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MINIREVIEWS

Complex ankle arthrodesis: Review of the literature

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Abstract

Complex ankle arthrodesis is defined as an ankle fusion that is at high risk of delayed and nonunion secondary to patient comorbidities and/or local ankle/hindfoot factors. Risk factors that contribute to defining this group of patients can be divided into systemic factors and local factors pertaining to co-existing ankle or hindfoot pathology. Orthopaedic surgeons should be aware of these risk factors and their association with patients' outcomes after complex ankle fusions. Both external and internal fixations have demonstrated positive outcomes with regards to achieving stable fixation and minimizing infection. Recent innovations in the application of biophysical agents and devices have shown promising results as adjuncts for healing. Both osteoconductive and osteoinductive agents have been effectively utilized as biological adjuncts for bone healing with low complication rates. Devices such as pulsed electromagnetic field bone stimulators, internal direct current stimulators and low-intensity pulsed ultrasound bone stimulators have been associated with faster bone healing and improved outcomes scores when compared with controls. The aim of this review article is to present a comprehensive approach to the management of complex ankle fusions, including the use of biophysical adjuncts for healing and a proposed algorithm for their treatment.

Key words: Ankle; Arthrodesis; Ilizarov; Reconstruction; Salvage

Core tip: This research article aims to review the definition, current trends and future direction of complex ankle arthrodesis surgery. To our knowledge, there has not been a review article in the literature on this important and challenging topic. This article discusses the major risk factors that entail this type of ankle fusion surgery. It brings forth the debate in recent literature on how to treat this complex pathology, mainly in regards to internal *vs* external fixation, and various adjuncts that are available to promote healing.

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INTRODUCTION

Ankle fusion is often a limb salvage procedure in patients with end-stage or complex pathologic conditions of the ankle joint that may warrant a below-knee amputation as the only alternative. Complex ankle fusion is defined by certain risk factors of patients undergoing the procedure and includes individuals with comorbidities associated with poor surgical healing or with local healing problems that predispose to a high rate of delayed and nonunions. In addition to the technical demands of lower extremity surgery, concomitant suboptimal patient profiles impart significant challenges and constraints. The risk factors of patients undergoing complex ankle fusion can be organized into systemic and local factors that pertain to co-existing ankle or hindfoot pathology.

ETIOLOGY AND RISK FACTORS

Systemic factors

Systemic factors including patient comorbidities and global risk factors are frequently associated with failed or complication-ridden ankle arthrodesis. The spectrum of these factors is vast and includes advanced age, smoking, alcohol abuse, worker's compensation, non-compliance, obesity and systemic conditions (*i.e.*, atherosclerosis, immune suppression, diabetes mellitus and connective tissue diseases). Several studies convey the higher association of nonunion in patients who smoke or have a significant smoking history, which is even further heightened as the patient's age increases[1-4]. In a study by Fragomen *et al*[5] more than 50% of the patients who smoked failed to achieve healing of their ankle fusion. Alcohol abuse is another factor associated with nonunion in patients undergoing ankle fusion. Frey *et al*[6] displayed a greater than 85% nonunion rate among patients with major medical problems, which included alcohol abuse. Worker's compensation patients undergoing ankle fusion have been linked to poorer outcomes in comparison to provincial/third-party insured patients[2,3]. Patient compliance is imperative for attaining successful ankle fusion. The importance of restricted weight-bearing following ankle fusion with internal fixation cannot be emphasized enough as well as proper pin-care management in patients managed with external fixation in order to prevent failure and complications after the operation[7]. Although there is little evidence supporting obesity as a direct risk factor for nonunion, it has been proposed to interfere with the healing process for bony union. Obese patients are faced with several challenges, including adequate cast or brace fitting as well as maintaining non-weight bearing status post-operatively. These circumstances have the potential to compromise the fixation and place increased mechanical load on the implant's fusion site, leading to unwanted motion at the arthrodesis[8]. Major complication rates seem to be relatively higher for smokers, patients with an increased BMI, and diagnosis of diabetes mellitus with rates of 80%, 70% and 65% of these patients, respectively, after ankle arthrodesis with external fixation[9]. The analysis of patients' concomitant diseases show that the incidence of systemic compromises associated with chronic local ischemia and disturbances of proprioception is three times higher in patients who developed nonunions. These chronic circulatory disturbances in combination with multiple operative procedures decreases the local healing potential of bone and soft tissue[10]. Chahal *et al*[3] found that patients who had noninsulin-dependent diabetes mellitus had an 18.7 times higher likelihood of varus malunion than nondiabetic patients. These patients also had poor clinical outcomes when compared with the remainder of the patients. Rheumatoid arthritis also adds a degree of complexity in ankle arthrodesis surgery. Bone stock and ankle deformity are frequently poor and necessitate more difficult and demanding operative treatment than osteoarthritis. In rheumatoid bone, it is typically difficult to achieve adequate purchase of screws and stable fixation. External fixation is more often complicated because of increased risk of pin tract infections and patients often receive high doses of corticosteroids and cytotoxic agents, leading to fragile skin and loss of subcutaneous tissue that impairs wound healing and increases infection. Patients with rheumatoid arthritis who are taking medications known to impede wound and bone healing require a drug-free interval during the perioperative period. Belt *et al*[11] study of rheumatoid patients undergoing the Dowel technique demonstrated a significantly high complication rate of infection and non- and malunion. Although the complication rate can be high, successful fusion can be achieved with a reported fusion rate of 90%[12]. Other systemic factors include major medical problems, such as end-organ failure, immunosuppresion, malnutrition, malignancy and chronic infections. In Frey *et al*[6] review of the predisposing factors leading to nonunion in ankle arthrodesis, patients with major medical problems (including renal failure, a significant smoking history, diabetes, and alcohol abuse) suffered an 85% nonunion rate. Saxena *et al*[13] demonstrated that the need for additional surgery was more likely if two or more of the high-risk designated criteria were met, which included immunosuppression, obesity and diabetes.

Local ankle and hindfoot factors

Local factors that define a complex ankle fusion include bone loss, a compromised soft-tissue envelope, presence of infection, ankle or hindfoot deformity, and neuropathy. Frey *et al*[6] reviewed 78 patients who underwent ankle fusion and revealed a nonunion rate of 83% in patients who had an open fracture, 89% in patients with AVN and 60% in those with a history of infection.

Bone loss typically manifests as a result of high-energy trauma leading to comminution or bone expulsion, bone resorption secondary to chronic infection and avascular necrosis or bone stock deficiency post-TAR. Bone loss can also create a significant degree of shortening, leading to leg-length discrepancy. Tibial plafond fractures can present with a significant degree of periarticular comminution and metaphyseal bone loss, which makes compression fixation with internal fixation difficult or impossible. This renders neutralization fixation *via* ankle fusion an option to prevent secondary deformities that could result from compression fixation in the presence of bone defects.

In the setting of high-energy trauma, the soft tissue envelope is often significantly compromised by multiple traumatic and surgical scars, edematous, fibrous skin that is not pliable, or by draining sinus tracts if infection develops. This can be a risk when performing surgical approaches for fusion of the ankle[14].

Infection is often chronic and involves septic arthritis or osteomyelitis. Complex ankle arthrodesis success rates are decreased in the presence of infection. To achieve successful fusion in the setting of local infection, radical debridement, bone contact, stable fixation, and minimal compromise of the marginal blood supply are necessary. It is also of vital importance to avoid introducing foreign bodies at the site of infection and thus, external fixation should be highly considered. Antibiotic coated IMN can also be considered if acute shortening and bone contact can be achieved.

Deformity poses another obstacle to ankle fusion, often arising from the nature of the trauma itself, the result of malunion or nonunion from previous ankle fusions, or from co-existing neuropathy, which may lead to a Charcot arthropathy. Instability and progressive deformity in Charcot arthropathy can ultimately result in ulceration in a high percentage of cases. This leads to a high risk for progression to osteomyelitis and subsequent need for amputation[15].

SURGICAL TECHNIQUES

Surgical treatment for complex ankle pathology is often demanding and difficult due to the limitations imposed by the etiology of the patient's condition. There are over forty techniques documented in the literature which range from open crossed screw constructs to plates, intramedullary nails (IMNs), and external fixation devices. Although the most widespread operative strategy for achieving arthrodesis is internal fixation, the role for other methods of fixation and stabilization become more apparent as complexity of ankle pathology increases[16-18].

Both external and internal fixations have demonstrated positive outcomes with regards to achieving rigid fixation, union and minimizing infection. The pitfalls and advantages of each arthrodesis strategy must be considered in deciding the course of management that is most likely to achieve an optimal clinical outcome. Advantages of internal fixation include the ready availability of screws, the relatively low cost, the ease of application, and the documented clinical efficacy under favorable patient conditions[19]. Reduced rates of complications (such as non-union and infection) and neutralization of biomechanical forces have also been reported[20]. Relative to external fixation, it may provide earlier and higher fusion rates, a greater degree of patient satisfaction and decreased complications, especially soft tissue infections.

However, there are situations in which adaptation of the modular circular external fixator for ankle arthrodesis offers significant advantages over screw fixation. The Ilizarov ring system is indicated in difficult cases, especially when additional distal tibial pathologic conditions, bone defects, length discrepancies, or the need for early weight bearing are present[10]. Several of the indications for ring external fixation include: (1) bone quality that is subjectively and radiographically deemed to be insufficient to support internal fixation; (2) a history of infection at the tibiotalar nonunion site; and (3) expected patient compliance with external fixator pin care [7]. The combination of dynamic axial compression and demonstrated ability to resist bending, shear, and torsional forces allows the option of early weight-bearing. These features make it an ideal fixation tool for patients with complex ankle pathology. Unlike screw fixation, external fixation arthrodesis can be performed in poor bone and soft tissue conditions and can be used in the presence of active infection as a one-stage procedure. Typically after debridement of the tibial plafond and talus, flat surfaces are left for apposition. Compression with a circular frame provides excellent mechanical stability in this setting[21]. This allows the surgeon to employ this technique with confidence in patients deemed unsuitable for reliable screw fixation[17]. Another advantage of the Ilizarov method for ankle fusion is its ability to equalize limb length discrepancies through simultaneous tibial lengthening using distraction osteogenesis. Performing a tibial osteotomy in the setting of an ankle fusion has also been thought to enhance healing at the arthrodesis site[22]. In addition to limb lengthening, the principles of distraction osteogenesis can be used to correct malalignment. The ability to correct the position of the hindfoot and forefoot by adjusting the frame as needed during the regeneration phase is a unique advantage of the Ilizarov method. It allows the surgeon to address any intraoperative errors or early postoperative loss of position, ultimately leading to improved success when treating severe malalignment, failed fusion, and septic arthritis[23,24]. Thordarson *et al*[16] reported that screws provided better resistance to torsional loading in specimens with higher bone quality, whereas external fixation resulted in better resistance to torsion in specimens with lower bone quality. The authors concluded that screw fixation is "essentially useless" in osteopenic bone. When Hoover *et al*[25] compared traditional crossed-screw fixation to bimalleolar external fixation, the bimalleolar external fixator revealed to be the more rigid construct in both bending and torsion as compared to traditional lag-screw technique. External fixation is not without its pitfalls, which may include increased risk of pin tract infections, wire breakage, decreased patient comfort with application of the device and the need for additional surgeries, including removal or repair of the fixator.

From a biomechanical point of view, the choice of combined internal and external fixation is reasonable. Compared with stabilization with external skeletal fixation alone, additional internal osteosynthesis offers the opportunity of early removal of the fixator and consecutive mobilization of the adjacent tarsal and metatarsal joints. With the protection of the internal osteosynthesis, beginning early partial weight bearing of the limb increases further bony healing[10]. Thordarson *et al*[16] demonstrated that the external fixator gives good protection against torsional rotation but lacks good stability against plantar flexion-dorsiflexion movements at the fusion gap. However, these forces can be neutralized by cancellous bone screws. Hybrid techniques such as lengthening and then nailing (LATN) and lengthening and plating (LAP) can reduce the amount of time spent in external fixation and the risk of early regenerate fracture[26,27].

INTERNAL *VS* EXTERNAL FIXATION

Internal fixation

Internal compression or neutralization plating: For many years, the most widely applied techniques for ankle arthrodesis were crossed lag screws and IMN. Recently, the use of compression or neutralization plating has become increasingly more common. This approach, often with the use of proximal humeral and pediatric blade plates, offers another option for stabilization of the arthrodesis, especially in the setting of high-energy trauma or osteoporotic bone. From a biomechanical perspective, internal compression plating has been shown to have similar initial stability when compared with IM nailing (IMN), both in uni-directional[28] and multi-directional loading planes. When comparing the stability of IMN and blade plate constructs in fresh-frozen cadaveric models with reduced bone mineral density, the results were also very similar. The relationship between bone density and plantar/dorsiflexion and torsional stability was not significantly different in either construct; only in inversion/eversion was there a difference between the two, with blade plates exhibiting a reduction in stability as compared to IMNs[29]. Independent studies evaluating union rates in patients with tibiotalocalcaneal (TTC) arthrodesis *via* either blade plate fixation or IMN yielded similar fusion rates and clinical findings between the two constructs[30,31]. In a biomechanical study by Nasson *et al*[20] comparing the compression blade plate to crossed screws, crossed screws proved to make a stronger ankle fusion construct than the compression blade plate in valgus and dorsiflexion testing and trended to achieve greater resistance to plantarflexion, varus and torsional loads. However, in the presence of severe metaphyseal comminution and nonreconstructable joint incongruence, screw fixation techniques may be compromised while the blade plate demonstrates an attractive option. Ankle arthrodesis using a cannulated blade plate is a viable option to treat a nonreconstructable articular surface and metaphyseal bone defects in complex tibia pilon fractures. The cannulated blade-plate used in Bozic *et al*'s[32] series offered several advantages over other implants. Its use with a guide-wire allowed for precise placement of the blade, decreasing the likelihood of malposition and successfully maintaining correct foot position. It provided stable fixation with axial and rotational control in comminuted fractures with extensive bone-loss or non-union without requiring compression across the fusion site. Similar results were seen in Morgan *et al*[33] study where tibiotalar arthrodesis and metaphyseal reconstruction was achieved in all patients using a fixed-angle cannulated blade-plate with no mechanical or fixation failure. In comparison to IMN, the blade plate avoids the subtalar joint, preserving motion and decreasing the likelihood of arthrosis of adjacent joints. The use of the cannulated blade-plate allows for direct insertion with its thin leading edge of the blade, decreasing the likelihood of iatrogenic talar fracture. Complications seen with blade plate fixation include breakage of the plate and deep infection, especially in patients with a history of infection, which may require IV antibiotics and removal of the hardware. Disadvantages of the technique are related to prominence of the plate when it is placed anteriorly or laterally, which can lead to local irritation and need for subsequent removal of the plate[33].

Retrograde IMN: Ankle arthrodesis with a retrograde retrograde IMN has been shown to be an effective method for complex reconstructive procedures of the ankle and hindfoot. Recent biomechanical studies have shown superior strength with the use of IMN fixation over that of conventional cross screw techniques for ankle and hindfoot fusion, offering the advantage of being useful in conditions of either distal tibial and talar bone loss or when conventional screw fixation is suboptimal. Upon biomechanical comparison of IMN fixation and lag screw fixation for TTC arthrodesis, the IMN construct was shown to be significantly stiffer than the crossed lag screw construct after cadaveric specimens were subjected to cantilever bending tests in plantarflexion, dorsiflexion, inversion, and eversion as well as in internal and external rotation[34,35]. Thus, the IMN can be seen as more helpful in aiding the maintenance of hindfoot alignment during union, which ultimately increases the rate of fusion. IMN also allows for immediate stability and alignment with less dependence on external immobilization. Indications for tibiotalar, TTC or TC fusion with the IMN include salvage of failed tibiotalar arthrodesis, globular avascular necrosis of the talus, failed TAR, rheumatoid arthritis, inflammatory arthropathies, Charcot arthropathy, and gross instability presenting as a flail ankle as well as other neuromuscular conditions[36]. Ankle arthrodesis using the retrograde IMN is an effective method of correcting deformity and providing a plantigrade, braceable foot in patients with severe Charcot arthropathy and diabetes mellitus. Dalla Paola *et al*[37] achieved complete bony union of the ankle panarthrodesis with use of the IMN in 14 of 18 patients with Sanders pattern IV Charcot neuroarthropathy with no intra- or perioperative complications. In a similar subset of patients, Pinzur *et al*[38] investigated the use of a longer, femoral nail for ankle arthrodesis and its role in decreasing the risk of tibial stress fractures compared with shorter nails. All 9 patients achieved fusion of their ankle arthrodesis with a longer retrograde femoral nail. There was no evidence of infection, stress fracture or stress concentration at the proximal metaphyseal tip of the nails and all patients were ambulatory without localized pain. Ankle fusion with longer IMNs dissipates the stress along the entire shaft of the tibia and prevents its concentration at the tip. In patients with tibial fractures previously treated with external fixation, there is a greater risk for infection with ankle arthrodesis using the IMN. Pawar *et al*[14] were able to achieve union and eradicate infection with an antibiotic-coated locked IMN in five patients with infected Charcot ankles, 3 of whom had failed treatment with circular external fixation for infected ankle neuroarthropathy. Retrograde IMN is associated with several complications which include wound slough, infection, malunion, delayed union and nonunion, hardware failure, plantar foot pain, stress fractures, cortical hypertrophy, or stress risers at the proximal nail junction. Deep infection with proximal extension often requires removal of the implant, debridement and salvage with an external fixator if arthrodesis is incomplete. Initial treatment for delayed unions and nonunions includes removal of the proximal locking screws and adjunctive use of bone stimulator. If nonunions are symptomatic, reaming and exchange to a larger rod, or alternatively salvage with blade plate and bone grafting augmented with compression screw fixation may be necessary. Plantar foot pain is minimized with placement of the nail flush with the plantar cortex of the calcaneus and avoiding insertion on the weight-bearing heel pad[36].

External fixation

The Ilizarov technique harbors several advantages in the management of patients undergoing complex ankle arthrodesis. Several circumstances, especially settings of infection, bone loss, osteopenia and poor soft tissue coverage, provide an inclination for the use of external fixation. As with any active infection, the introduction of foreign bodies (*i.e.,* internal fixation with plates and screws) poses a major risk for failed fusion and continued infection. External fixation bypasses implant usage and can be used in the presence of active infection as a one-stage procedure. With major bone loss or other defects, the principles of distraction osteogenesis can be used to correct limb length discrepancies and malalignment. It allows the surgeon to address any intraoperative errors or early postoperative loss of position. External fixation provides adequate dynamic axial compression of flat, otherwise unstable surfaces that may be continued in the postoperative period and is able to resist bending, shear, and torsional forces. Thus, the rigid fixation provided, allows for the option of earlier weight bearing than seen with other arthrodesis techniques. The following sections hereunder aim to discuss in further detail the outcomes of external fixation in various clinical scenarios.

SPECIAL SITUATIONS, OUTCOMES AND COMPLICATIONS

External Fixation in patients with multiple comorbidities

Achieving arthrodesis in a Type B host presents a reconstructive challenge to the orthopaedic surgeon[5]. A Type B host is a patient with malnutrition, immune deficiency, chronic hypoxia, malignancy, diabetes mellitus, renal/liver failure, tobacco use, chronic lymphedema, major vessel disease, or extensive scarring. These patients have compromised bone healing and have traditionally been treated non-operatively or with amputation. External fixation has been used in the setting of these complex cases as a last resort treatment for limb salvage. Fragomen *et al*[5] achieved a fusion rate of 78% in Type B host patients, compared to a 94% fusion rate in Type A hosts. When smokers were excluded from the Type B hosts there was no difference between host type, demonstrating how smoking is one of the strongest predictors of failure among the factors that define a Type B host. Similarly to Fragomens' study, Cierny *et al*[39] reported success rates of 100% in Type A hosts and 83% in Type B hosts. Additional studies have demonstrated successful results in patients with multiple pathologies undergoing ankle arthrodesis utilizing the Ilizarov method. Kugan *et al*[40] demonstrated an 83% fusion rate with clinical functional improvement and no recurrence of previous deep infection in 48 patients with multiple comorbidities using the Ilizarov technique alone. Despite a few expected complications, most of which can be controlled and treated if recognized early, external fixation serves as a reasonable limb salvage alternative to amputation in this subset of patients.

External fixation in patients with infected and non-infected Charcot arthropathy

Severe foot and ankle deformity frequently arises as a consequence of peripheral neuropathy, which ultimately leads to Charcot arthropathy. Charcot neuroarthropathy is most serious when the ankle is involved because of the instability and progressive deformity, which often leads to ulceration, osteomyelitis, and amputation. Limb salvage is considered superior to amputation if a stable, well-aligned, lower extremity can be achieved due to the excessive weight-bearing and potential increase in severe diabetic complications the contralateral limb will likely face. Ankle arthrodesis, even in cases before ulcerated lesions appear, is considered a limb salvage treatment for this condition. External fixation has been routinely applied for arthrodesis in patients with Charcot arthropathy. Among patients with complex ankle pathology undergoing arthrodesis *via* the Ilizarov method, the fusion rate for patients with Charcot neuroarthropathy has been shown to be lower than for patients without Charcot neuroarthropathy. These patients exhibit numerous complications, including tibial stress fractures, subtalar joint collapse after frame removal, total collapse of the calcaneal body, and return to the operating room for frame revision and have often ended with a below knee amputation[5]. Utilization of a neutrally applied three-level circular external fixator in diabetic patients affected by Charcot neuroarthropathy with midfoot deformities and open wounds has shown excellent results. Pinzur *et al*[41] demonstrated 24 of 26 patients to be ulcer and infection-free and able to ambulate with commercially available depth-inlay shoes and custom accommodative foot orthoses. Although complications such as amputation for persistent infection, stress fractures and recurrence of plantar ulcers were seen, the study concludes that adequate correction and maintenance of the fixed midfoot deformity with a neutrally applied ring external fixator can be achieved in morbidly obese diabetic individuals with multiple co-morbidities complicating severe Charcot foot deformity. Hybrid external fixation has also been used for ankle fusion in patients with Charcot neuroarthropathy complicated by ulcers with isolated tarsal or ankle osteomyelitis[15]. This technique has demonstrated an 87% fusion rate and achievement of a stable, plantigrade foot. The key elements of treatment using this method include: (1) complete debridement of the infected tissue; (2) application of the external fixator with pins and wires not interfering with the infection site; (3) the use of only tensioned thin wires on the foot; (4) 6 to 8 wk of parenteral antibiotics in the postoperative period; (5) strict non-weight bearing post-operatively for 8-12 wk; and (6) the use of negative pressure wound therapy for the postoperative treatment of open wounds.

External fixation in patients with failed total ankle replacement

Total ankle replacement (TAR) is often indicated in patients with end-stage tibio-talar arthritis. Although survivorship of the implant has improved, failure rates still remain elevated with revision arthroplasty being imminent within 10 years of the index procedure[42]. TAR failure results in bone defects, significant limb length discrepancy (LLD) and poor soft tissue envelope quality, limiting many surgical options. In addition to revision arthroplasty, arthrodesis serves as an alternative and is often the preferred salvage procedure. Several approaches to achieve arthrodesis have been reported, ranging from external and internal fixation (plates, screws and retrograde nails) with or without structural bone or trabecular metal graft. Salvaging failed TAR with ankle arthrodesis has the potential to create significant bone deficits. This issue can be addressed in several ways including shoe lifts, placement of auto- or allograft within the bone defect or staged tibial lengthening *via* the Ilizarov method. A retrospective case series by McCoy *et al*[43] investigated the utilization of the Ilizarov method for complex ankle fusion in 7 patients with failed TAR, 5 of whom had undergone prior revisions and re-revisions. External fixation demonstrated an ability to produce an excellent fusion rate in complex, possibly infected, failed TARs with no evidence of fixation failure, re-fracture, or infection in all patients and all achieving a stable, plantigrade foot with minimal limping. In the setting of failed TAR, the Ilizarov method evinces a particular appeal because the staged lengthening modality allows for limb length optimization to be achieved after ankle fusion and bony apposition has already been set in the frame. Optimal bone contact can be achieved at the ankle fusion site and accurate assessment of the postarthrodesis LLD can be done. The patient and surgeon can then make a more informed decision regarding further treatment with limb lengthening or a shoe lift. Both options allow precise adjustment of limb length to patient comfort. Additionally, since the reconstruction does not rely on indwelling hardware or allograft bone, there is less concern when working in an infected field.

External fixation in patients with septic arthropathy and bone loss

Injuries involving bone loss around the ankle are often secondary to high-energy trauma and present a unique challenge for reconstruction and limb salvage efforts. These injuries are frequently compounded by infection, scarring, poor bone quality and shortening, either due to the primary insult or after initial surgery. The ability to achieve a painless, stable limb with eradication of infection using internal fixation is difficult and often contraindicated, setting forth the option of external fixation. The Ilizarov technique has shown to be a viable alternative to amputation in patients with these difficult cases. The rationale is to provide fixed angle stable fixation of the bone fragments, a percutaneous approach that is particularly useful in the presence of poor skin, and avoid the use of internal implants in the presence of infection[44]. Zarutsky *et al*[9] exhibited circular wire external fixation to be a viable treatment for the complex ankle salvage pathology. In a setting where implantable hardware is an absolute contraindication, only 2 of 12 patients with unilateral septic ankles achieved an unstable nonunion after external fixation. Salem *et al*[45] demonstrated the need for additional surgery and high complication rates despite successful fusion and clinical function using the Ilizarov frame for ankle arthrodesis in patients with significant bone loss and infection. Several patients, nearly all with septic ankle arthritis, needed repeat postoperative wound revisions or resection and renewed frame application to achieve union or to eradicate infection. With infection or AVN of the talus, complete or partial talectomy is often necessary which results in bone loss and LLD. This problem can be resolved with bone transport using the Ilizarov fixator for proximal tibial distraction osteogenesis. Of note, when comparing complex ankle fusion healing time in septic verus aseptic patients, a longer mean time to fusion for the infected cases has been shown[22,41].

External fixation in patients with revision ankle arthrodesis

Malunion and nonunion of an ankle fusion site are frequently complicated by persistent pain, infection, limb-length discrepancy and deformity. Revision surgery with the Ilizarov technique has been used to treat these complex conditions. The ultimate goals of revision ankle arthrodesis are a pain-free ankle, an almost normal gait pattern, and a foot capable of wearing a regular shoe. These goals can be met after obtaining solid union and correcting any deformity or malposition of the ankle, hindfoot, and forefoot. Advantages of external fixation over other methods for revision arthrodesis include rigid immobilization, resistance against shear and torsional stresses, axial loading with the ability for early return to weight bearing status, wound access, and manageability of large soft tissue and bony defects[36]. Excellent results have been achieved for revision ankle arthrodesis using external fixation with successful union being achieved in over 80% of patients and outcomes being comparable to those of primary arthrodesis. These patients who achieved successful fusion exhibited marked improvement in clinical outcomes scores[7,46,47]. The subgroup of patients undergoing revision arthrodesis present a unique challenge because most of them have coexisting pathological conditions and multiple previous operations[23]. Although achieving excellent radiographic and clinical results, the 22 (of 45) patients in Easley *et al*[7] study who had undergone revision tibiotalar arthrodesis with ring external fixation experienced the most complications in comparison to the groups with revision using internal fixation. Most of the complications were minor, not requiring surgical intervention. Although ring external fixation proved to have the highest rate of union among the methods of revision ankle arthrodesis and was effective for achieving union in several re-revision cases, it was associated with the majority of complications. Similarly to patients with other complex ankle pathologies, many patients undergoing revision ankle arthrodesis with external fixation face major complications such as, persistent nonunion, the need for additional surgical procedures (*e.g.,* frame revisions, re-debridement of residual bone infections), as well as other issues such as pin-site infections, adjacent joint arthrosis and tibial fractures and below knee amputation. Patients undergoing revision arthrodesis with external fixation have also required longer periods of immobilization in comparison to primary arthrodesis surgery[12].

Patients undergoing simultaneous tibial lengthening

Many patients requiring ankle arthrodesis have a significant degree of limb-length discrepancy as a result of severe bone loss; often secondary to trauma or removal due to infection or AVN. Significant LLD presents a major issue in that a greater discrepancy is associated with a higher risk of ankle nonunion[5]. Patients with this issue undergoing ankle fusion using external fixation are at a major advantage in that the limb-length discrepancy can be addressed with either a distal or a proximal corticotomy, followed by distraction osteogenesis and compression at the arthrodesis site[22]. Not only can the external fixator correct limb length inequality, it allows partial weight-bearing during the reconstruction, which enhances rehabilitation and stimulates healing of the arthrodesis and the proximal bone transport[48]. The ideal candidate for tibial lengthening is a nonsmoker, young adult, with a strong family support system, who has greater than 3 cm of shortening[44]. The procedure should be staged several weeks after the index fusion procedure. Abiding to the Ilizarov technique, a seven-day latent period after the corticotomy should be followed by gradual distraction at 1 mm per day. The goal of treatment is for the operatively treated limb to be 0-1 cm shorter than the normal limb. This slight amount of limb shortening is necessary for toe clearance during the swing phase of gait. Several studies have demonstrated excellent results with simultaneous tibial lengthening during complex ankle arthrodesis. Of the 18 patients (with an average LLD of 4 cm) in Katsenis *et al*[23] study, 16 patients' limbs were able to be successfully lengthened to 1.5 cm shorter than the contralateral limb. Among 48 patients with complex ankle pathology that underwent ankle fusion, 11 patients underwent simultaneous tibial lengthening. Bifocal compression-distraction in 10 patients and bone transport in one patient resulted in both fusion and leg length equality. Similarly, eight patients in Rochman *et al*[48] study underwent proximal tibial distraction osteogenesis in the Ilizarov frame to achieve equal limb length. Aside from the common complications associated with external fixation, complications that may arise with bone transport include premature consolidation or delayed maturation of the regenerate bone at the osteotomy site as well as angulation at the site of transport. These complications may require the need for correction with surgical intervention. The advent of the Taylor Spatial Frame

(TSF), which enables correction of residual deformity by computer-generated software and gradual strut adjustments, can negate the need for surgery. Although lengthening adds to the complexity of treatment and prolongs the overall treatment time, it allows limb length equalization after aggressive debridement of all necrotic, infected, and poor quality bone. It also provides a biological stimulus for bone healing, alleviating the need for bone grafts. Studies have demonstrated a 2 to 3-fold increase in blood flow in the bone segment under distraction arthrodesis as compared to the contralateral side. This has been shown to accelerate bone union and control of sepsis[45]. The theory that performing a tibial osteotomy in the setting of an ankle fusion enhances healing at the arthrodesis site by promoting blood flow is, however, of much debate. Fragomen *et al*[5] study disproved the notion of increased fusion rates with osteotomy and simultaneous tibial lengthening. Patients with lengthening had a lower fusion rate, which the authors attributed to compromised healing seen with the increased complexity of patients with LLD that might require lengthening surgery. Simultaneous tibial osteotomy with ankle fusion also exposes the patient to increased swelling, blood loss, and increases the risk of thromboembolism and compartment syndrome.

BIOLOGICAL AND PHYSICAL AUGMENTATION FOR COMPLEX FUSIONS

Biological augmentation

With the progression of technical advances in external and internal fixation, complex ankle fusion outcomes have seen improvement. In addition to better surgical technique, a better understanding of bone healing biology has certainly contributed to these improved outcomes. The manipulation of bone biology to promote healing can be achieved with 2 types of biological agents, osteoconductive and osteoinductive agents. Osteoconductive agents serve as a scaffold matrix for cells to infiltrate, which allows bone to grow across the material. Osteoinductive agents are growth factors that stimulate nondifferentiated mesenchymal cells to differentiate into osteoblasts and other bone or cartilage forming cells. Osteobiologic agents that have been of current research focus include structural allografts, demineralized bone matrix (DBM) and bone morphogenetic proteins (BMPs).

The operative management of complex ankle and hindfoot pathology with large structural bone deficits can be difficult owing significant shortening of the limb. Fortunately, these conditions can be treated with arthrodesis in combination with implantation of bone graft. The foot and ankle is an area of great mechanical stress, rendering corticocancellous (structural) grafts to be frequently used due to the support and rigid fixation they facilitate. The use of frozen femoral head allograft has proven to be useful and safe for the treatment of these complex cases[49]. Although its use is technically demanding because of difficulty maintaining the position of the allograft during preparation and placement of the IM nail, the use of the "cup-and-cone" technique described by Cuttica *et al*[50] has shown to be helpful. After reaming the distal tibia and remaining talus or calcaneus with an acetabular reamer, a concave surface is created for secure placement of the convex interpositional femoral head allograft. The fusion interface leading to increased bone-to-bone contact between the allograft and the residual host bone in combination with the structural strength of the femoral head leads to a stable construct that more readily maintains the alignment and placement of the IMN while preserving the limb length of the patient's affected lower extremity.

A novel substitute to conventional bone graft measures is DBM, a form of allograft bone which preserves the proteinaceous growth factors present in bone that stimulate the induction of non-differentiated bone cells into osteoblasts[51]. It's use as a substitute for other forms of bone graft in complex ankle fusion surgery has demonstrated a mixed array of outcomes in regards to improved union rates[51-53]. Thordarson *et al*[51] was not able to demonstrate fusion rates superior to those observed with historical trials of DMB or standard forms of bone graft (*e.g.,* iliac crest autograft). Although DBM' s osteoinductive properties have not exhibited superior results to gold standard autogenous iliac crest bone graft, its use does convey lowered risk of complications such as donor site infection, pain, neurovascular injury, and fracture. In addition, there may be insufficient autograft in cases with large bone defects and operative time is decreased when allograft is used. It is important to be aware of the risks carried with allograft, these include latent infection, decreased mechanical strength following sterilization, and an increased risk of fracture, collapse, or nonunion[43].

BMPs exert a wide range of osteoinductive growth factor functions, with most BMPs (except BMP-1 and 3) promoting cellular proliferation, apoptosis, differentiation, and morphogenesis. They induce bone formation by way of endochondral ossification and in high concentrations may form bone by way of intramembranous ossification[48]. They are key modulators of osteoprogenitor and mesenchymal cells during fracture healing. In a prospective randomized clinical trial of 450 patients who had open tibia fractures, patients who received an IMN in combination with high-dose BMP had significantly fewer hardware failures, shorter time to union, fewer infections, faster wound healing, and fewer nonunions when compared to the patients who only received the IMN[54,55]. Currently, recombinant BMP-2 (INFUSE®) is FDA approved for use in anterior lumbar interbody fusions (with fusion cages) and open tibia fractures treated with IMN fixation. Encouraging results in Bibbo *et al*[55] experience with rhBMP-2 in high-risk ankle and hindfoot fusions promotes its clinical use in this spectrum of patients with an excellent safety profile. A case-control study[56] involving 82 high-risk patients who underwent complex ankle fusion with an Ilizarov frame showed promising results in the patients treated with rhBMP-2. The patients were more likely to obtain fusion after the initial surgery, spent less time wearing the frame and showed more bone bridging on CT scans in comparison to the control group of patients. A reduction in time wearing the frame in patients treated with rhBMP-2 could signify decreased morbidity and complications, particularly superficial and deep infections, pin loosening or failure, and tibial fractures. Recent literature cites unexpected complications such as heterotopic ossification and retrograde ejaculation in patients treated rhBMP for spinal procedures in close proximity to the presacral sympathetic plexus[57,58]. In the case-control study mentioned, there were no differences in the frequency of complications between the groups and no heterotopic ossification, deep vein thrombosis, compartment syndrome, wound breakdown, or focal neurologic deficiency was observed in either patient group. However, another case-control study by DeVries *et al*[59] failed to show significance in the fusion rate and time until radiographic union for rhBMP-2-treated and untreated groups after TTC fusions secondary to failed initial arthrodesis. Even with these encouraging results, it must be stressed that osteobiologic agents, including rhBMP-2, are adjuvant agents; the use of rhBMP-2 alone will not ensure osseous healing and thus it cannot yet be solely relied upon on to bridge bone gaps, especially in high-risk patients.

Physical device augmentation

In addition to the wide array of adjunctive bone grafts and growth factors for complex ankle fusion, various external and internal osteobiologic devices have showed promising results. Three commercially distinct modalities have been of investigation for bone stimulation, which include: pulsed electromagnetic field (PEMF), internal direct current (DC), and low intensity pulsed ultrasound (LIPUS)[55].

PEMF have been approved by the FDA for stimulation of bone growth in the treatment of nonunions following fractures and failed arthrodesis. PEMF seems to stimulate healing of a nonunion through TGF-B-mediated differentiation of fibrocartilage cells and increased expression of BMP-2 and 4, leading to the stimulatory effect on osteoblasts[60,61]. Initial preclinical studies on the application of PEMF treatment on osteotomized rat fibula and canine tibia models demonstrated significant reduction in the amount of time-dependent bone volume loss and osteotomy gap size as well as faster recovery of dynamic load bearing with increased load-bearing capacity compared with the non-PEMF treated controls[62,63]. Use of PEMF devices less than the recommended minimum period of 3 h has been demonstrated to significantly reduce the efficacy of this modality of bone stimulation in union rates, with approximately 2.3 times less union reported compared with when PEMF is used for the recommended periods[55]. Saltzman *et al*[64] investigated the use of PEMF, immobilization, and limited weight-bearing to treat 19 cases of delayed union after foot and ankle arthrodesis in 334 patients. The treatment protocol was successful in 5 of the 19 cases, with the remainder resulting in nonunion, thereby directing the authors to not recommend their PEMF protocol in treating delayed union in foot and ankle arthrodesis. They attributed the lower success rate, relative to fusion of long bones, to the geometric difficulties in orienting the coils to induce a current through the asymmetric foot and ankle.

The application of implantable DC bone stimulation for the treatment of complex ankle fusion has shown positive outcomes in several studies. Although the implantable DC stimulator may necessitate the need for a secondary procedure to remove the device in light of infection, local irritation, prominent hardware, or pain, it has several distinct advantages, which include increased compliance and constant, DC application to the site of interest with maximal intensity. Despite the absence of controlled studies directly comparing patients with and without implanted DC stimulators, several studies suggest that internal electrical bone stimulation may assist in fusions of the foot and ankle in high-risk patients. Saxena *et al*[13] demonstrated an 86% fusion rate utilizing implantable DC stimulation in conjunction with the standard arthrodesis protocol of bone graft and internal fixation in patients with diabetes, obesity, alcohol abuse, smoking history, previously failed arthrodesis or history of immunosuppressive drug use. Several complications did arise with 2 of the patients sustaining cable breakage of the implanted bone stimulator and 5 needing additional surgery, 4 of whom in order to achieve arthrodesis, which was subsequently successful. On a similar note, Donley *et al*[65] study exhibited a significant decrease in nonunion rate among high-risk patients, with 12 of 13 achieving fusion and improvement in mean pain scores after placement of an implantable DC stimulator during the arthrodesis surgery. Complications included a successfully treated superficial breakdown of a wound and 4 reoperations to remove the implant's batteries. Hockenbury *et al*[66] achieved a 90% fusion rate as well as improved clinical function in 10 patients with severe Charcot neuroarthropathy with the use of rigid internal fixation, autogenous bone graft and an implantable bone growth stimulator. In addition to complex primary arthrodesis procedures, implantable DC bone stimulation was analyzed in 10 consecutive revision arthrodeses for patients who had aseptic nonunion of the ankle. All 10 patients obtained solid fusion with good clinical outcome scale measurements[67].

The concept of LIPUS has also been applied to the arsenal of treatment for foot and ankle fusion. LIPUS has shown to accelerate the fracture healing rate for fresh fractures[68,69] as well as fracture nonunions[70]. It has received more attention for patients or fractures with potentially negative factors for fracture healing, such as delayed unions and nonunions[71,72]. Jones *et al*[73] were the first to prospectively investigate the use of LIPUS in the treatment of hindfoot nonunions after revision hindfoot arthrodesis. Although the study was not a controlled series and included a variety of hindfoot nonunions and revision surgeries, it demonstrated improved clinical function and only one nonunion from a total of 19 joints (13 patients) that had been revisioned with arthrodesis in combination with LIPUS. An important disadvantage of LIPUS that was mentioned in the study was the high cost of the ultrasound units and reimbursement that varied between carriers and location. Jones *et al*[73] were also the first to complete a prospective comparative study evaluating clinical and radiographic healing of patients undergoing primary subtalar arthrodesis with LIPUS and demonstrated a 100% fusion rate with significantly faster healing rates on plain radiographs and CT in addition to improved clinical function 12 mo post-operatively compared to the control. Although the mentioned studies did not include high-risk nonunion patients, the outcomes demonstrated hold promising results for the treatment of a more complex group of patients. Because of the paucity of literature evaluating electrical and ultrasound bone stimulation with complex hindfoot and ankle arthrodesis, it is difficult to clearly define its role. Sufficient clinical evidence does not exist to support the use of one modality over another. Although the most important aspect in any fusion surgery is meticulous technique, advances in technology with bone stimulators and osteobiologic agents seem to be useful additions in the quest to achieve solid fusions with decreased complications[55].

CONCLUSION

Complex ankle fusion remains a challenging problem, with multiple factors ranging from local ankle and hindfoot pathology to systemic conditions and risk factors. Careful clinical and radiographic assessment, including CT and MRI might be warranted for proper decision making and formulating plan of management. Despite the limitations imposed by the etiology of the patient's condition, both internal and external fixation techniques have shown to be viable limb salvage alternatives, with each having there advantages and disadvantages. Both modalities have demonstrated very good fusion rates in a wide array of conditions including high-energy trauma, significant bone loss, deformity, and Charcot arthropathy. External fixation *via* the Ilizarov method has proved to be invaluable in cases with active infection, significant LLD as well as poor bone quality and soft tissues for adequate coverage. The antibiotic coated locked IM nail can be used in the setting of infection and bone loss if acute bony apposition can be achieved. Lastly, the use of biophysical adjuncts provides a promising field that requires additional randomized controlled trials to further justify their use in light of their expense.

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