General Considerations About Foot and Ankle Arthrodesis. Any Way to Improve Our Results?

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KEYWORDS

• Arthrodesis • Nonunion risk factors • Ankle arthrodesis • Ankle osteoarthritis
• Foot arthrodesis

KEY POINTS

- A successful joint fusion depends on a complex relationship of several factors, such as patient-related factors, intraoperative, and postoperative factors.
- With smoking cessation, good diabetic control (HbAc1 <7%) and vitamin D supplementation before the procedure, the outcomes after foot and ankle arthrodesis can be improved.
- Patient outcomes and postoperative complications can be improved by using less invasive techniques, even in the presence of more severe deformities.
- Using bone grafts in more complex cases, high-risk patients, nonunion revision surgeries, and filling in bone voids at the arthrodesis site, should be considered.
- The incidence of surrounding joint osteoarthritis after foot and ankle fusion seems to increase progressively with time. Owing to its progression and high probability of being symptomatic, patients must be informed consequently, as they may require additional joint fusions, resulting in further loss of ankle/foot motion.

INTRODUCTION

The etymology of the word arthrodesis shows that it originated from *arthro(English)* + "*dese*," from the Greek meaning binding together.[1] The first known use of arthrodesis was in 1888, suggesting that surgeons for thousands of years have performed this procedure.[1] Historically, its main indication was to treat painful osteoarthritis, but with the arrival of arthroplasty, joint arthrodesis for osteoarthritis

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has been decreasing and almost not performed, namely in hip and knee. However, in foot and ankle surgery, arthrodesis procedures remain an essential treatment tool for foot and ankle surgeons, as joint fusions are performed to treat a variety of pathologies from an isolated Hallux Rigidus to a complex midfoot/hindfoot deformity, tendon dysfunction, and neurologic foot problems.[2–4]

Nonunion and adjacent joint osteoarthritis are known complications after a fusion procedure, and foot and ankle surgeons are commonly exposed to such disabling complications. Nonunion has been associated with high patient morbidity and increased health costs, which justifies the resources and research focused on improving fusion rates in elective fusion procedures.[2] As a result, reducing nonunion rates has been a goal in foot and ankle surgery.[2] Nonunion rates of standard foot and ankle arthrodesis are illustrated in **Table 1**.

Determining who is at risk of developing nonunion is essential to reducing nonunion rates and improving patient outcomes. Several patient-related risk factors such as smoking and diabetes have been strongly associated with nonunion in foot and ankle surgery.[5–7] However, a successful bony fusion depends on a more complex relationship of several factors other than patients' comorbidities as several technical and mechanical factors have also been related determinants for nonunion development.[8]

This article exposes the most frequent factors related to nonunion and adjacent joint osteoarthritis after foot and ankle arthrodesis procedures. It provides the insight and necessary knowledge to properly inform patients about potential adverse outcomes and how to improve outcomes after foot and ankle arthrodesis. With this in mind, we have divided these factors into 3 main categories according to their relationship with the surgery into (1) preoperative; (2) intraoperative; (3) postoperative (**Table 2**).

Preoperative Factors

This group includes all the modifiable risk factors in patients who could benefit from focused preoperative education and treatment modification to improve patient outcomes and decrease the nonunion rate. Most of these risk factors are related to the patient's comorbidities or health habits.

Smoking

The effect of smoking on foot and ankle procedures is likely to be more pronounced when compared with other orthopedic surgical subspecialties. Peripherally, nicotine decreases prostacyclin, leading to vasoconstriction and tissue hypoperfusion.[9] Nicotine also potentiates platelet adhesion resulting in microvascular clot formation.[9,10] Carbon monoxide in cigarette smoke binds to hemoglobin and shifts the oxygen

Table 1
Nonunion rates in common arthrodesis performed in foot and ankle surgery

Fusion Procedure	Non-union Rates (%)
Ankle arthrodesis	3%–11%[2]
Subtalar arthrodesis	10%–23%[111–113]
Talonavicular arthrodesis	4%–7%[3]
Midfoot arthrodesis	7%–13%[4,114]
First TMT arthrodesis	2%–10%[64]
First MTP arthrodesis	3%–5%[115,116]

Abbreviations: MTP, metatarsophalangeal; TMT, tarsometatarsal.

Table 2
Modifiable risk factors for adverse outcomes after foot and ankle arthrodesis according to the operative period

Preoperative	• Smoking • Diabetes • BMI • Vitamin D levels • Medications (Corticosteroids)
Intraoperative	• Open surgery vs less invasive procedures • Joint alignment • Method for joint preparation • Interfragmentary gap • Use or not use bone graft and which type
Postoperative	• NSAID medication • Early vs delayed weight bearing • Surrounding joint OA and additional fusions

dissociation curve to the left, which causes oxygen dissociation from hemoglobin and further tissue hypoperfusion.[9] In addition, there is evidence showing an association between smoking and low bone mineral density, delayed fracture union, and implant failure.[10] A recent review of literature involving 91 studies assessing the effect of smoking in trauma and elective foot and ankle procedures concluded that it seems to be a significantly increased risk of nonunion in ankle, hindfoot and midfoot arthrodesis performed in smokers.[11] The odds ratio of smokers in hindfoot and midfoot arthrodesis nonunions was reported as 3.9 and 8.5, respectively. Moreover, major postoperative complications such as deep infections and wound healing problems were significantly higher in smokers. In another study, Thevendran and colleagues[12] completed a review on the risks of nonunion in foot and ankle arthrodesis. Although all included studies were level III and IV evidence, they concluded that there was enough evidence to support a grade B recommendation on smoking as a risk factor for nonunion in foot and ankle fusions.

In clinical practice, patients are often requested to stop or reduce tobacco smoking to improve postoperative outcomes. It has been reported that self-reporting of tobacco use is underestimated by up to 25% of actual smoking status.[13] Thus, on occasions, it can be helpful to determine the right level of tobacco smoking. The 2 most common methods of smoking assessment currently in use are exhaled carbon monoxide and saliva cotinine measurement. Passive smokers usually have cotinine concentrations in saliva below 5 ng/ml. Levels between 10 and 100 ng/mL may result from infrequent active smoking and levels >100 ng/mL from regular active smoking.[14]

It is known that immune and pulmonary function improves after smoking cessation.[15] Moreover, a comparative level- I study has shown that smoking cessation for 4 weeks preoperatively reduced the risk of postoperative complications comparable to nonsmoking patients.[16,17] Although evidence is quite limited, it seems that smoking has a significant negative impact on foot and ankle fusion procedures outcomes. Thus, it is recommended that active smokers decrease or stop smoking in the perioperative period (4 weeks ideally) of a surgical procedure.

Obesity

In orthopedic surgery, obesity has often been associated with increased postoperative complications, such as wound healing problems and fracture nonunion.[18–21] Obese patients may encounter cast and brace fitting challenges and may have

difficulty maintaining non–weight-bearing postoperatively. These circumstances can compromise the fixation and increase the mechanical load on the implant's fusion site, leading to unwanted motion at the arthrodesis. The available literature assessing the impact of BMI on the outcome of arthrodesis procedures is exceptionally scarce or inexistent. However, studies assessing the outcomes of femur and proximal tibial realignment osteotomies have shown significantly higher rates of nonunion in obese patients.[22,23] Nevertheless, there is no evidence supporting obesity as an independent risk factor for arthrodesis nonunion in the foot and ankle field.

Diabetes

The pathophysiology of diabetic bone healing has been studied extensively in animal and clinical models.[24] Through several mechanisms such as sustained hyperglycemia and increased the activation of proinflammatory factors, diabetes disrupts the homeostasis between osteoblasts and osteoclasts' activity.[25] In the process of fracture healing, the reparative stage involves the formation of cartilage during endochondral bone formation by chondrocytes and bone production by osteoblasts. Moreover, angiogenesis enhances cartilage transition into bone. Impaired osteoclasts and osteoblasts function to organize bone into its final form, and states of hyperglycemia and insulin insufficiency are proposed mechanisms that alter chondrocyte and osteoblast apoptosis, interfering with bone healing.[24] Diabetes increases blood viscosity and is associated with tissue hypoxia.[26] In addition to affecting the angiogenesis process, tissue hypoxia slows inflammatory responses, thereby altering wound healing and increasing the risk of infection, particularly in the lower extremity.[25,26]

The negative impact of diabetes on fracture healing is widely supported. For example, a recent systematic review comparing rates of adverse healing outcomes in patients with diabetes versus nondiabetes following surgical treatment of a lower extremity fracture concluded that patients with diabetes are at a significantly higher risk of nonunion (approximately six times) especially in fractures involving the lower leg.[25] A retrospective comparative study assessing the outcomes of ankle and hindfoot fusions in patients with and without diabetes found that the overall rate of postoperative complications (infection and nonunion) was significantly higher in patients with diabetes (45% vs 22%, $P < .005$).[27] Moreover, patients with diabetes had a two times higher likelihood of developing a nonunion when compared with patients with nondiabetes.

It is well known that patients with poorly controlled diabetes are more likely to experience complications of diabetes, such as neuropathy, foot ulcer, and Charcot foot condition.[28] Poorly controlled glucose (Hgb A1c greater than or equal to 7%) in patients with diabetes has been associated with two- and five-times higher likelihood of developing a postoperative nonunion and infection, respectively.[27,29]

There is fair evidence supporting diabetes as a risk factor for postoperative complications after foot and ankle arthrodesis. In addition, poorly controlled glucose with Hgb A1c superior to 7% seems to increase complications incidence in patients with diabetes. Therefore, close glycemic control and multidisciplinary diabetic consultation are recommended before any foot and ankle surgery.

Vitamin D

Vitamin D is essential in maintaining bone health through calcium and phosphate metabolism regulation. When vitamin D levels are low, the absorption of calcium and phosphate in the intestine decreases, causing an increase in parathyroid hormone, which results in increased osteoclastic activity.[30] Hypovitaminosis D is not rare as we might think. Vitamin D levels have been reported as low in 70% of orthopedic patients and as severely low in 22% of patients undergoing elective foot and ankle procedures.[31]

Inadequate sun exposure, gastrointestinal malabsorption syndromes, and renal failure are frequent causes of insufficient levels of vitamin D. Current evidence about the role of vitamin D on foot and ankle conditions are limited owing to the anecdotic number of high-level evidence studies. One study comparing vitamin D levels between patients with ankle fractures and patients with ankle sprains has shown significantly lower vitamin D levels in the ankle fracture group.[32] Another case-control retrospective study compared 29 patients with nonunion following elective foot and ankle reconstruction with a control group of 29 patients with a successful union.[33] They assessed the prevalence of modifiable risk factors for nonunion and found statistically significant lower vitamin D levels in the nonunion group. Moreover, patients with vitamin D deficiency or insufficiency were 8.1 times more likely to experience nonunion.

Animal models suggest that vitamin D supplementation facilitates fracture healing.[30] In addition, a randomized clinical trial after proximal humerus fracture in humans showed increased fracture callus formation with vitamin D and calcium supplementation compared with placebo.[34] For an adult, vitamin D levels of 75 mmol/L or superior are considered as normal or sufficient to maintain bone health, and the recommended daily intake of vitamin D for healthy individuals is 600 IU (international units) for those younger than 70 and 800 IU after age 71.[33]

Based on the limited evidence, hypovitaminosis D in foot and ankle patients is a frequent condition. Therefore, screening and hypovitaminosis D treatment supplementation is recommended as the benefits seem to outweigh the drawbacks, and outcomes of the arthrodesis procedure may be improved as a result.

Patient Medications

Several medications used to treat chronic medical conditions, especially those commonly prescribed to treat rheumatologic and inflammatory diseases have come under consideration for their theoretical ability to alter the early inflammatory pathway and the later molecular environment involved in bone and wound healing, thereby potentially resulting in undesirable postoperative complications. For example, animal studies have shown that long-term use of corticosteroids leads to osteoblast apoptosis, osteocyte apoptosis, and inhibition of osteoblastogenesis, resulting in decreased bone density and callus formation.[35,36] In an experimental model of posterolateral lumbar spinal arthrodesis in rabbits, dexamethasone administration inhibited graft incorporation and increased rates of nonunion.[37] Although the inhibitory effect of corticosteroids on bone healing seems logical, these results have been found primarily in animal studies.

For other drugs, such as methotrexate, the effect on bone healing seems to be dose-related as a low dose of methotrexate did not affect the early process of endochondral bone formation in experimental studies.[38] Regarding wound healing, in vitro and experimental animal studies suggest that methotrexate can adversely affect wound healing, whilst the clinical studies show that lose-dose methotrexate is safe and does not affect the incidence of postoperative wound complications.[39]

The effect on bone healing of oncologic drugs has been investigated. The antiproliferative and cytotoxic properties of chemotherapeutic agents seem to alter neovasculogenesis, proper callus formation, and host bone-allograft incorporation resulting in higher nonunion rates.[40] Quinolones have been associated with decreased chondrocyte number, abnormalities in cartilage morphology and impaired fracture healing in rats.[41]

Today's knowledge of the effect of several drugs on bone healing is characterized by inconclusive and controversial results from several animal models. However, evidence suggests that some pharmacologic agents can be detrimental to bone healing

and affect patient's outcome following arthrodesis surgery. Considering this, physicians should inquire about patients' medications, perform necessary adjustments, and, perhaps, consider delaying surgery whenever indicated.

Intraoperative Factors

This group includes all the modifiable factors during the surgical procedure. Most of them are related to surgical techniques and surgeons' choices.

Open vs. arthroscopic surgery: does it matter?

Foot and ankle joint arthrodesis have been traditionally performed through open techniques. The small size of most joints has been the main drawback of using less invasive techniques such as arthroscopy. However, improved instrumentation and more significant experience have facilitated the development of new and less invasive approaches. As a result, arthroscopic arthrodesis procedures have gained increasing popularity among foot and ankle surgeons. Owing to their minimally invasive nature, arthroscopic techniques provide specific benefits: minimal soft tissue damage with less blood supply disruption, improved intra-articular visualization, minimal bone resection, improved fusion surface preparation, reduced postoperative pain, diminished wound healing complications, and a superior cosmetic result.[42–44] The majority of studies comparing open versus arthroscopic joint fusion assess the ankle and subtalar joints. A recent systematic review compared the outcome of arthroscopic ankle fusion in 303 patients with open ankle arthrodesis in 214 patients.[45] Only ankle arthrodesis for ankle osteoarthritis was included. Overall, the arthroscopic group had significantly higher fusion rates, less blood loss, shorter tourniquet times, shorter length of hospitalization, and better recovery at 1 year. Another multicentric comparative study found shorter length of hospitalization and significantly better outcomes one and 2 years after arthroscopic ankle fusion.[46] Moreover, arthroscopic ankle fusion has been associated with less postoperative pain and fewer complications such as wound healing problems and nerve injury.[47,48] In patients at high risk of postoperative complications, arthroscopic fusion significantly decreased major surgical-site-infections.[49]

The use of arthroscopic arthrodesis in patients with more severe angular deformities has been a debatable question. Whereas initially it was considered suitable only for minimally deformed arthritic ankles, evidence shows that similar good results can be obtained in more severe deformities.[50,51] Issac and colleagues compared the results of arthroscopic and open ankle fusions in patients with less than 15° of coronal plane angulation versus patients with more than 15° of coronal plane deformity.[52] They found equal good deformity correction with both techniques, and the degree of deformity did not adversely affect the outcome of arthroscopic ankle arthrodesis compared with an open procedure. Moreover, significantly higher rates of nonunion were observed in patients with more than 15° of deformity treated with open techniques. An example of a severe ankle valgus ball and socket deformity treated with arthroscopic ankle fusion is illustrated in **Fig. 1**.

Although there is strong evidence supporting the benefits of arthroscopic over open techniques in ankle arthrodesis, the available evidence comparing both procedures in other foot joints is still limited. A recent prospective multicenter randomized controlled trial compared the results of open posterior subtalar fusion in 28 patients with posterior arthroscopic subtalar arthrodesis (PASTA) in 28 patients.[53] Union time (9.4 vs 12.8 weeks) and recovery time (time to return to activities of daily living [8.4 vs 10.8 weeks]) were significantly shorter with PASTA than with the open technique. Other outcomes, including tourniquet time (55.8 vs 67.2 min), union rate (96.3% vs 100%), and

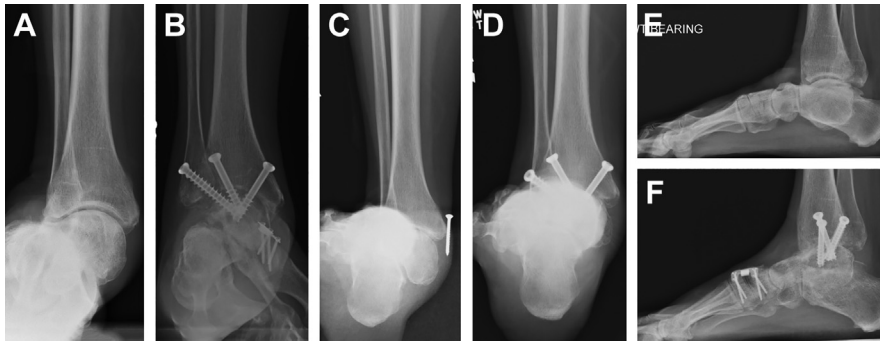

Fig. 1. Pre and postoperative imaging of a 34-year-old patient with severe ankle valgus ball and socket deformity treated with arthroscopic ankle fusion. (*A*) Preoperative weight-bearing AP ankle radiograph. (*B*) Postoperative weight-bearing AP ankle radiograph. (*C*) Preoperative weight-bearing hindfoot view. (*D*) Postoperative weight-bearing hindfoot view. radiograph. (*E*) Preoperative weight-bearing lateral ankle radiograph. (*F*) Postoperative weight-bearing lateral ankle radiograph.

complication rate, were not significantly different between the techniques. Similar results were observed by Rungprai and colleagues in another retrospective comparative study with 57 patients in the open group and 64 patients in the arthroscopic group.[54-] Because of their size and limited motion, midfoot joints were traditionally fused with open techniques. However, with new techniques, arthroscopic arthrodesis of midfoot joints such as the talonavicular, calcaneocuboid, and first TMT joint is becoming more frequent.[55–57] A recent retrospective study compared the radiographic correction and complication rates between 47 patients treated with arthroscopic first TMT fusion and 44 patients treated with open first TMT fusion for hallux valgus deformity.[57] Both techniques showed comparable good to excellent deformity correction. However, wound complications and non-union rates trended higher in the open group (4 vs 0, P=.051).

Based on the available evidence, it seems that patient outcomes and postoperative complications can be improved by using less invasive techniques, even in the presence of more severe deformities.

Malalignment

The position of each lower extremity joint intimately affects adjacent joint function as well as whole-limb performance. For instance, ankle fusion in the equinus position may result in accelerated subtalar changes and has been associated with recurvatum and laxity of the medial collateral ligament at the knee caused by back-kneeing and externally rotating the limb and stance.[58] Excessive hindfoot varus is often mal tolerated as can lead to excessive lateral column loading.[59] In triple hindfoot arthrodesis, residual hindfoot valgus and forefoot supination may cause subfibular impingement and deltoid failure resulting in ankle valgus.[60] An example of an ankle valgus after a triple arthrodesis with residual hindfoot valgus and forefoot supination malalignment is illustrated in **Fig. 2**.

Nevertheless, some degree of malalignment can be beneficial and improve outcomes in certain type of patients. For example, posterior displacement of the talus under the tibia is thought to reduce distal tibial pain and midfoot stress. This posterior displacement, combined with external rotation of 5 to 10°, reduces the foot lever arm and the tendency of the proximal joints to rotate externally during gait.[59] Thus,

Fig. 2. Postoperative weight-bearing foot and ankle radiographs showing a triple hindfoot fusion with residual hindfoot valgus and inadequate plantar flexion of the first ray resulting in deltoid ligament insufficiency and ankle valgus. (*A*) Postoperative lateral foot view showing absence of first ray plantar flexion. (*B*) Postoperative hindfoot view showing residual hindfoot valgus. (*C*) Postoperative ankle view showing nonconcentric valgus ankle.

ankle fusion with slight posterior displacement of the talus may improve outcomes in patients presenting with concomitant midfoot degeneration. When performing first tarsometatarsal joint fusion for midfoot osteoarthritis and hallux valgus deformity in patients with early features of progressive collapsing foot deformity, surgeons should consider increasing first ray plantar flexion to stabilize the medial column, correct hindfoot alignment, and bring the foot to a plantigrade position that protects the whole foot construction and ankle joint.[61]

Joint preparation

Joint preparation can be performed through several different techniques. Tools such as osteotomes, curettes, and rongers are frequently used to remove the cartilage. Because thorough joint preparation with these tools can be time-consuming, power tools such as saws, burrs, and reamers have been developed and adapted to facilitate foot and ankle joint arthrodesis procedures. However, the use of power tools in joint preparation has several nonnegligible drawbacks. Firstly, they can be a source of thermal bone necrosis, as higher burr and reamer speed causes an increase in bone temperature.[62] One systematic review comparing the effect of joint preparing in first metatarsophalangeal arthrodesis found higher rates of nonunion when power tools are used for cartilage removal.[63] Therefore, temperature control with saline solution irrigation should be applied when high-velocity surface preparation methods are used. Secondly, joint preparation with power tools can cause excessive subchondral bone removal with secondary joint and bone shortening.[64] This concerns more mid and forefoot arthrodesis procedures such as tarsometatarsal joint arthrodesis as excessive metatarsal shortening can lead to postoperative metatarsalgia.[61] Using saw cuts in Lapidus arthrodesis has been associated with excessive first ray shortening compared with more conservative methods such as curettes.[65]Once the cartilage is removed, sequentially drilling multiple holes in bone is often used to aid fusion.

However, drilling induces a significant amount of heat and accumulates after multiple passes, resulting in thermal osteonecrosis and detrimental to patient outcomes.[66] Although available evidence does not support one specific standard preparation method, the surgeon must be aware of the risks when using high-velocity tools for joint preparation, and actions to mitigate such risks should be employed. Several factors, such as tool selection and geometry, the time interval between passes, and drilling technic, can be modified to reduce heat-related bone injuries during joint preparation.[66,67] Ideally, surgeons should: use twist drills rather than Kirschner wires to improve bone chips evacuation; prefer drill bits of small diameter (<2.0 mm) to decrease bone contact; decrease the time interval between passes to reduces the total heat exposure time; optimize the drilling sequence and technic applying more perpendicular drill angles; perform irrigation and bone chips evacuation regularly.

Interfragmentary bone gap

The notion that increasing the interfragmentary gap would impair bone healing and alter the outcome is strongly supported mainly by animal studies.[68,69] It has been shown that a higher bone gap is associated with delayed bone healing, decreased callus and bone volume formation.[68] Although evidence on animal studies seems to be unanimous, there is a paucity in human studies, mainly owing to the difficulties in isolating bone gap as the only risk factor for bone healing. Perhaps, the only study assessing the role of poor bone apposition and the presence of bone gaps in achieving fusion in foot and ankle arthrodesis involving human subjects has been performed by DiGiovanni et al.[70] In their level- II study, the authors evaluated the importance of adequate graft material (defined as graft material filling >50% of the gap between bones) to obtain fusion in hindfoot and ankle arthrodesis. In their results, 81% of joints with good graft fill were successfully fused at 24 weeks compared with only 21% without adequate graft fill ($P < .001$). Furthermore, the OR for successful fusion with or without adequate graft fill did not differ significantly when stratified by joint type, the number of joints fused, sex, age, BMI, diabetes, or smoking status. Joints that had undergone a previous operation (other than fusion) at a fusion site had a significantly lower OR of successful fusion, although having good graft fill was still beneficial for fusion. They concluded an association between the amount of graft material, adequate graft filling, and successful ankle and hindfoot arthrodesis. Therefore, when a surgeon can eliminate bone-to-bone gaps in any joint intended for fusion, whether via the use of autograft or similar orthobiological, such a joint has a significantly better chance of ultimately achieving fusion.

Bone graft: use or not use?

Using bone graft to improve outcomes and achieve fusion in arthrodesis surgeries is a common procedure in foot and ankle surgery. However, the question of whether bone graft should be performed in primary arthrodesis procedures, in high-risk patients, or only in nonunion revision surgeries is still unanswered. Despite extensive literature citing the use of autograft or suitable alternatives to promote fusion in ankle and hindfoot arthrodesis, there is a remarkable paucity of level-I or II studies directly comparing rates of union with and without the use of graft material. In a recent systematic review including 27 studies, Heifner and colleagues assessed the role of bone grafting on fusion rates in primary open ankle arthrodesis.[71] Their results showed equivalent fusion rates between the graft and no graft group, and the authors conclude that the routine use of bone graft may not be needed in primary ankle arthrodesis in low-risk patients. However, the evidence seems to suggest the opposite regarding arthrodesis involving other foot joints.[72] Buda and colleagues assessed the effect of

bone grafting on union rates in 88 patients undergoing primary tarsometatarsal arthrodesis for tarsometatarsal osteoarthritis and concluded that the use of autologous bone grafting significantly reduced the risk of nonunion. Thus, for primary tarsometatarsal joint arthrodesis, the use of bone graft can be advantageous in improving outcomes.

The decision to use a bone graft or any orthobiologics in arthrodesis procedures seems to be driven by a combination of radiological and clinical considerations. In a survey inquiring foot and ankle surgeons about the need for bone graft in arthrodesis procedures, the top 3 clinical factors motivating the use of bone graft were the presence of nonunion or previous history of nonunion, followed by smoking and concomitant medications that are known to impede bone healing.[73] On the other hand, evidence of nonunion, avascular necrosis, and incongruous bone apposition with bone gap were the main radiological factors influencing surgeons' decision on using a bone graft. Although bone grafting in high-risk patients and nonunion revision surgeries is common, the evidence supporting it is unclear or insufficient. As a successful union depends on multiple factors (mechanical stability, comorbidities, surgical technic, and complexity) it is extremely difficult to obtain non-union rates based purely on the use of bone graft. The review by Lareau and colleagues is perhaps the most extensive analysis made up today.[74] They performed a logistic regression analysis of 159 studies in the foot and ankle literature comparing the use of autograft, allograft, and no bone graft for foot and ankle arthrodesis. Among other results, they demonstrated a trend toward higher union rates with autograft and cancellous allograft relative to no graft. Although no differences were statistically significant, the addition of bone graft approximately halved the nonunion rate. They conclude that considering the frequency, expense, functional impairment, and comorbidity of failed arthrodesis, this difference could be viewed as clinically substantial.

Overall, insufficient evidence supports the routine use of bone autograft or suitable alternatives to enhance fusion in ankle and hindfoot arthrodesis. Nevertheless, using bone grafts in more complex cases, high-risk patients, nonunion revision surgeries, and the filling-in of bone voids in the arthrodesis site to improve bone apposition should be considered to improve results and union rates, as the benefits of their use outweigh the drawbacks.

Autologous bone graft: Anterior iliac crest or proximal tibia?

Despite the dramatic advances in the orthobiological industry during the past decades, the autologous bone graft is still the gold standard for improving healing in arthrodesis and nonunion revision surgeries. This is mainly owing to its naturally osteoconductive, osteoinductive, and osteogenic characteristics.[74] Furthermore, it negates the potential risk of immunologic and infectious complications associated with the use of allograft.[75]

Traditionally, autologous bone is harvested from the anterior iliac crest. Because it can provide large quantities of cancellous and cortical bone, the iliac crest is ideal in situations whereby structural support may be required, such as ankle arthrodesis with more significant bone defects and subtalar distraction arthrodesis. Additionally, the iliac crest bone possesses higher marrow content, resulting in greater osteogenic potential compared with other anatomic sites.[76] For these reasons, the iliac crest is considered the gold standard site for bone harvesting. However, high incidence (20%–40%) of potential complications and several drawbacks have been associated with bone harvesting at the iliac crest, including hematoma, infection, chronic pain, nerve injury, fracture, and hypertrophic scar.[76] As an alternative, other sites for bone harvesting have gained increased popularity, namely the calcaneus and

proximal and distal tibia.[75] In addition to being close to the operative site, which facilitates tourniquet and draping placement, a significant amount of bone graft can be obtained. On average, 30 cc can be harvested from the proximal tibia, which is suitable for most foot and ankle procedures.[77] The incidence of complications related to proximal tibial bone grafting has been reported as extremely low (1.3%) and include tibial tubercle fracture, hematoma, and superficial infection.[78]

Although the iliac crest presents superior histologic features, there is no evidence supporting the use over other sites in terms of union rates for foot and ankle surgery. However, proximal tibial bone harvesting can be a valid alternative because of its simplicity and low incidence of associated complications.

Orthobiologics

Orthobiologics are biologically active substances used therapeutically for their positive effects on healing skeletal and soft-tissue injuries. Several orthobiologics products are currently available to the foot and ankle surgeon, including bone allografts, bone substitutes, and growth factors. To better elucidate their role in foot and ankle arthrodesis, these different types of orthobiologics can be grouped according to their primary function: (1) to provide structural support; (2) to address bone defects; (3) as augmentation in joint fusion surgeries.

Structural support is often required in complex hindfoot reconstruction and arthrodesis procedures, such as subtalar distraction and ankle arthrodesis with substantial bone defects. Of the orthobiologics, the cortical and cortico-cancellous bone allografts are frequently used to provide structural support as they are more rigid and resistant to loading forces.[79] Bone allografts obviate the inherent donor site problems of autogenous bone grafts but are beset by issues with graft rejection, low osteogenic and osteoinductive properties, and slower graft incorporation, particularly in areas whereby the blood supply is comparatively tenuous. Nonetheless, there seems to be no significant difference in well-vascularized bone sites when comparing incorporation and complication rates of allografts versus autogenous grafts.[79]

Bone defects whereby no physical support is needed can be addressed with different orthobiologics such as cancellous bone allograft, demineralized bone matrix (DBM), and bone graft substitutes.[80] Cancellous bone graft is often used but has the issues inherent to all allografts. DBM is a form of allograft prepared by acid extraction, so it retains bone morphogenetic proteins (BMP) and bone collagens. Therefore, DBM has improved osteoinductive capacity compared with traditional allograft, and available evidence seems to support the use of DBM in ankle and hindfoot joint fusion procedures.[79,80] However, the data are essentially retrospective with small samples and typically involves short-term follow-up. As an alternative to allografts and associated complications, synthetic bone graft substitutes, such as calcium phosphate and calcium sulfate, can be implanted to treat bone defects.[79] The clinical utility of these materials lies in their 3D porous structure that provides an osteoconductive scaffold, which enhances the adhesion and proliferation of osteoprogenitor cells, and correspondingly promotes the growth of new bone.[79] They are commonly used as an adjunct to bone reconstruction in trauma surgery, and their use in foot and ankle arthrodesis surgery seems more uncommon.

The use of augmentation products to improve fusion in foot and ankle arthrodesis has been gaining popularity as their use in foot and ankle procedures has been approved in different countries worldwide.[80] Platelet-derived growth factor (PDGF) and platelet-rich plasma (PRP) are perhaps the products more commonly used and with the more available evidence.[81] PDGF is a polypeptide growth factor released by platelets and macrophages in the injury site and plays a role in embryogenesis,

angiogenesis, and osteogenesis.[80] The use of rhPDGF in foot and ankle arthrodesis procedures has shown significant equivalent clinical outcomes in bone fusion performance compared with the autologous bone graft.[82] Moreover, compared with autologous bone graft, the use of rhPDGF was associated with fewer adverse events such as chronic graft site pain.

The rationale for using PRP lies in the anabolic and immune-modulatory properties of platelet concentrates. When activated, platelets release a group of biologically active proteins, such as growth factors and cytokines, crucial for bone, cartilage, and soft-tissue healing.[83] In the foot and ankle, PRP is frequently used in cartilage and soft tissues lesions, and its safety has been demonstrated.[84] However, the evidence supporting PRP to enhance bone healing seems to be scarce and quite contradictory. The use of PRP augmentation has been associated with higher fusion rates and reduced time to fusion in some studies, while others have shown no differences.[85,86] Regardless of this disparity, it seems to be unanimous that PRP augmentation is a safe method to deliver active biological factors to the fusion site, with few risks associated.

Postoperative Factors

Pain medications

The impact of nonsteroid antiinflammatory (NSAID) medications on bone healing is a topic of intense discussion. It is thought that the use of NSAID medication in postoperative pain management can affect the typical inflammatory cascade needed for new bone formation, thus, increasing the risk of developing a nonunion.[87] Most of the available data assessing the effects of NSAID in bone healing involves patients with bone fractures, and little is known about the influence of these medications in foot and ankle arthrodesis outcomes. A recent meta-analyis of 16 studies with a total of 15,242 bones included investigated whether the use of NSAIDs increased the risk of delayed and nonunion in the setting of fracture, osteotomy, or fusion procedure.[88] Their results revealed that the effect of NSAIDs on delayed or nonunion is strongly related to patients' age. There was an increased risk of delayed or nonunion with NSAID exposure (OR 2.07) in the adult population, suggesting that this medication can be safely administered in pediatric patients without compromising bone healing. In addition, this study found that a low dose or short postoperative exposure to NSAIDs did not substantially increase the risk of delayed or nonunion. NSAIDs seem to have dose-dependent and duration-dependent effects on fusion rates. However, short-term (<2 weeks) postoperative use seems to have no effect on nonunion rates.[89]

Because there are multiple confounding factors in the bone healing process, the actual role of these medications as a non-union risk factor is still not fully determined. Nevertheless, based on current evidence, pain management with NSAIDs should be limited to a short period and avoided in high-risk patients after an arthrodesis procedure.

Early vs. delayed weight-bearing

Non-weight-bearing has been traditionally recommended after foot and ankle arthrodesis as early weight-bearing and repetitive loading may increase micromotion at the fusion site, increasing the risk of nonunion. On the other hand, it has been demonstrated that bone healing is enhanced by micromovements of bone fragments, as bone remodeling and mass density are directly linked with direct load-bearing.[90] In addition, non–weight-bearing after lower extremity surgeries is associated with increased bone demineralization, muscle atrophy, and thromboembolic events.[91,92] For these reasons, historical non–weight-bearing protocols have been questioned

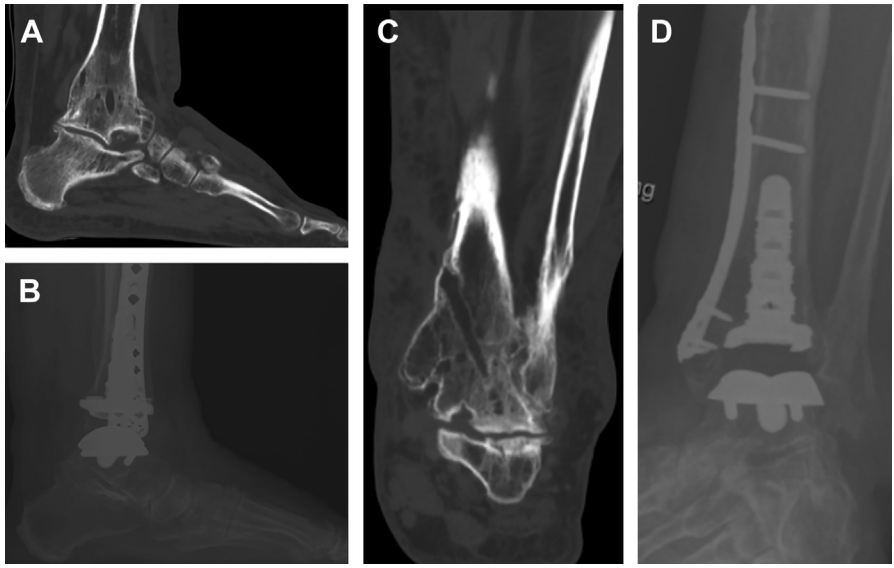

Fig. 3. Pre and postoperative imaging of a 59-year-old female patient presenting with symptomatic end-stage subtalar osteoarthritis 4 years after an ankle fusion for ankle osteoarthritis. For this patient, a take-down fusion and conversion to total ankle arthroplasty (Inbone, Wright medical) was performed. (*A*) Preoperative ankle CT sagittal view showing ankle fusion with subtalar osteoarthritis. (*B*) Postoperative weight-bearing lateral ankle radiograph. (*C*) Preoperative ankle CT coronal view showing ankle fusion with subtalar osteoarthritis. (*D*) Postoperative weight-bearing AP ankle radiograph 6 months after total ankle conversion with a medial malleolus plate reinforcement.

by an increasing number of studies being conducted in this field and recent randomized controlled trials comparing short-term outcomes of early versus delayed weight-bearing after ankle fracture fixation has shown that early weight-bearing is associated with better general health status, better function, earlier return to work, and sport without increased postoperative complications.[93–95] Although short-term outcomes are pretty promising, these studies did not investigate the influence of early weight-bearing in time-to-union and nonunion rates.

Early weight-bearing after arthrodesis surgery in the foot and ankle remains poorly researched without high-level evidence studies. A recent systematic review aiming to compare outcomes between early and delayed weight-bearing protocols after ankle arthrodesis was conducted by Potter and colleagues in 2019.[96] A total of 2426 ankles were included and divided into 4 groups according to the duration of the postoperative non–weight-bearing period: zero to 1 week (group A), 2 to 3 weeks (group B), 4 to 5 weeks (group C), or 6 weeks or more (group D). Mean union rates for groups A to D were 93.2%, 95.5%, 93.0%, and 93.0%, respectively. No clear trend was found between groups when comparing the time required to achieve union. Mean time to union was 10.4 weeks, 14.5 weeks, 12.4 weeks, and 14.4 weeks for groups A to D, respectively. The shortest time to union was found in the group with early weight-bearing supporting the hypothesis that early weight-bearing may promote faster union.

Regarding complication rates, the mean was 22.3%, 23.0%, 27.1%, and 28.7% for groups A to D, respectively. Although similar rates were generally found between groups, early weight-bearing was associated with a slightly lower incidence of

Box 1
Main clinic care points relevant to improve outcomes of foot and ankle arthrodesis procedures

- There is fair evidence supporting smoking and diabetes as a risk factor for nonunion following foot and ankle arthrodesis for preoperative factors. However, through smoking cessation and good diabetic control before the procedure, surgeons may improve outcomes. Moreover, screening and hypovitaminosis D treatment supplementation is recommended as the benefits seem to outweigh the risks.
- When technically feasible, less invasive techniques should be the first choice as patient outcomes and postoperative complications can be improved by using less invasive techniques, even in the presence of more severe deformities.
- Regarding joint preparation, surgeons should use twist drills rather than Kirschner wires, prefer drill bits of small diameter, decrease the time interval between passes, drilling at more perpendicular angles, apply regular irrigation and bone debris evacuation.
- There is insufficient evidence supporting the routine use of bone autograft or suitable alternatives to enhance fusion in primary ankle and hindfoot arthrodesis. Nevertheless, using bone grafts in more complex cases, high-risk patients, nonunion revision surgeries, and filling in bone voids at the arthrodesis site, should be considered to improve results and union rates, as the benefits of their use outweigh the risks.
- Although the iliac crest presents superior histologic features, there is no evidence supporting its use over other sites in terms of union rates for foot and ankle surgery. Because of its simplicity and low incidence of associated complications, proximal tibial bone harvesting can be a valid alternative.
- The use of orthobiologics, namely rhPDGF, in foot and ankle arthrodesis procedures has shown equivalent clinical outcomes and bone fusion performance compared with autologous bone graft. Moreover, the use of orthobiologics may obviate adverse events and morbidity related to autologous bone graft harvesting.
- Based on current evidence, pain management with NSAIDs should be limited to a short period (<2 weeks) and avoided in high-risk patients after an arthrodesis procedure.
- Although evidence is quite limited, early postoperative weight-bearing has shown to be beneficial, and it does not seem to increase postoperative complications. Therefore, it seems reasonable to start weight-bearing at an early phase when the arthrodesis is performed in loading joints with low shear forces.
- The incidence of surrounding joint osteoarthritis after foot and ankle fusion seems to increase progressively with time. Owing to its progression and high probability of being symptomatic, patients must be informed consequently, as they may require additional joint fusions, resulting in further loss of ankle/foot motion.
- In patients with symptomatic adjacent joint OA and unsatisfactory results after an ankle arthrodesis, conversion to total ankle arthroplasty (TAA) has become a potential option in managing these complex and challenging situations.

complications overall. The authors conclude that outcomes following ankle arthrodesis seem to be similar regardless of the duration of postoperative non–weight-bearing period, although, the existing literature is insufficient to make definitive conclusions.

Early weight-bearing versus delayed weight-bearing after midfoot joint arthrodesis has also been investigated. In a comparative, multicenter retrospective study involving 367 patients undergoing modified Lapidus arthrodesis with various fixation constructs, early weight-bearing did not increase the risk of nonunion than delayed weight-bearing.[97] These results support previous findings, suggesting that non–weight-bearing after tarsometatarsal arthrodesis may not be necessary.[98,99] Regarding arthrodesis of

the first metatarsophalangeal, similar conclusions can be made as evidence shows no differences in nonunion rates with early weight-bearing.[63,100]

Overall, the heterogenicity of the available studies and paucity of level I-II studies do not allow definite conclusions and correctly recommend early over delayed weight-bearing in foot and ankle arthrodesis. However, there is a general trend to abandon long, non–weight-bearing periods as current evidence favors early weight-bearing. Early postoperative weight-bearing has shown to be beneficial, and it does not seem to increase postoperative complications. It is possible that although early weight-bearing may enhance compression and coaptation in some joints (eg, ankle and subtalar), a similar protocol in other joints (eg, talonavicular) may increase shear under physiologic loads and compromise fusion site stability. Therefore, given patients' satisfaction with early weight-bearing and low compliance to long periods of non–weight-bearing, it seems reasonable to start weight-bearing at an early phase when the arthrodesis is performed in loading joints with low shear forces.

FUTURE OF SURROUNDING JOINTS

Osteoarthritis in surrounding joints is a major concern after foot and ankle arthrodesis procedures. It has been demonstrated that fusion of the ankle joint results in decreased eversion/inversion and internal/external rotation of the subtalar joint, which increases the mechanical stress of the subtalar joint during walking.[101] Consequently, this joint overloading can lead to progressive joint degeneration, which results in later osteoarthritis. It seems that the overloading of surrounding joints starts a few months following the arthrodesis procedure, as demonstrated in a recent study whereby postoperative SPECT-CT performed in patients undergoing ankle arthrodesis showed significantly increased activity in surrounding joints 6 months after surgery.[102] In addition, the incidence of surrounding joint osteoarthritis after ankle fusion seems to increase progressively with time. Coester and colleagues reported that secondary subtalar OA developed or progressed in 33% of patients at 9 years and 90% at 22 years after the primary ankle fusion.[103] Regarding talonavicular OA, 37% of patients developed or progressed OA at 9 years and 55% at 22 years after the ankle fusion. One could say that this degenerative process is bidirectional, as ankle OA seems to develop or progress in 55% of patients 15 years after a triple hindfoot arthrodesis.[104] Similar overloading mechanisms seem to explain the 30% midterm incidence of adjacent joint OA after isolated talonavicular arthrodesis.[105]

Overall, adjacent joint OA after arthrodesis procedures is frequently encountered in the foot and ankle. Owing to its progression and high probability of being symptomatic, patients must be informed consequently, as they may require additional joint fusions, resulting in further loss of ankle/foot motion. For instance, a young patient who undergoes ankle arthrodesis is likely to develop hindfoot osteoarthritis during the next 20 years, which may lead to additional hindfoot fusion surgery.[103,106,107] In this scenario, the risk of nonunion in the setting of previous ipsilateral ankle/hindfoot fusion is substantially higher as 40%.[108] Additionally, patients undergoing multiple foot and ankle fusions often have difficulties performing daily-basis activities such as climbing stairs, getting out of a chair, walking on uneven surfaces, and running.[109] Thus, patient satisfaction and disability level seem to decline with time.[103]

In patients with symptomatic adjacent joint OA and unsatisfactory results after an ankle arthrodesis, conversion to total ankle arthroplasty (TAA) has become a potential option in managing these complex and challenging situations. As improved instrumentation and more significant experience with TAA have facilitated this procedure, the number of reports involving patients undergoing take-down fusion and conversion

to TAA has been increasing during the last decade. A recent systematic review involving 172 patients submitted to this procedure with a mean follow-up of 62.8 months, reported substantial pain (mean preoperative VAS 7.8 vs 2.5 postoperatively) and ankle function improvement (mean preoperative AOFAS score 32 vs 72.4 postoperatively) after surgery.[110] However, long-term outcomes have not been reported. An example of pre and postoperative imaging of a take-down ankle fusion and conversion to TAA is illustrated in **Fig. 3**.

Take-down fusion is a complex procedure and should be performed by surgeons with extensive experience in total ankle arthroplasty procedures. Although the evidence is scarce, conversion of ankle arthrodesis to total ankle replacement seems to be a viable option to improve patient outcomes and prevent extensive hindfoot arthrodesis.

SUMMARY

Determining who is at risk of developing complications is essential to reduce the nonunion rates and improve patient outcomes after foot and ankle arthrodesis. However, a successful joint fusion depends on a complex relationship of several factors, such as patient-related factors, intraoperative, and postoperative factors. Therefore, research performed in this field often has inherent methodological limitations, which difficults to provide a definitive conclusion. Based on the current evidence, several conclusions can be drawn and are summarized in **Box 1**.

CLINICS CARE POINTS

- There is fair evidence supporting smoking and diabetes as a risk factor for non-union following foot and ankle arthrodesis for preoperative factors.
- Less invasive techniques should be the first choice as patient outcomes and postoperative complications can be improved.
- There is insufficient evidence supporting the routine use of bone autograft or suitable alternatives to enhance fusion in primary ankle and hindfoot arthrodesis.
- Although the iliac crest presents superior histological features, there is no evidence supporting its use over other sites in terms of union rates for foot and ankle surgery.
- The use of orthobiologics, namely rhPDGF, in foot and ankle arthrodesis procedures has shown equivalent clinical outcomes and bone fusion performance compared to autologous bone graft.
- Although evidence is quite limited, early postoperative weight-bearing has shown to be beneficial, and it does not seem to increase postoperative complications.
- Based on current evidence, pain management with NSAIDs should be limited to a short period (<2 weeks) and avoided in high-risk patients after an arthrodesis procedure.

DISCLOSURE

The authors have nothing to disclose.

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