Current Management of Acute and Posttraumatic Critical Bone Defects

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Summary: Limb reconstruction in patients with critical-sized bone defects remains a challenge due to the availability of various technically demanding treatment options and a lack of standardized decision algorithms. Although no consensus exists, it is apparent from the literature that the combination of patient, surgeon, and institutional collaborations is effective in providing the most efficient care pathway for these patients. Success relies on choosing a particular surgical approach that manages infection, soft tissue defects, stability, and alignment. Recent systematic reviews demonstrate high success rates with the following management options: Ilizarov bone transport, Masquelet (induced membrane) technique, cancellous bone grafting, and vascularized bone grafts.

KEY WORDS: bone defects, limb reconstruction, acute, posttraumatic

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INTRODUCTION

The management of bone defect reconstruction has evolved and now includes multiple surgical options. Successful limb salvage for complex fractures requires considerations for patient characteristics, soft tissue, and fracture components of the injury. Patients who sustain fractures with bone loss may have soft tissue defects that require an orthoplastic approach.[1] As limb salvage options have expanded into various all-internal, integrated, and external fixator options,[2–5] it is effective to incorporate patient factors into the treatment algorithm.[6] Collaboration among orthopaedic and plastic surgeons expands the limb salvage options but increases decision complexities. Host factors, such as diabetes, obesity, malnutrition, and peripheral vascular disease, complicate the treatment plan and may affect the success of limb reconstruction.[7,8] Most published data are small retrospective series and do not provide a complete description of the episode of care (including adverse events).[9] A recent systematic review by Bezstarosti et al[9] reported on 43 studies in 1530 patients with fracture-related infections and a critical-sized bone defect. The mean bone defect size in all studies was 6.6 cm, and 86% were localized to the tibia.[9] Although methodological limitations prohibit drawing robust conclusions regarding the superiority of one method of limb reconstruction over another, a 94% success rate, 8% recurrence rate, and amputation rate of 3% were reported.[9] Techniques compared represent the contemporary strategies used by limb salvage surgeons (Ilizarov bone transport, induced membrane technique, cancellous bone grafting, and vascularized bone grafting).

Patient considerations include social support, ability to appreciate the gravity and duration of limb salvage strategies, and ability to comply with multiple visits, reoperations, and time off work.[10] In the end, due to heterogeneity of the clinical problems, surgeons use a pragmatic approach relying on their technical expertise, local institutional constraints, soft tissue defects, and the bone affected. The magnitude and location of the defect and history of infection remain additional considerations.

A critical-sized bone defect is one that will never heal without a secondary surgical intervention. Such defects are typically 2.5 cm or twice the diameter of the affected long bone.[11,12] Options can be divided into biologic and nonbiologic reconstructions. Biologic reconstruction includes distraction osteogenesis (the Ilizarov method), autograft, vascularized bone grafting, and the induced membrane (Masquelet) technique. Nonbiologic strategies include allografting and three-dimensional (3D) printing metal implants.[5] Treatment costs and efficiency of care are important factors that health care providers will continue to use in decision making.[13]

Distraction Osteogenesis (The Ilizarov Method)

Distraction osteogenesis was developed by Gavril Ilizarov[12,14,15] in the 1950s and included invention of his apparatus, the Ilizarov circular ring fixator. Ilizarov's thesis was on the Law of Tension Stress, which he described a low-energy osteotomy, bony stability, and distraction with a specific rate and rhythm. Interestingly, as the science of the Ilizarov method has remained the same, there has been an evolution of internal and external fixation (and computerized software) to move bone segments.[2,16–19] The original stainless steel ring–block fixators have evolved into aircraft aluminum hexapods supported by web-based software and

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motorized automatic struts.[20–22] All-internal techniques have evolved to improve the patient's experience and limit ring fixator–associated complications, such as pin-tract infections and scarring.[23] The Ilizarov method of distraction osteogenesis can reliably reconstruct limbs that would otherwise not be salvageable.

The Ilizarov method is a versatile yet demanding management strategy in biologic reconstruction of bone defects (Fig. 1). It allows for concurrent treatment of infection, malalignment, limb length discrepancy, and localized transport for osteogenesis. The premise relies on a surgical low-energy osteotomy (corticotomy) followed by a latency period and a daily distraction rate of no more than 1 mm divided at a rhythm of 4 times.[14,15] Finally, the consolidation phase occurs after all transport and alignment correction has been completed, and it is when the immature regenerate forms bone. Once the bone is fully mature, the external fixator, if present, can be removed. Regardless of the transport method, the formula must be adhered to.

It is important to segregate the science from the device. Figure 1 presents various forms of bone transport using the Ilizarov method. Indications for the use of distraction osteogenesis strategies are massive bone loss (greater than 5 cm), infection, periarticular segments (stability implications), surgeon experience, and hospital resource support.[3,4,9,18,22,24,25] Classic Ilizarov transport involves stacked Ilizarov style ring fixators or hexapods (Fig. 1A), with one focus that is the osteotomy and another the docking site (bifocal bone transport).[26–32] In bone defects larger than 8 cm, special considerations are required to reduce the time spent in the fixator—external fixation index.[4,18,26–34] These include plate-assisted bone transport (Fig. 1C),[33–36] cable pulley transport over an intramedullary rod (Fig. 1B),[2] and cable pulley transport with subsequent intramedullary nailing (Fig. 2).[19] The main advantage of cable pulley transports includes its ease of use around soft tissue flaps, less scarring, and modifications to automate the process.[2,19,37–39] Additional advantages include the ability to speed up the healing of the regenerate (improved bone healing index) and significantly decreased external fixation index.[19]

Structural Graft

When considering how to reconstruct a bone defect, certain cases and/or patients may require immediate structural stability or may be unsuitable for prolonged reconstruction due to medical or social factors. In these cases, some surgeons elect for reconstruction with structural allograft. Allograft use has expanded overall in orthopaedic surgery—notably for osteochondral defects but is used in other areas.

Structural allograft is commonly used in foot and ankle reconstruction and postoncologic reconstruction. A recent meta-analysis for the use of structural allograft in hindfoot reconstruction demonstrated a union rate of 67% and limb salvage rate of 92.5%.[40] Femoral head was the most used allograft and primarily for large hindfoot defect after failed total ankle replacement or talar osteonecrosis. The use of allograft for reconstruction after oncologic resection is common but is associated with nonunion rates from 0% to 53% and allograft fracture rates from 0% to 75%.[41] Allograft incorporation remains a challenge. Vercio et al[42] demonstrated excellent union when using a motorized magnetic lengthening nail in compression mode for allograft reconstruction after tumor. Some surgeons have proposed combining allograft with a vascularized bone graft, commonly referred to as the Capanna[43] or modified Capanna technique.[44] One similar alternative is the combination of allograft with vascularized periosteum, which has shown promising results in animal models.[45,46] In addition, animal models suggested that pulsed parathyroid hormone analog may aid with allograft incorporation.

Generally, the use of structural allograft is uncommon for traumatic defects. Viale et al[47] combined the induced membrane technique with structural allograft for a 10-cm femoral defect after trauma. Recently, Dheenadhayalan et al[48] described 20 patients in whom they used structural allograft combined with autologous grafting at the host–allograft junctions for reconstruction of open distal femoral fractures with bone loss. Thirteen of 20 patients achieved uneventful union, and all but one achieved union after

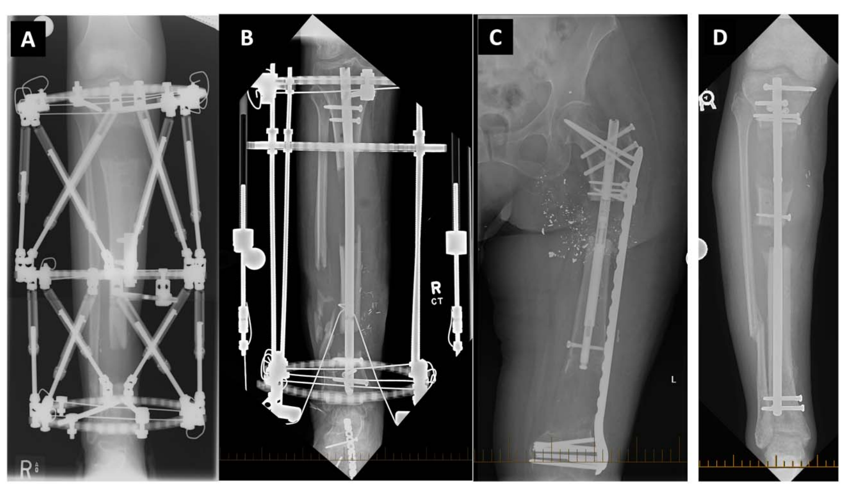

FIGURE 1. The images represent 4 different bone defect reconstruction strategies using the Ilizarov method of distraction osteogenesis. A, A 24-year-old man with a 72-mm infected bone defect after a motorcycle collision. He underwent successful limb salvage with a bifocal bone transport using stacked hexapod ring fixators. B, A 35-year-old man with a 118-mm tibial diaphyseal defect who was treated with bone transport using cable and pulleys over an intramedullary rod. C, Example of an all-internal technique. A 65-year-old woman with a self-inflicted accidental shotgun injury to her left thigh. She had successful limb reconstruction of a 112-mm bone defect using plate-assisted bone transport. D, A 45-year-old man who sustained an open type IIIB tibia fracture. After debridement, a 92-mm bone defect was reconstructed using a bone transport, magnet-controlled intramedullary rod.

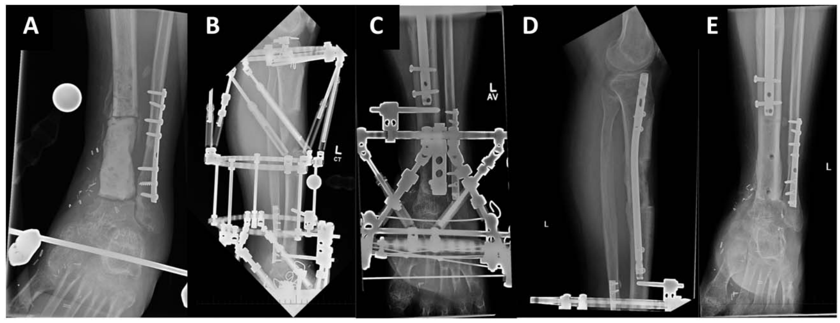

FIGURE 2. A, A 29-year-old male with a 74-mm distal tibial bone defect. B, Bone transport into an ankle fusion using lengthening and then nailing technique. B, C, Intramedullary rod to stabilize the regenerate. Hexapod was maintained to provide sustained compression and stability for the ankle fusion site. E, Successful ankle fusion.

a secondary procedure(s). Four patients developed deep infections. Structural allograft is a viable option when other biologic reconstruction techniques are contraindicated or cannot be performed.

Vascularized Bone Transfer

Certain bone defects may present such a large defect or challenging biologic environment (eg, irradiated tissue or scarred, multiply operated tissue beds) such that grafting or distraction osteogenesis is unlikely to succeed. Advances in microsurgical techniques have allowed surgeons to transplant viable bone, with or without accompanying soft tissue, on a vascular pedicle to address the defect.

Free vascularized fibular transfer was first described by Taylor et al[49] in 1975. Over time, the uses and indications for free vascularized bone transfer have expanded. It is possible to transfer vascularized rib, iliac crest, scapula, or medial femoral condyle. However, owing to the achievable length and superior mechanical properties, the fibula is used most often. The fibula is typically transferred to the upper extremity, where the caliber of the bone makes it a good match for defects in the clavicle, forearm, or humerus. The fibula can be used in the lower extremity, although additional considerations are warranted.

The indications for free fibula transfer are a defect for which the fibula can provide sufficient length and the ability to provide stability to allow for postoperative motion and prescribed weight-bearing. The patient must have blood vessels amenable for microsurgical anastomosis and a clean and viable tissue bed. Contraindications are patients whose lower extremity vasculature will not permit harvest of the fibula. The blood supply to the fibula is from the peroneal artery. Occasionally, foot perfusion is dependent on the presence of the peroneal artery. A magnetic resonance arthrogram or traditional lower extremity angiography can be used to identify any vascular abnormalities present.

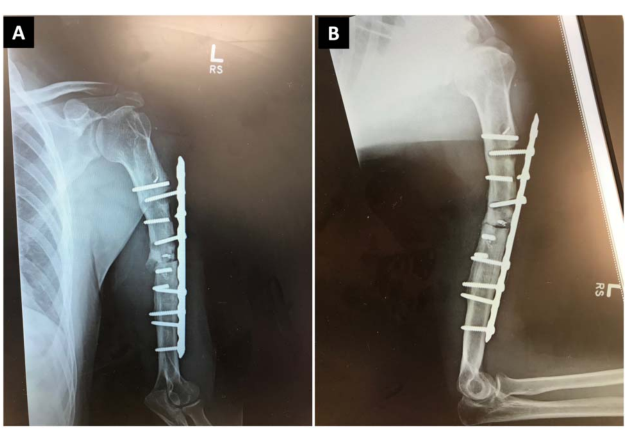

FIGURE 3. AP (A) and lateral (B) images from a 35-year-old male patient who has had multiple revisions for an infected nonunion of the left humerus.

In the upper extremity, several factors can improve results during free fibula transfer (Fig. 3). Good bony contact and compression is desirable. When possible, removing the periosteum from the end of the fibula, tapering it, and potting it within the canal of the native improves stability and bony contact (Fig. 4). This technique, as well as the use of bone graft at the ends of the fibula, has been shown to improve healing.[50–52]

In the lower extremity, additional considerations exist. The fibula is not sufficiently large to support weight-bearing by itself but can hypertrophy over time.[53,54] Some authors have successfully used circular external fixators to support the leg with gradual changes to the stability of the frame to promote successful hypertrophy. It is also possible to use a "double-barrel" fibular reconstruction to improve surface area[55] or to place the fibula within allograft to allow for healing and stability.[43,44,56]

The outcomes from vascularized fibula transfer are generally good, with union rates between 80% and 100%, and may be dependent on etiology of the defect, with oncologic and infectious defects having lower union rates.[50,56–61] The primary concerns with free vascularized bone transfer when compared with other types of defect management are donor site complications. These can include infection, hematoma, peroneal nerve palsy, compartment syndrome, and gait changes.[52,62,63]

The Induced Membrane Technique (Masquelet)

The induced membrane (Masquelet) technique was discovered and initially published by Masquelet.[64–66] This technique relies on the creation of a foreign body induced biologically active membrane to protect cancellous autograft and stimulate new bone growth.[65–71] The Masquelet technique is indicated in bone defects secondary to a variety of causes (Figs. 5A, B).[70] The formed membrane protects autograft against resorption, maintains positioning of the

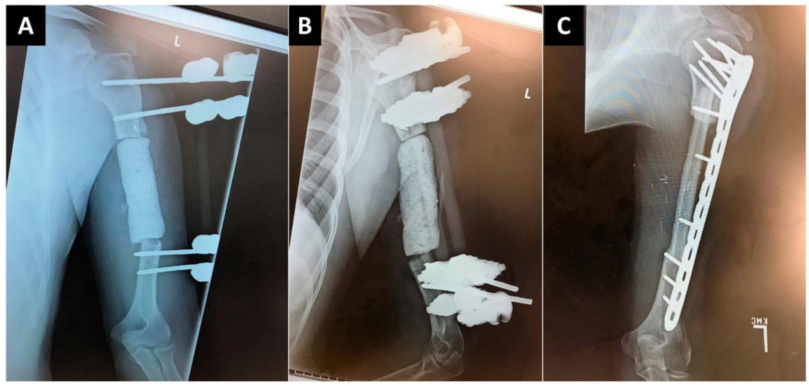

FIGURE 4. A, B, Same patient, as in Figure 3, PMMA spacer insertion, debridement and external fixator with targeted antibiotics as stage 1. C, Six months post ipsilateral vascularized free fibula transfer. Telescoped fibula into the humerus for added stability.

autograft, prevents soft tissue growth into the defect cavity, and protects the bone graft from the patient's immune reaction.[72,73] The technique is still considered among the gold standards in the care of critical bone defects. It relies on a two-stage process.[64,70,74,75]

Technique Stage 1

An aggressive debridement of any necrotic or infected bone, skin, or muscle in the region is first performed (Fig. 5C). All synovial tissue, tumor, or scar tissue is similarly excised to prevent recurrent tissue or fluid from forming in the defect cavity. Cultures and pathological specimens are obtained to direct oncologic or antibiotic treatment. In addition, the medullary canal should be made permeable by drilling any closed regions.[75]

Stability is critical for successful and eventual incorporation of the graft. This can be achieved with internal or external fixation. After debridement and osseous fixation, the bone defect should be filled with polymethylmethacrylate (PMMA) which overlaps the bone edges to create a large cavity with continuity from the defect to intact, viable bone.[70] The original technique described by Masquelet used PMMA without antibiotics present to prevent local antibiotics from masking an inadequate first-stage debridement.[65,66] Nau et al[76] demonstrated that the use of antibiotics in the PMMA provides bacterial inoculation while promoting higher osteogenic gene expression and current treatment strategies recommend antibiotics to enhance local bacterial eradication (Figs. 6A, B).[67,70,77] Definitive soft tissue closure with free tissue transfer, local rotational flaps should be performed during this first stage of care if necessary. The presence of a stable, subtle, and mobile soft tissue envelope is critical to bone grafting during stage 2 of this surgical technique.

Similar to withholding antibiotics from the PMMA spacer, the initial treatment strategy avoided systemic antibiotic treatment to prevent bacterial suppression in case of inadequate soft tissue debridement.[66,70,76] As the technique has continued to advance, it is now recommended that patients are treated with culture directed or empiric antibiotics for at least 6 weeks before the second stage to decrease risk of reinfection.[67,70]

Technique Stage 2

The optimal timing for the second stage of the procedure is between 4 and 8 weeks to allow for soft tissue readiness, completion of antibiotic treatment, increased membrane strength, and increased membrane biologic activity

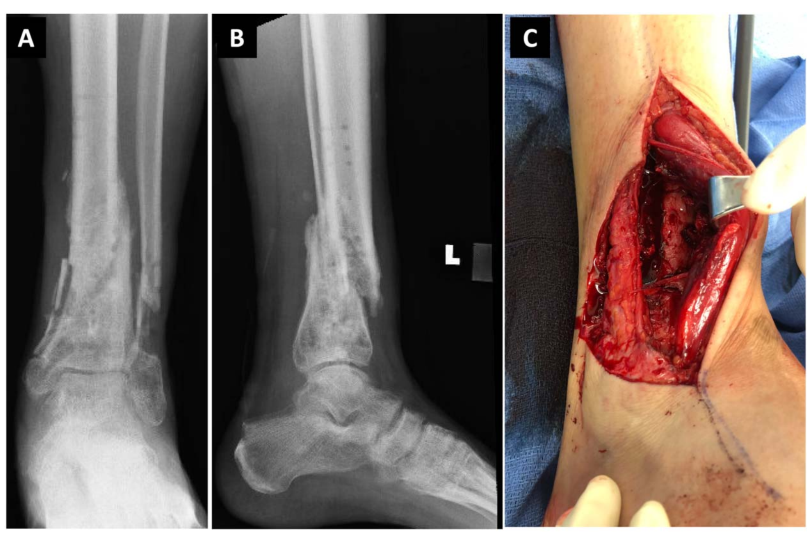

FIGURE 5. Mortise (A) and lateral (B) ankle images of a 51-year-old man presenting with infected distal third tibia fracture after multiple surgical procedures. C, Clinical image of the patient during stage 1 of induced membrane technique before excision of nonviable bone.

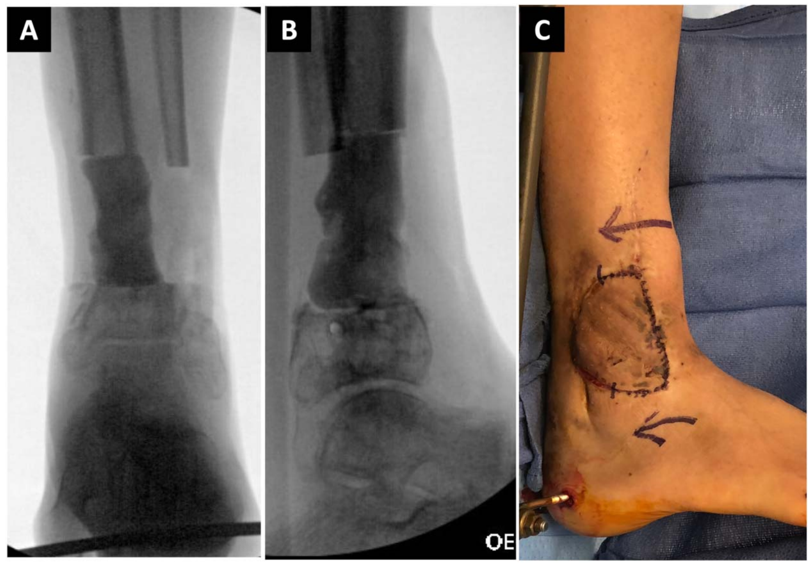

FIGURE 6. Mortise (A) and lateral (B) ankle images after bone resection and antibiotic PMMA cement spacer insertion. Steinman pins placed in the intramedullary canal and extension of cement over the viable bone edges can improve spacer stability and size of membrane at stage 2. C, Clinical image of free tissue transfer before incision during stage 2.

(Fig. 6C).[67,72] At 4 weeks, the membrane is most biologically active with higher concentrations of vascular endothelial growth fracture, interleukin-6, and bone morphogenic protein-2 which stimulates bone growth.[70,72,78] After skin incision or flap elevation by the plastic surgery team, the membrane must be identified, incised, and maintained while the cement is removed (Figs. 7A, B).[70,72,75] In the setting of intramedullary nailing, there will be a second membrane that must be removed as well. The proximal and distal cortical bone should be freshened up in addition to opening the intramedullary canal to allow for improved endosteal communication with the bone graft.[70] Cultures should be taken early in the procedure with gram stain and frozen pathology to confirm a sterile cavity. Any positive cultures or concern for persistent infection warrant aggressive debridement and placement of a second cement spacer an additional 6-week waiting period before grafting. If revision or definitive surgical fixation is essential, this should be performed before bone grafting as well (Figs. 7C, D).

Autograft can be harvested from the iliac crest or the long bone medullary canals. Bone graft can be combined with cancellous chips at a 70 (autograft)/30 (allograft) ratio[70] for larger defects. Giannoudis et al[74,79] described the addition of concentrated bone marrow aspirate to allograft to enhance bone healing during the second stage. The graft should be packed gently to allow for vascularization throughout the cavity during healing, and the membrane should be closed over the graft. The wounds should be closed without any surgical drains. Definitive form of fixation dictates weight-bearing for the patients. Intramedullary nailing can allow for early weight-bearing, while plate fixation of long bones may require up to 12 weeks of protected weight-bearing to allow for improved graft consolidation.

Outcomes

Union rates have been reported between 70% and 90% using the Masquelet technique.[74,75,80,81] A recent systematic review reported a union rate of 87% overall, almost 95% in

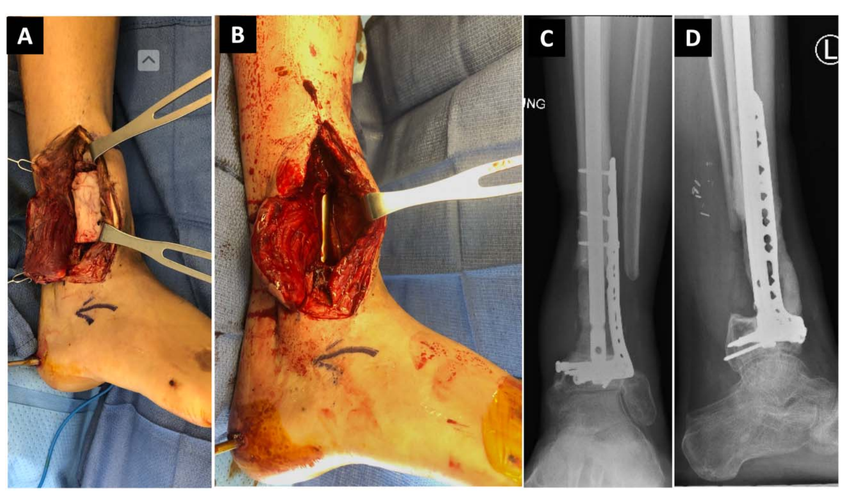

FIGURE 7. A, PMMA in place after flap elevation. B, Intramedullary nail in place with membrane in place. Mortise (C) and lateral (B) ankle images at 6 months post stage 2.

infectious cases and 85% in noninfectious cases.[77] Antibiotic PMMA during the first stage, preoperative infection, and intervals less than 8–12 weeks between the first and second stages were associated with higher rates of union.[77] Younger patients, femoral defects, and bone cement in the antibiotics were protective factors against nonunions and the need for additional surgical procedures.[77] Other studies have reported initial procedure healing rates of 86% in adults and 60% in pediatric patients. Those rates improve to 90% in patients who undergo additional grafting or additional surgical procedures.[67] The original publications report no correlation with length of defect and union rate, but the time to union did correlate with the length of defect. For every 1 cm of bone defect, there was 1.24 months until union, and the mean time to radiographic union has been reported anywhere from 5 months to 14 months.[74,75] There are very few studies investigating functional outcome following the induced membrane technique. In one of the first analyses, 50% of patients still used an assistive device for mobilization, 15% had resumed sports, and only 8% of patients had resumed running.[75] Grün et al[82] used the Short Form 36 (SF-36) (higher score = better function), and Lower Extremity Functional Scale (range 0–80 points), to evaluate functional outcomes in their series of patients treated with the induced membrane technique. The median Lower Extremity Functional Scale was 59 (15–80), the SF-36 Physical Component summary was 41.3 (24.0–56.1), and SF-36 Mental Component summary was 56.3 (13.5–66.2).

Complications

Complication rates have been reported as high as 40%, and in most cases, patients sustained more than 1 complication.[78] Infection (21%–60%) is the most common reported complication, and it is most commonly due to insufficient first-stage debridement.[77,81,83] Nonunion rates have been reported as high as 11.2%, and amputation rates have been reported in up to 4% of patients.[77] Masquelet's publication from the series of patients in the French Society of Orthopaedic Surgery and Traumatology evaluated alignment in their patients and reported 17% malunion rate with 16% of their patients requiring corrective procedures for deformity.[75] In that series, the failures occurred in the open tibias and 2 patients had associated vascular injuries. Further investigation into induced membrane technique is indicated to assess patients who best respond to this treatment strategy, those at highest risk of complications and the long-term functional outcomes of these patients.

CONCLUSIONS

Current techniques for reconstruction of segmental posttraumatic defects exist and demonstrate high success rates. The similarities between strategies drawn on orthopaedic trauma pearls: soft tissue coverage, skeletal stability, debridement of nonviable tissue, and targeted antibiotics in septic cases. Surgeons must consider the defect size, location, and the presence of concurrent infection. In addition, their own skill and institutional resources, as well as the patient's psychosocial situation, are critical for success.[5,13] Medical literature on the subject still fails to demonstrate one specific treatment algorithm over another. The Ilizarov method of distraction osteogenesis, Masquelet (inducible membrane) technique, cancellous grafting, vascularized grafting, and custom metallic implant continue to provide successful limb salvage options for patients. Research collaboration driving evidence-based approaches combined with continued patient-specific solutions will drive innovation into more efficient methods.

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