TIBIAL FRACTURE NONUNION: Troubleshooting

Jordan Z. Tacktill, DPM
Donald R. Powell, DPM

According to the national center of health statistics, tibial fractures comprise approximately 500,000 cases per year (1). These common high velocity injuries are wrought with difficulty in management and maintenance. The AO Foundation (Arbeitsgemeinschaft für Osteosynthesefragen) has classified these fractures based on the fracture pattern and force of trauma. The classifications devised by the AO foundation have driven future treatment protocols through research directed at optimal healing for osseous injuries. Tibial fractures have been treated based on severity with casting, internal fixation, and external fixation. It is important to maintain certain parameters when treating these difficult cases, in order to have a successful outcome. El-Rosasy et al developed five management objectives for tibial nonunions including union of bone and soft tissue healing (2). The remaining objectives involve complete eradication of bone and soft tissue infection as well as eliminating any limb length discrepancy and maintaining limb function (2).

Many factors contribute to a delay in bone healing. Fractures without boney union at 6 months are classified as delayed union whereas fractures without union at 9 months following the initial injury are classified as nonunion fractures. The degree of velocity of the injury and post injury conditions such as open versus closed, soft tissue loss, bone loss, soft tissue interposition, compartment syndrome, infection and fracture motion are all influences that contribute to the predictive value of bone consolidation. When focusing on occurrence, the diaphyseal tibial fracture has a higher incidence of nonunion due to the avascular component of bone at this location. The location of the fracture with regard to the region of the bone is only one aspect that leads to further incidence of poor healing. The rate of nonunion increases with the compound nature due to the tremendous force of the fracture's pathophysiology and the extent of external contamination introduced to the internal environment (3). It is for these reasons that open fractures are over three times more likely to lead to a nonunion at the fracture site (4, 5). Systemic issues such as long-term steroid use, diabetes, peripheral vascular disease, hyperparathyroidism, Paget's disease, smoking, alcohol abuse, and poor nutritional status can also impede the healing status of a fracture.

Weber and Cech described a classification of nonunions based on the radiographic presentation (6). Atrophic or avascular nonunions present as tapered and sclerotic edges with the absence of callous formation at the fracture site. They are caused by many factors including infection, lack of reapproximation, diet, and medications. Hypertrophic, or hypervascular nonunions present as abundant callous formation at the fracture site. They are most commonly due to instability of fixation, however, there are some rare cases of malignancy that should be considered. Normotrophic nonunions share features of both atrophic and hypertrophic conditions (6). Other classifications such as Paley and Herzenberg base the treatment protocols of nonunions by their degree of motion at the fracture site (7). These treatment protocols correlate with the Weber and Cech classification using clinical mobility and noting the amount of stiffness of the fracture with manipulation (7).

A diagnostic work-up of the patient is essential to the success of the treatment. The clinician's investigation into the patient's social background, including nutritional status and compliance to prior treatments are crucial to ideal outcomes. Other negative contributions to wound healing from tobacco and alcohol intake have obvious repercussions that deter the healing process. Dinah concluded a nonunion rate of over three times in smokers than nonsmoking patients with similar fractures (8). Laboratory assessment includes white blood cell count (WBC), C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR) and alkaline phosphatase (Alk Phos), all of which aid the clinician's investigation to determine the etiology of the nonunion. Normal laboratory values should be expected but inquiry into the patient's complete health is a necessity.

Brinker et al found that endocrine disorders are a major contributing factor leading to tibial nonunions. The causative factors leading to tibial nonunions include vitamin D deficiency, calcium deficit, hypogonadism, thyroid disorders, and parathyroid disorders. Of the 37 patients involved in the study, the overwhelming majority had vitamin D deficiency (9).

The clinician may become suspicious of tibial nonunion following initial treatment of the fracture with or without prior surgical intervention. Continued pain, swelling, motion, and increased skin temperature are associated with nonunions and should be correlated with further workup. The fracture line may be obscured by callus formation or hardware placement on radiographic examination and further imaging including computed tomography scan or radioisotope bone scan will aid in the diagnosis of nonunions (10).

Pharmaceuticals designed for enhancement of bone quality may contribute to fracture care. Bisphosphonate therapy is most commonly employed for the treatment of osteoporosis in the elderly community. Patients with decreased bone mineral density have previously been advocated for bisphosphonate therapy in rehabilitation of osseous nonunions. Bisphosphonates decrease the osteoclastic activity while stimulating the production of osteoblasts deterring the natural bone turnover process. It is intuitive that the positive relationship between building bone for patients with osteoporosis would translate into increase union rates for patients with fractures. However, Solomon et al found that individuals are twice as likely to develop a nonunion if nitrogen-based bisphosphonates were initiated after analyzing 19,000 humeral fractures (10).

The management of tibial nonunions must be tailored to the genre of patient. In the elderly population, amputation should be avoided due to its connection with increased mortality rate. It has been reported that amputations in the elderly population are consistent with a 5-year survival rate as low as 25% (11, 12). While remaining a last resort, amputation may be the best option for those patients whose overall health condition does not permit them to undergo a lengthy treatment and recovery period (13).

Nonsurgical treatment should be considered first if normal anatomic alignment and fracture end proximity is maintained. Management consisting of Low-Intensity Pulsed Ultrasound (LIPUS) has been introduced and tested on tibial nonunion stress fractures. The LIPUS treatment stimulates an acute inflammatory reaction. The inflammatory reaction cultivates the differentiation of osteoblasts resulting in the generation of new bone and contributing to the union of bone ends (14). Studies have shown that LIPUS allowed the patients to resume sports activity and other activities of daily living faster than other conservative treatments (15, 16, 17).

Adjunctive therapy, such as hyperbaric oxygen, has been significant in the treatment of atrophic tibial nonunions. Kürklü et al studied the effects of hyperbaric oxygen therapy (HBOT) on mice with a 5 mm bone block of tibia surgically excised and a circular ring external fixator applied to the lower extremity. Ten of the mice underwent HBOT and ten mice did not. All were evaluated radiograpically at 30 and 90 days. The mice were also assessed with scintographic studies including Technetium-99m. Little difference was seen at the 30-day interval but full boney union of the HBOT group was seen at 90-days. The progression to boney union in 6 of the 9 mice undergoing HBOT treatment is a significant finding where no boney union was seen in the control group. Osteoblastic activity was also increased in the HBOT group at both the 30- and 90-day evaluation via technetium-99m. It should be noted that in this experiment, none of the nonunion sites were opened, cleaned, or compressed at any time for the duration of the study (18).

Minimally invasive approaches have been reserved for atrophic nonunions. Procedures preformed by the acquisition of progenitor cells by way of bone marrow aspirate are concentrated into a graft and injected through a small stab incision at the nonunion site (19). The fracture site is then compressed via an external fixation device. This procedure is only indicated for a nonunion free of infection, but has shown promising results (19).

Infected nonunion rates are directly correlated with the amount of soft tissue coverage lost at the time of the injury. Infections are treated most commonly with intravenous antibiotics and lavage at the time of injury. The extent of the infectious process will determine the necessity and extent of staged procedures to follow. Eradication of the infection and prevention of bacterial colonization is the primary goal of the surgeon. Serial debridements, antibiotic impregnated beads and concomitant intravenous antibiotics, assist in the suppression and elimination of bacterial burden following a compound fracture.

While most surgeons have relied on a multi-stage approach for infected nonunions of the tibia including stability, suppression of infection, and finally resection of the affected portion of tibia with final definitive fixation. A single-stage, surgical approach for the treatment of infected nonunion of the distal tibia has been illustrated by Wu (20). The surgical technique entails correction of any malalignment with resection of the nonunion site to healthy bleeding bone both proximally and distally while a second incision is placed medial to the patellar tendon. A guide wire is placed into the medullary canal of the tibia spanning the section of resected nonunion following removal of cancellous bone graft from the proximal tibia. Vancomycin and Gentamycin impregnated cement is then placed within the medullary canal of the tibia. The bone graft is then placed within the nonunion site previously obtained, which has been mixed with the antibiotic powders. A static external fixation device is then applied to the lower extremity and maintained until boney union. Wu noted a 100% healing rate of all 22 infected tibial nonunions within 6 months. No further pain or recurrence was observed during the 2-year follow-up period (20).

Previous surgical intervention may help dictate further treatment. In the instance of tibial fractures treated with antigrade intramedullary nails, a technique of exchange nailing has been adapted to the correction of tibial nonunions. The technique of exchange nailing requires reaming of the medullary canal for insertion of a larger boar intramedullary nail than previously placed. The advocacy of exchange nailing was studied by Court-Brown et al who found that 87.9% of 33 patients united the nonunion site following one nail exchange and the remaining patients united after the second nail exchange (21).

Bone transport osteosynthesis has become popularized by the Ilizarov treatment for tibial nonunion with bone loss. Bone transport procedure protocol accounts for complete resection of the nonunion site with a proximal corticotomy at the metaphyseal-diaphyseal junction. A multi-level circular external fixation is applied to the lower extremity to allow bifocal osteosynthesis compression at the resection site with distraction at the corticotomy site until the limb length discrepancy is eliminated. An additional complication encountered in distraction osteosynthesis is the lack of radiographic confirmation of growth. Callus formation within the proximal corticotomy site must be appreciated to ensure osteogenesis is occurring.

The accordion technique is a method of manipulating the corticotomy site and stimulating bone growth. Manipulation implemented by consecutive intervals of compression and distraction at the corticotomy site provokes the formation of and osseous foundation for callous distraction. Execution of the accordion method is accomplished with the aid of an external fixation device until radiographic evidence of bone formation is observed.

The Ilizarov bone transport is the gold standard for treatment of segmental bone defects (22). Resection of boney nonunion results in a deficit of bone at the fracture site. Paly et al combined limb lengthening with bone resection and accounted for union rates at 100% (23). Similar findings were conveyed by Sala et al, who concluded that infectious processes and malalignment are remedied with radical bone resection and bone transport (22). Application of the Taylor Spatial Frame (Smith and Nephew) device, contributed to the 100% union rate of the nonunion site with subsequent bone resection and bone transport. (22).

External fixation devices allow for versatility of adjunctive treatment modalities while maintaining stability. The Ilizarov method for treatment of tibial nonunion has proven itself in all aspects including stability, ease of use, and ease of manipulation. Brinker concluded that within the elderly population, the Ilizarov external fixation device had a positive effect on the overall quality of life (13). It was also noted within the same study that the average length of time that the external fixator remained intact on the lower extremity was considerably longer in patients with infected tibial nonunions (426 days) when compared to the uninfected tibial nonunions (277 days) (13).

As stated, open fractures more often result in a nonunion scenario. Initial treatment of these injuries includes the application of an external fixation device to avoid hardware placement in a potentially infected fracture. If a tibial nonunion results even after an external device is placed, attempts to stimulate osseous union at the fracture site can be preformed without further surgical treatment. Dynamization is a method of converting the rigid external fixation frame to a dynamic compression device.

An additional study produced by El-Rosasy described acute shortening and lengthening performed on 21 patients with bone loss of three to eleven centimeters (2). The surgical planning must include resection of the boney defect but also contraction and expansion of the soft tissues surrounding the surgical site. A z-plasty of the soft tissue structures adjacent to the nonunion adequately accommodates the manipulation of the bone greater than 5 cm. If acute shortening is a greater distance than the soft tissue will allow before necrosis, then a period of gradual shortening of 2 mm to 3 mm per day is preformed to rectify the diminished length of the boney deficit. Once boney apposition is accomplished, a corticotomy at the metaphyseal junction furthest from the nonunion is preformed. The corticotomy permits the initiation of the callous distraction technique to the desired limb length. Distraction is initiated 7 days following the operation at a rate of 1 mm per day until equivalent limb length is attained. Achieving the surgical and functional goals of deformity correction with substantial bone loss are attained with this procedure (2).

While autogenous cancellous bone graft is the gold standard for filling osseous defects, finding a source within the body to fill large deficits has been difficult. Recently, Synthes has introduced the Reamer-Irrigator-Aspirator (RIA), which harvests cancellous bone graft from the femur gathering 20-80 cc with a single use. Bone graft has been combined with rhBMP-2 (Infuse, Medtronic) for the purpose of filling boney voids following wide resection of tibial nonunion 15-20 cm in length. The RIA procedure also compliments the bi-Masquelet well, in which the infected nonunion is resected and filled with an antibiotic impregnated polymethylmethacrylate spacer for 6 weeks. Following the latency period the antibiotic spacer is removed and the RIA bone graft with Infuse is then placed in the spacer's position. Stability is preserved throughout this period with an ante-grade tibial intramedullary nail. Pratik et al found the mean time to union at 27.6 weeks using this method (25).

Central bone grafting for tibial nonunions has traditionally been reserved for more complex defects including bone loss, recalcitrant infection, or both. Bone grafting is performed following the resolution of infection confirmed by elimination of sinus tract, constitutional signs of infection, negative C-reactive protein, normal erythrocyte sedimentation rate, and negative cultures. Central bone grafting is harvested from the iliac crest and transferred to the anterior lateral leg incision where the tibia is decorticated through a periosteal flap anterior to the interosseous membrane. The nonunion remains undisturbed while the medial cortex of the fibula is decorticated and the iliac bone graft is placed anterior to the interosseous membrane between the tibia and fibula. The lower extremity nonunion site is stabilized by external fixation. This procedure has been shown to achieve boney union of defects up to 5 cm in length (26).

Yajina et al proposed a treatment modality for infected tibial nonunion with vascularized fibular bone graft. The treatment suggests that the nonunions undergo serial lavage to clear infectious debris followed by implantation of antibiotic impregnated cement beads (27). The vascularized fibular bone graft was applied subsequently to diminishing inflammatory response and fixated utilizing an external fixator. While there was a recurrence of infection in 6 of the 18 patients requiring lesional debridement, union was visualized within 6 months. Only one failed union was reported following this technique, which required excision of the vascularized fibular graft. Elimination of the nonunion and replacement of the denuded bone site with a healthy vitalized graft promotes and supports an environment for healing (27). Management of infection while replacing the denuded bone site with a healthy vitalized graft is an innovation in the opportunity to treat infected nonunion with minimal failure (27).

The Papinaeu technique has been described as a single or multi-staged procedure for the treatment of a nonunion due to osteomyelitis. The procedure requires the resection of the infected portions of bone with the conservation of the posterior cortex. The area of boney resections is then replaced with corticocancellous bone chips as foundation for ossification at the previous nonunion site (28).

Research has shown that autogenous bone graft has all properties of osteoconduction, osteoinduction, and osteogenesis. Date et al proposed a procedure, which introduces management of gap nonunion of tibia by tibialization of the ipsilateral vascular fibula. Gap nonunions as described have particular difficulty with achieving a functional limb. Date's technique entails grafting a portion of the fibula 2 inches longer than the gap required and fusing it to the posterior aspect of the tibia. The graft retains its soft tissue envelop and is therefore transferred with an axial pedicle. Date et al concluded that 16 of 17 patients completed treatment with complete union and a functional full weightbearing limb (29).

CONCLUSION

Treatment of tibial nonunion is a multifaceted process, which entails optimization of the patient both medically and surgically. Rectification of the underlying etiology of the nonunion must be the objective of the treating physician. Each type of nonunion, whether infected, atrophic, normotrophic, or hypertrophic are managed based on their physiologic influence. The defect may require metabolic, antibiotic, or operative correction. New technology including bone grafting products as well as fixation devices both internal and external fixation are becoming available to combat this pathology by minimizing physiologic insult. As these injuries proceed to nonunion state, the patient is presented with all options consisting of conservative and surgical methods for reconstruction as well as end-stage amputation. The surgeon must be aware of all options to convert the nonunion site to a union site by increasing the level of stability following failure of the initial hardware construct. Tibial nonunions are inherently challenging situations for both the patient and surgeon. Attaining the 5 goals of treatment as set forth by El-Rosasy et al requires a keen intellect that incorporates all assets medically and surgically.

REFERENCES

1. Poduval M, Kale S. Diaphyseal tibial fractures. URL: http://emedicine.medscape.com/article/1248857-overview.
2. El-Rosasy MA. Acute shortening and re-lengthening in the management of bone and soft-tissue loss in complicated fractures of the tibia. J Bone Joint Surg Br 2007;89:80-8.
3. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty- five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am 1976;58:453-8.
4. Audige L, Griffin D, Bhandari M, Kellam J, Ruedi TP. Path analysis of factors for delayed healing and nonunion in 416 operatively treated tibial shaft fractures. Clin Orthop Relat Res 2005;438:221-32.
5. Will RE, Fleming ME, Lafferty PM, Fletcher JW, Cole PA. Low complication rate associated with raising mature flap for tibial nonunion reconstruction. J Trauma 2011;71:1709-14.
6. Weber BG, Cech O. Pseudoarthrosis: Pathology, Biomechanics, Therapy, Results. Berne, Switzerland: Hans Huber Medical Publisher;1976.
7. Paley D, Patel M, Herzenberg JE. Treatment of complex hypertrophic nonunions by closed ilizarov distraction. J Bone Joint Surg Br 2005;87 Supp III:311.
8. Dinah AF, Vickers RH. Smoking increases failure rate of operation for established non-union of the scaphoid bone. Int Orthop 2007;31:503-5.

9. Brinker MR, O'Connor DP, Monla Y, Earthman TP. Metabolic and endocrine abnormalities in patients with nonunions. J Orthop Trauma 2007;21:557-70.
10. Solomon DH, Hochberg MC, Mogun H, Schneeweiss S. The relation between bisphosphonate use and non-union of fractures of the humerus in older adults. Osteoporos Int 2009;20:895-901.
11. Frykberg RG, Arora S, Pomposelli FB Jr. Functional outcomes in the elderly following lower extremity amputation. J Foot Ankle Surg 1998;37:181-5.
12. Pell J, Stonebridge P. Association between age and survival following major amputation. The Scottish Vascular Audit Group. Eur J Vasc Endovasc Surg 1999;17:166-9.
13. Brinker MR, O'Connor D.P Outcomes of tibial nonunion in older adults following treatment using the ilizarov method. J Orthop Trauma 2007;21:634-42.
14. Suzuki A, Takayama T, Suzuki N, Sato M, Fukuda T, Ito K. Daily low-intensity pulsed ultrasound-mediated osteogenic differentiation in rat osteoblasts. Acta Biochim Biophys Sin 2009;42:108-15.
15. Batt ME, Kemp S, Kerslake R. Delayed union stress fracture of the anterior tibia: conservative management. Br J Sports Med 2001;35:74-7.
16. Retting AC, Shelbourne KD, McCaroll JR, Bisesi M, Watts J. The natural history and treatment of delayed union stress fractures of the anterior cortex of the tibia. Am J Sports Med 1988;16:250-5.
17. Orava S, Vaananen K, Hulkko A, Karpakka J, Takala T, Kallinen M. Diagnosis and treatment of stress fractures located at the mid-tibial shaft in athletes. Int J Sports Med 1991;12:419-22.
18. Kurklu M, Yurttas Y, Kose O, Demiralp B, Yuksel HY, Komurcu M. Adjunctive hyperbaric oxygen therapy in the treatment of atrophic tibial nonunion with Ilizarov external fixator: a radiographic and scintigraphic study in rabbits. Acta Orthop Traumatol Turc 2012;46:126-31.
19. Hernigou P, Mathieu G, Poignard A, Manicom O, Beaujean F, Rouard H. Percutaneous autologous bone-marrow grafting for nonunions. Surgical technique. J Bone Joint Surg Am 2006;88 Suppl 1:322-7.
20. Wu CC. Single-stage surgical treatment of infected nonunion of the distal tibia. J Orthop Trauma 2011;25:156-61.
21. Court-Brown CM, Keating JF, Christie J, et al. Exchange intramedullary nailing. J Bone Joint Surg BR 1995;77:407-11.
22. Sala F, Thabet AM, Castelli F, Miller AN, Capitani D, Lovisetti G, et al. Bone transport for postinfectious segmental tibial bone defects with a combined Ilizarov/Taylor spatial frame technique. J Orthop Trauma 2011;25:162-8.
23. Paley D, Maar DC. Ilizarov bone transport method for tibial defects. J Orthop Trauma 2000;14:76-85.
24. Wu CC, Shih CH. Effective dynamisation of a static interlocking nailing on fracture healing. Can J Surg 1993;36:302-6.
25. Desai PP, Bell AJ, Suk M. Treatment of recalcitrant, multiply operated tibial nonunions with the RIA graft and rh-BMP2 using intramedullary nails. Injury 2010;41 2:S69-71.
26. Ryzewicz M, Morgan SJ, Linford E, Thwing JI, de Resende GV, Smith WR. Central bone grafting for nonunion of fractures of the tibia: a retrospective series. J Bone Joint Surg Br 2009;91:522-9.
27. Yajima H, Kobata Y, Shigematsu K, Kawamura K, Kawate K, Tamai S, et al. Vascularized fibular grafting in the treatment of methicillin-resistant Staphylococcus aureus osteomyelitis and infected nonunion. J Reconstr Microsurg 2004;20:13-20.
28. Polyzois VD, Galanakos SP, Tsiampa VA, Papakostas ID, Kouris NK, Avram AM, et al. The use of Papineau technique for the treatment of diabetic and non-diabetic lower extremity pseudoarthrosis and chronic osteomyelitis. Diabetic Foot Ankle 2011;2:5920.
29. AS Date, SB Solanki, NP Badhe, PD Sonsale, HG Pandit. Management of gap non-union of tibia by tibialisation of ipsilateral vascular fibula. J Postgrad Med 1996;42:109-11.