can be described with Winquist's classification system. This system was originally created to describe femur fractures; however, it has been subsequently applied to tibial shaft fractures[3,11]. Battiston *et al.*[3] recommend non-vascularized bone grafting for Winquist grade 1 or 2 fractures (no or minimal comminution and more than 50% contact between fragments with moderate comminution, respectively). For fractures with less than 50% contact between fragments, more severe comminution, or segmental bone loss (Winquist grades 3 and 4), reconstruction with bone transport or vascularized bone grafting is suggested[3]. While several techniques have been described for bony reconstruction, vascularized bone grafting remains the modality of choice in the setting of large bony defects (> 6 cm)[12,13]. Additional indications for vascularized bone grafting include poor vascularity of the recipient site, repeated failure of non-vascularized bone grafts, and fracture nonunion[14].

BIOLOGY

The proposed advantages of vascularized bone grafting for reconstruction of post-traumatic lower extremity bone defects include a sturdier immediate reconstruction and the capacity for osteogenesis, which ultimately allow for faster incorporation and primary bone union times[3,12]. Unlike avascular bone grafts, the process of creeping substitution is bypassed. Therefore, vascularized bone grafts have less resorption with better retention of bony architecture, resistance to infection, mechanical strength, and healing potential[15,16]. Additionally, vascularized bone grafts are capable of responding to applied biomechanical stresses with hypertrophy[17].

GRAFT TYPES

The three primary donor site options for vascularized bone grafting for the lower extremity include the fibula, iliac crest, and medial femoral condyle [Figure 1]. Historically, vascularized rib grafts have been described; however, they have fallen out of favor. Flap selection is determined predominantly based upon the size and location of the bony defect, flap availability, donor site morbidity, and flap success rates. General considerations when selecting the ideal vascularized bone graft for a post-traumatic bone defect in the lower extremity are outlined in Figure 2.

The fibula flap is the most commonly used vascularized bone graft for extremity reconstruction. It provides a strong cortical strut that is straight, and therefore ideal for extremity reconstruction. The vascularized fibula flap can be used to reconstruct defects up to 26 cm in length[18]. The flap pedicle is the peroneal artery with associated peroneal veins. The composition of this flap can vary to include skin, fascia and muscle as indicated by the defect requirements. A skin paddle up to 20 by 10 cm can be reliably transferred and used
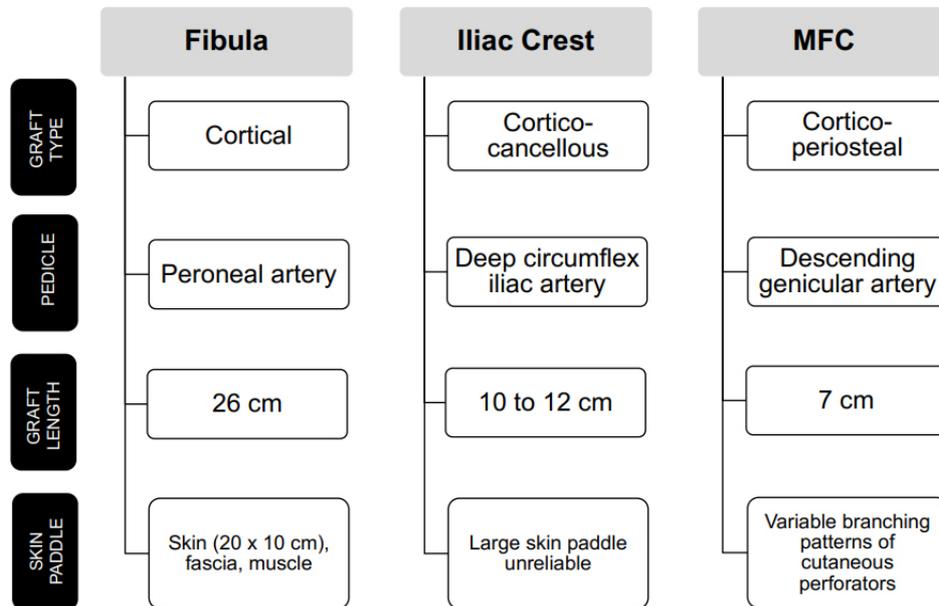
Figure 1. Characteristics of vascularized bone graft options for traumatic lower extremity bone defect reconstruction.
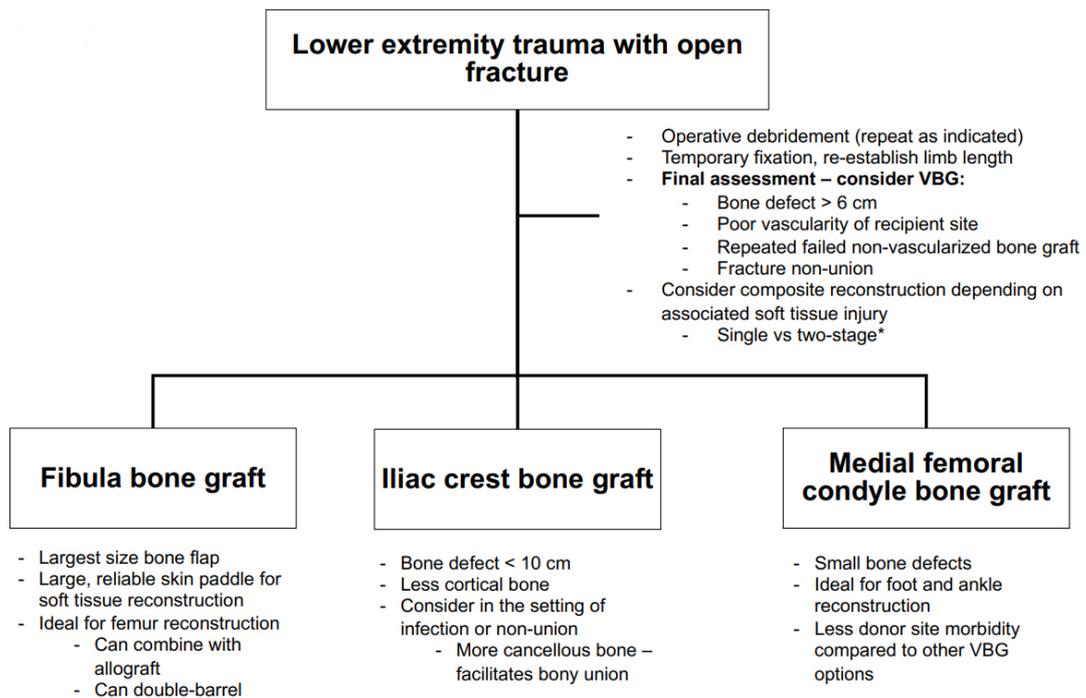
Figure 2. Selecting a vascularized bone graft for lower extremity traumatic bone defects in adults. *The optimal timing for soft tissue reconstruction and vascularized bone grafting should be determined on a case-by-case basis, keeping in mind the limitations of each approach. VBG: Vascularized bone graft.

for flap monitoring. Additionally, this bone flap has an endosteal and periosteal blood supply, which allows for the option to create a double-barrel construct with a single pedicle using a transverse osteotomy in the diaphysis of the graft for femur or tibial reconstruction[18]. For large intercalary defects of the femur, the vascularized fibular graft can be combined with a massive cortical allograft (Capanna technique). The

allograft provides immediate strength to the construct, while the fibula graft provides the previously noted biologic benefits of vascularized bone graft (potential for osteogenesis, ability to hypertrophy, and faster time to the union)[12].

Vascularized iliac crest bone grafts have been described for lower extremity bone reconstruction. This corticocancellous bone has a slight curve, which is undesirable in long bone reconstruction. This maximal graft length from this donor site is only 10 to 12 cm. The flap pedicle is the deep circumflex iliac vessel. An associated skin paddle based on the deep circumflex iliac vessels alone is reportedly unreliable - if a large skin paddle is required for osteocutaneous reconstruction, a double anastomosis including the superficial circumflex iliac vessels should be performed[14,18-20].

The medial femoral condyle (MFC) flap has been popularized for use in the setting of post-traumatic avascular necrosis of the talus and navicular bones and the setting of foot and ankle fracture nonunions. The MFC is typically a thin corticoperiosteal graft that includes periosteum and outer cortical bone, with or without underlying cancellous bone. The dominant flap pedicle is the descending genicular artery; however, the flap can be supported by the medial superior geniculate artery (though this results in a shorter pedicle length). The advantage of this flap is its thin, pliable nature which allows for shaping to fit small, irregular bone defects[9]. When used for structural support, the maximal graft length is 3 cm in length; however, flaps up to 5 cm × 7 cm have been described[21,22]. The MFC can be raised with an associated skin paddle based on the saphenous artery branch of the descending geniculate artery pedicle (medial knee, up to 70 cm^2) or a more distal descending geniculate artery cutaneous perforator (medial distal thigh and proximal leg, up to 361 cm^2)[23,24]. Because of variable branching patterns and available distal cutaneous perforators, the size of the skin paddle associated with an MFC flap is inconsistent[24,25].

PRE-OPERATIVE CONSIDERATIONS

In the post-traumatic setting, multiple operative debridements are often required to adequately address contamination and removal of devitalized bone and soft tissues with the goal of eradicating potential nidi for infection. Provisional bony stabilization is typically obtained with external fixation. In the setting of associated soft tissue loss (Gustillo IIIB or IIIC), some authors recommend single-stage reconstruction with composite bone grafting, while others advocate for soft tissue reconstruction followed by vascularized bone grafting in a second stage 6-8 weeks later. The advantages of one-stage reconstruction include reduction of overall healing time and simultaneous soft tissue and bone reconstruction, with the theoretical disadvantage of increased risk of infection and loss of the vascularized bone graft. The disadvantages associated with staged reconstruction include increased scar burden and limited availability of recipient vessels for subsequent vascularized bone grafting[26-31]. The optimal timing for soft tissue reconstruction and vascularized bone grafting should be determined on a case-by-case basis, keeping in mind the limitations of each approach.

Evaluation of the donor and recipient vascular anatomy in the setting of lower extremity trauma is an important component of the pre-operative workup. This includes clinical evaluation and Doppler ultrasound examination. Angiography of the recipient and/or donor sites can be performed if there are abnormalities on exam and for pre-operative planning. In the setting of high-energy trauma, the extent of injury to the potential recipient vessels can be assessed with angiography[18,20]. However, pre-operative angiography may not reliably delineate the extent of vascular injury in the recipient vessels following trauma or in patients with chronic infections. Vein grafts may be required based on the availability of healthy recipient vessels outside of the zone of injury[13].

Patient age is also an important consideration. Traumatic bone defects in the pediatric population are more rare and have better prognoses compared to the adult population. The integrity of their relatively thick, vascular, and cellularly active periosteum can be used to guide the reconstruction of pediatric traumatic bone defects. If the periosteum is intact, bone reconstruction may not be necessary with appropriate stabilization. A non-vascularized autograft may be used for bone defects with partially intact periosteum. In patients with no periosteum or with nonunion due to infection, bony reconstruction using the induced membrane technique followed by autograft bone, bone transport, or vascularized bone grafting has been described. Case series describing outcomes following reconstruction of pediatric bone defects in the setting of trauma are limited[32]. However, the use of vascularized bone grafts in the pediatric population has been shown to be a reliable reconstructive option following tumor resections of the extremities with flap survival rates of over 92%-92% for fibula, 100% for iliac crest, and 96% for MFC flaps[33-36]. Long-term outcomes following vascularized fibula flaps for bone sarcoma reconstruction in pediatric patients were evaluated by Ruiz-Moya *et al.*[37] and Ghoneimy*et al.*[38]. In these series (68 patients total), the rate of graft fracture was 33.3% to 34%, and the rate of non-union was 11% to 13.8%[37,38].

DEFECT RECONSTRUCTION

Following vascularized bone graft harvest and recipient site preparation, the bone graft is inset to bridge the bony defect, and the flap is revascularized. Several options have been described in the literature for graft stabilization including plates and screws, screws only, k-wire fixation, intramedullary nail, press-fit (MFC flaps), and external fixation[3,18,25,39,40]. Stability can also be augmented with graft inset into the medullary canal of the recipient bone[18]. Many authors advocate for ancillary cancellous bone graft placement at the junction between the graft and the recipient bone has been to accelerate healing[18,40]. Han *et al.*[40] compared vascularized bone graft fixation techniques (stable internal fixation *vs.* unstable internal fixation *vs.* external fixation). They reported significantly higher rates of primary bone union with stable internal fixation ± ancillary bone grafting (71%) compared to external fixation ± ancillary bone grafting (47%). The type of skeletal fixation with or without ancillary bone grafting had no significant effect on overall bone union rates[40]. Many authors describe a preference for stabilization with Ilizarov frames - the reported advantages include the ability to adjust bone compression/distraction, early weight-bearing, and decreased risk of infection with an external device[3,41]. The use of large plates for fixation can provide too rigid fixation , which can result in a stress-shielding effect on the bone graft[18,42].

OUTCOMES
Bone union
Osseous union is an indicator of bone healing. This can be assessed using plain film radiographs to evaluate for the presence of a bridging callus or absence of the fracture line. Reported rates of primary union for vascularized bone grafting in the post-traumatic setting range from 79% to 88.5% (Minami *et al.*[43], 26 of 33 flaps; Yazar *et al.*[39], 54 of 61 flaps)[39,43]. Han *et al.*[40] evaluated vascularized bone grafting with the fibula and iliac crest flaps to all skeletal defects (mandible, clavicle, upper extremity, pelvis, lower extremity). They reported significantly lower rates of primary and overall union in patients with osteomyelitis - 46% (29 of 60 flaps) rate of primary union, 76% (46 of 60 flaps) rate of overall union[40]. In a systematic review by Kazmers *et al.*[44] in 2018, MFC flaps performed for talus avascular necrosis and nonunion had an 86% union rate (6 of 7 flaps), while flaps performed for navicular avascular necrosis (2 patients) had a 100% union rate. Stranix *et al.*[25] reported a series of 30 MFC flaps for foot and ankle reconstruction with a primary union rate of 74% and overall union rate of 89% - of note, the etiology of hindfoot pathology was a history of trauma in 73% of these patients.

Several authors have attempted to compare primary union rates between vascularized bone flaps. Lin *et al*.[14] found no significant difference in the rate of primary union between fibula, rib and iliac crest bone flaps (82%, 73.7%, and 75%, respectively). Han *et al*.[40] were unable to detect a statistically significant difference between the rate of primary union, rate of overall union, time to union, or return to full activity following vascularized fibula and iliac crest bone grafts. However, 32% of patients who underwent vascularized iliac bone graft required a secondary procedure to achieve union, compared to only 17% of patients following vascularized fibula graft. Secondary procedures included cancellous bone grafting and external electrical stimulation followed by cast immobilization[40].

The time to union of vascularized bone grafts in the setting of lower extremity trauma has been evaluated by Yazar *et al*.[39] and Pelissier *et al*.[13] in single center retrospective reviews. It is reported as an average time to union for all included vascularized bone grafts (regardless of donor site). Yazar *et al*.[39] evaluated one-stage composite bone and soft tissue reconstruction in the setting of lower extremity trauma using fibula (50), iliac crest (6) and rib (5) vascularized bone grafts. The average time to primary union in this series of 61 patients was 6.9 months, with an average time to overall union of 8.5 months[39]. Pelissier *et al*.[13] reported a series of 24 patients who underwent vascularized bone grafting (10 iliac crest, 12 fibula, 2 lateral arm flaps), with an average time to primary union of 11.5 months. Another single center review of 14 patients who underwent vascularized fibula flap for post-traumatic lower extremity reconstruction reported an average time to union of 3.9 months[45]. The average time to union following MFC flaps for all lower extremity reconstruction is 3.5 months in a systematic review of the literature by Kazmers *et al*.[44]. However, the average time to union in the setting of foot and ankle reconstruction with MFC flap was reported to be 7.1 months in a retrospective review of 30 MFC flaps by Stranix *et al*.[25].

Flap failure
The reported rate of flap failure, defined as unsalvageable vascular thrombosis resulting in total flap loss, in the setting of post-traumatic bone defect ranges from 3.1% to 10% (Yazar *et al*.[39], 2 of 63 flaps; Lin *et al*.[14], 3 of 68 flaps; Hierner and Wood[19], 1 of 10 flaps). Higher rates of flap failure following reconstruction for chronic osteomyelitis compared to post-traumatic bone defects have been reported - 20.7% (Lin *et al*.[14], 6 of 29 flaps) to 25% flap failure rate (Hierner and Wood[19], 6 of 24 flaps)[39].

The rate of flap failure based on donor site was assessed by Lin *et al*.[14]. Ninety-seven vascularized bone transfers to the lower extremity from 1991 to 1995 were included for retrospective review. The indications for bone reconstruction were post-debridement of osteomyelitis and post-traumatic bone defects. The flap failure rates in this series were 4.7% following fibula flaps, 13.6% following rib flaps, and 27.3% following iliac bone flaps. Stranix *et al*.[25] reported no total flap losses in their 30 patient series of MFC flaps for foot and ankle reconstruction.

Stress fracture
Stress or fatigue fractures of the vascularized bone graft can occur, especially in lower extremity reconstruction. Following vascularized bone graft reconstruction, excessive mechanical loading before the graft has had an opportunity to adequately hypertrophy can result in fracture. The rates of stress fracture following vascularized fibula grafts for post-traumatic bone defects ranges from 11.5% to 13.1%[14,26,39,43]. Lin *et al*.[14] compared the rate of stress fracture following vascularized fibula, rib and iliac bone grafting to the lower extremity and found no significant difference (13.1%, 15.8%, and 12.5%, respectively). Two strut bone constructs had lower rates of stress fracture (6.7% compared to 15.2% for one strut construct); however, this difference was not statistically significant. No significant association between the length of the bone graft and the incidence of stress fracture was identified. Of note, indications for bone grafting in this series included post-traumatic defects and chronic osteomyelitis[14]. Management of stress fractures included

cast immobilization, application of external fixation, and open reduction with internal fixation[14,39].

Donor site morbidity

Donor site morbidity profiles can have a significant impact on the surgical decision-making process. Limited donor site morbidity has been described following MFC flaps when compared to vascularized free fibula flap and iliac crest bone graft. Multiple systematic reviews have been performed to elucidate the true incidence of complications associated with these vascularized bone graft donor sites. The donor site morbidities based on vascularized bone graft are outlined in Table 1.

Ling *et al.*[46] performed a systematic review of the literature and calculated weighted mean incidences for early and late donor site complications following free fibula flap. Early complications included infection (1.1%), dehiscence (7.0%), necrosis (7.3%), delayed wound healing (17.4%) and skin graft loss (8.1% partial graft loss, 4.7% complete graft loss). Of note, the incidence of wound healing complications was higher in donor sites that were skin grafted compared to those that were closed primarily (19.0% *vs.* 9.9%). The most common late complication was a limited range of motion of the ankle (11.5%) followed by altered sensation (7.0%), persistent pain (6.5%), claw toe (6.1%), ankle instability (5.8%), reduced muscle strength (4.0%), gait abnormality (3.9%), and dorsiflexion of the great toe (3.6%)[46]. Compartment syndrome of the lower leg is rare, however severe, complication following vascularized free fibula flap - a rate of 3% was reported in a recent meta-analysis by Gu *et al.*[47] in the setting of mandibular reconstruction.

Early and long-term donor site morbidities following vascularized iliac bone flap for mandibular reconstruction were evaluated by Gu *et al.*[47] in a 2021 systematic review and meta-analysis. The most common donor site morbidities were late complications - chronic altered sensation (43%), pain (26%), and gait disturbance (20%)[47]. The altered sensation is likely related to injury to the lateral femoral cutaneous nerve with resulting lateral thigh numbness/tingling. The reported early donor site morbidities (wound infection, dehiscence, and hernia) ranged from 3% to 16%[47]. The iatrogenic hernia is a rarely reported complication (3% in the previously cited meta-analysis) and is thought by some authors to correlate with the size of the flap[47,48]. Donor site morbidity has been compared in the craniomaxillofacial literature between free fibula flaps and vascularized iliac bone grafts. The fibula group had less immediate post-operative pain and returned to unaided walking faster, while patients who underwent iliac bone graft had a higher incidence of altered sensation and gait abnormality[49].

A systematic review of the literature evaluating donor site morbidity following vascularized bone grafts from the distal femur by Giladi *et al.*[50] found a low rate of donor site complications. The most commonly reported donor site morbidities included persistent knee pain (which commonly lasts up to 3 months), and temporary altered sensation (parethesias or sensitivity) - < 2% of patients in the included studies had permanent altered sensation. The authors suggest that sensory changes could be related to saphenous nerve injury associated with osteocutaneous flap harvest. There are no reports in the literature of post-operative knee instability or limitations to knee range of motion. Secondary procedures were performed in 2.5% of patients included for review (6 flaps); procedures included: hematoma evacuation, seroma evacuation, wound debridement, and open reduction and internal fixation of femur fracture[50]. Post-operative femur fracture has been reported in two patients in the literature[22].

CONCLUSIONS

Vascularized bone grafts may be required for the reconstruction of bone defects in the setting of lower extremity trauma. Indications include bony defect greater than 6 cm, fracture non-union, and previously failed reconstruction with non-vascularized bone grafts[12-14]. Single-stage and two-stage approaches have

Table 1. Donor site morbidity following vascularized bone graft for lower extremity traumatic bone defects

Fibula	Iliac crest	MFC
EARLY COMPLICATIONS		
Infection dehiscence necrosis Delayed wound healing Skin graft loss Compartment syndrome	Infection Dehiscence hernia	Altered sensation Hematoma seroma Delayed wound healing
LATE COMPLICATIONS		
Decreased ankle range of motion Altered sensation Persistent pain Claw toe Ankle instability Reduced muscle strength Gait abnormality Reduced muscle strength	Altered sensation Persistent pain Gait disturbance	Persistent knee pain Femur fracture

MFC: Medial femoral condyle.

been described in the literature - immediate, often composite, free flap reconstruction *vs.* immediate soft tissue coverage followed by second stage bony reconstruction[26-31]. Free fibula flaps provide the largest size bone flap, ideal for larger bone defects and femur defects that would benefit from double-barreled reconstruction[18]. Vascularized iliac bone flaps provide less cortical bone for reconstruction, and are therefore ideal for defects that are less than 10 cm in length. However, it can be harvested with associated cancellous bone which can facilitate bony union[14,18-20]. MFC flaps are ideal for smaller bone defects, and can be implemented in the setting of foot and ankle trauma[25].

DECLARATIONS
Authors' contributions
Made substantial contributions to conception and design of the paper and provided mentorship and revisions on the manuscript: Stranix JT
Performed literature review, composition of manuscript: Schaeffer CV

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Not applicable.

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Conflicts of interest
Both authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

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