**Introduction**

The treatment of chronic infected nonunions is very difficult, and no consensus has been reached as yet. To manage this complex, three basic problems need to be settled, i.e. soft tissue damage, nonunion and chronic osteomyelitis, each alone is difficult, not to mention that the three challenging issues need to be resolved simultaneously, as they are closely inter-related.

Currently there are several manage strategies. The first one is that all pathologies should be treated in the same session (one-stage). The second one is two-stage approaches, which are preferred for nonunions with diffuse (type-IV) chronic osteomyelitis. In two-stage approaches, the infection is treated first, and then the nonunion. In the first phase, the key point is to manage the dead area after debridement. Many antibiotic-induced materials have been reported to be used to manage the dead area, but there is no consensus until now. The second phase treatment focuses on the nonunion. There are many techniques available, especially free vascularized bone and soft tissue flaps or nonvascular bone grafts. Each technique has its own advantages and disadvantages.

The aim of this study was to present the midterm results of atrophic tibial nonunion cases with diffuse (type-IV) chronic osteomyelitis managed using two-stage treatment with the fibular sliding technique.

**Purpose:** To assess the effectiveness of two-stage treatment with the fibular sliding technique in chronic infected nonunion of the tibia.

**Methods:** The study included patients who were diagnosed with long-term chronic infected tibial nonunion following trauma and treated with the two-stage technique between January 2010 and November 2017. Patients with (1) intra-articular fractures of the distal third of the tibia and fibula, (2) pathological fracture resulting in bone loss or (3) neurological and vascular pathologies of the limbs were excluded. The operation consisted of two stages and the main goal in the first stage was to control the infection and in the second stage to control the healing of the bone. Functional & radiographic results and complications were evaluated according to Paley’s criteria.

**Results:** The patients comprised 14 males and 5 females with a mean age of 37.4 years (range, 21–52 years). Patients were followed up for an average of 27 months (range, 15–38 months). The microorganisms produced from these patients were *Staphylococcus aureus* in 13 patients, *Pseudomonas aeruginosa* in 4 patients and no bacteria in 2 patients. After the first stage operation, superficial skin necrosis developed in 1 patient. In another patient, there was a persistent infection, although union was achieved. For the entire patient group, union was observed at the end of 7.44 months (range, 7–11 months). Based on Paley’s criteria, there were 16 (84.2%) patients with excellent scores, 2 (10.5%) good scores and 1 (5.3%) fair scores radiologically; while regarding the tibial function, 15 (78.9%) patients had excellent scores, 3 (15.8%) good scores, and 1 (5.3%) fair scores. No patients had poor radiological or functional score.

**Conclusion:** Two-stage treatment can be considered as an alternative for fractures in regions that are susceptible to many and persistent complications, such as the tibia. This technique has the advantages of short operation time, minimal blood loss, no excessive tissue damage and not very technique-demanding (a short learning curve with no requirement for an experienced team).
Methods

The study was approved by the Local Ethics Committee of Adana Health Practice and Research Center Hospital and the procedures adhered to the tenets of the Declaration of Helsinki. Written informed consent has been obtained from all subjects.

Patients

The study included patients with long-term chronic infected tibial nonunion who were treated with two-stage technique in the department of orthopaedics and traumatology or the department of plastic and reconstructive surgery between January 2010 and November 2017. All the patients had long-term and chronic infected nonunion secondary to trauma. Patients with intra-articular fractures of the distal third of the tibia and fibula, pathological fracture resulting in bone loss, or neurological/vascular pathologies of the limbs were excluded from the study.

Patients were operated on under spinal anesthesia. The operation comprised two phases: to control the infection in the first stage and to control healing of the bone in the second stage.

First stage operation

At this stage, a custom-made vancomycin-loaded bone cement was applied after thorough necrotic tissues debridement and irrigation.

First the sequestrum and other necrotic tissues were cleaned. Then the dead bone regions were gradually removed until bleeding bone was reached. For all the patients, posterior cortex continuity was maintained. In addition, an appropriate extent of the lateral cortex was resected for the preoperative preparation of the second phase. This was necessary for the fibula to slide.

After these procedures, the area was washed using saline solution with rifampicin at normal pressure. The medullary region of both fragments was opened and reamed. The irrigation process was repeated twice. Thereafter, the custom-made bone cement with vancomycin suitable for each defect was prepared. These segments were placed in the defect area. Finally, an external fixator was applied.

The patients were followed up for three weeks via physical exam, imaging exam and laboratory tests every week.

Second stage operation

This phase consisted of three processes. First, the foreign matter placed in the wound area was removed and debridement was applied again. Then the fibular sliding operation was performed. Finally, fixation of the fracture was done. The three procedures were performed in the same session.

Fibular sliding operation

The surgical plan was made before operation. A single incision was made on the lateral region of the tibia (Fig. 1A). After the infected area was re-debrided and culture samples have been taken, irrigation was applied (Fig. 1B). The length of the fibula that needs to be transferred was determined according to the cicatrized and infected region, varying between 5 and 10 cm. The muscles on the lateral and posterolateral fibula were released (Fig. 1C). Soft tissue or muscles in other parts of the fibula were left intact. Thus an intermediate corridor was created by moving the tibialis anterior, extensor hallucis longus and extensor digitorum longus muscles to the tibial defect zone; and the fibula, which was osteotomized at an appropriate length from proximal and distal, was slid and fixed to the tibia with cortical screws (Fig. 1D). Fluoroscopy was adopted to check all the procedures and then locking plate fixation was done. (Fig. 2).

Clinical and radiological assessment

At the time of final follow-up, the functional and radiographic results were evaluated according to Paley et al.'s criteria (Table 1). Using the Paley classification, complications were classified as minor (complications that do not require surgical intervention), major without sequelae (complications that require surgery but do not impact the outcome) and major with sequelae (complications that require surgery and impact the outcome).

Results

General data of the patients

Altogether 19 patients were included, comprised of 14 males and 5 females with a mean age of 37.4 years (range, 21–52 years). Patients were followed up for a mean of (27.00 ± 5.09) months (range, 16–38 months). Tibia fractures occurred in 9 patients due to

Fig. 1. The surgery technique of sliding fibular flap. (A) Location of the incisions for fibular sliding in the second stage. (B) Bone cement was removed from the area with nonunion and infection, and debridement irrigation was applied again. (C) The fibula to be slid was osteotomized in the distal and proximal. Lateral and posterolateral muscles were freed. (D) Tibialis anterior and extensor hallucis longus and extensor digitorum longus muscles, the fibula from the posterior slid to the tibial region and fixed with two screws.
traffic accidents, in 6 patients due to a fall from height and in 4 patients due to gunshot injury. All were open fractures and two patients had multiple fractures. All the fractures were localized in the middle third of the tibial diaphysis. These patients had undergone an average of 9 (range, 4–18) operations in various centers before presenting at our clinic.

The time from trauma to the first surgical procedure in our clinic was approximately 22 months (range, 12–45 months). The average duration of the operation was 122 min (range, 90–170 min), and the average blood loss was 400 mL (range, 330–540 mL). The microorganisms produced from these patients were Staphylococcus aureus in 13 patients, Pseudomonas aeruginosa in 4 patients and none in 2 patients.

Clinical and radiological results

After the first stage operation, superficial skin necrosis developed in one patient. At 6 weeks, all patients except one had normal levels of erythrocyte sedimentation rate, C-reactive protein and leukocytes. Antibiotic treatment continued for 4 weeks; in one patient the infection continued but union was achieved. In all patients, union was observed at a mean of 7.44 months (range, 7–11 months).

Only one of the current patients experienced delayed union, as the infection could not be controlled, so autogenous spongiosis graft with a plate exchange was applied.

Another condition observed in this technique is plantar flexion deformity on the first toe. This is because the flexor hallucis muscle is not released from the fibula posterior due to sliding the fibula to the defective tibial region, and therefore this muscle is stretched. However, all cases of this deformity were managed successfully with passive exercise and not any additional surgical interventions.

The radiological and clinical results according to Paley bone scoring system are shown in Fig. 3. Most of the patients obtained good-excellent radiologic (94.7%) and functional (94.7%) outcomes. And there is no poor or failure results.

Complications

There was one minor complication such as flexion deformity of the first toe, one major complication without sequelae as delayed union and no major complications with sequelae.

Discussion

All the 19 cases in this series had atrophic nonunion in the tibia diaphysis region with diffuse (type-IV) chronic osteomyelitis according to the Cierny-Mader classification. This complex, in particular chronic osteomyelitis and nonunion pathologies, is very difficult to treat, even individually. Moreover, each pathology is closely inter-related and thus the treatment needs to be adjusted with the progress of others. Many management strategies are now available. The pathological characteristics are important in selecting suitable treatment methods. Moreover, the type and localization of nonunion, the duration of infection (acute, chronic) and the type of osteomyelitis are important guiding parameters.

Currently, there are two different approaches in the treatment of patients with diffuse (type-IV) chronic osteomyelitis and tibial nonunion. The first is a radical approach, and the second is a...
two-phase approach, which we can call conservative surgery. In the radical approach, the disease is treated more like a malignant bone tumour and the infected area is resected. The intercalary defect is treated with techniques such as callus distraction or free vascularized bone flap, which are quite complex and have many complications.10,11

The callus distraction technique provides indications for the treatment of difficult and complex musculoskeletal system diseases. It is used in the treatment of internal defects of bone tissue depending on the various causes.10,12 However, this technique has many disadvantages, such as time-consuming, requirement for frequent controls, high risk of wire bottom or deep infection, neurovascular damage, non-compliance with the device used and psychological disorders.12,13

Another technique used to repair the defects is vascularized autogenous grafts. Vascularized fibula can be combined with allograft or autogenous grafts as well as used alone. Vascular fibula alone contains significant complications. The main advantages of such a reconstruction graft are having an independent vascular structure, healing to the original bone in a short time and the early advent of oppositional growth. However, in spite of all these features, it takes a long time for the fibular graft to thicken and reach a volume that is able to carry a full load. During this time, there is a high risk of micro-fractures turning into macro fractures. Therefore, single vascularized fibula flaps are generally preferred in the reconstruction of the upper extremity. Even in this region, in the upper extremity zone, which is not weight-bearing, the fracture rate varies between 30% and 50%.10,14

As for the two-stage surgical approach, which we call conservative surgery, is popular in the treatment of advanced nonunions with chronic osteomyelitis. Local antibiotics have been proven to be effective in prophylaxis and osteomyelitis treatment. However, high concentrations of an antibiotic release can cause cytotoxicity, which may inhibit osteogenesis and have negative effects on fracture healing.15,16

Various materials have been used in the management of infected dead areas. Currently, antibiotic-induced bone polymethylmethacrylate (PMMA) is most popular. Antibiotic-impregnated bone cement, which has been examined in detail in pharmacokinetic analysis, is used in the management of the case series. The materials have very important advantages. In general, approximately 5%–7% of the total amount of antibiotics is released quickly within the first 24 h. Then there is a biphasic release model characterized by a constant gradual decline in antibiotic release for weeks and months. However, this form of oscillation may not be effective in combating infection and can also cause microbial resistance and biofilm layer formation.17–19 It has been claimed that PMMA causes disturbances in the response and function of the immune system.20 There are also concerns about the long-term implantation and there is no consensus on the duration that it should be retained in the dead area. Most authors have suggested that beads be removed gradually 4–6 weeks after implantation.21

In our study, these chains were removed at the end of three week with the transition to the second phase. The main reason for using these chains for a short period of time was to maximize the antibacterial effect and meanwhile minimize the risk of microorganisms developing a biofilm layer and other complications. In addition, in these patients with prolonged nonunion, it was desirable to start the bone healing process as soon as possible.

The sliding fibular flap technique to reconstruct the tibial gap defect was first described in 1884. Although various modifications have been made over the years, the principle remained the same. In previous similar studies,17 Tuli12 evaluated 21 patients with tibia gap defect due to either infection or trauma, union was obtained in all the patients. In 8 of 11 patients with tibia gap defects ranging from 4 to 22 cm due to tumour resection, trauma or chronic osteomyelitis, Kassab et al.54 also reported success. Unlike these studies, a more homogeneous group was formed in current study, and similarly successful results were obtained. The infection could not be controlled in only one patient, who had type c according to the Cierny-Mader classification22 and severe local and systemic disease. However, recent clinical and experimental studies have shown that none of the materials used temporarily in the management of infected bone defects are optimal. In this study, diligent efforts were made to use the materials available in the optimum time frame. The results were satisfactory, although the small number of cases prevents a definitive result.

In his study, the average operation time was 122 min. There was no need for anastomosis surgery in this technique, and the fibula was slid to the tibial defect zone without causing damage to the soft tissues. This can be considered to have reduced the time and minimized the risk of vascular obstruction problems. In addition, since another important advantage is that the fibula is slid with a majority of the vascular and soft tissue of the fibula, an excellent biological environment can be considered to be provided in the dead area.

A limitation of this study was that because of the small number of cases it was impossible to make comparisons with other techniques on a solid basis. Another disadvantage is that this technique has localized indications, i.e. just in the tibial region. However, the data obtained from this small case series are important in terms of guiding a broader range of studies to be conducted in the future. It can be considered important to create an alternative for regions where many complications may develop and be persistent, such as the tibia. Other advantages of the technique are the short operation time, less excessive tissue damage and blood loss, no need for an experienced team and quick technique learning curve.
Funding

Nil.

Ethical Statement

The study was approved by the Local Ethics Committee of Adana Health Practice and Research Center Hospital and the procedures adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all subjects and the individual data are kept confidential.

Declaration of Competing Interest

The authors declare no conflicts of interest.

References

1. Deng Z, Cai L, Jin W, et al. One-stage reconstruction with open bone grafting and vacuum-assisted closure for infected tibial nonunion. Arch Med Sci. 2014;10:767–772. https://doi.org/10.5114/ams.2013.34411.
2. Alemdar C, Ashboy I, Atic R, et al. Management of infectious fractures with “Non-Contact Plate”(NCP) method. Acta Orthop Belg. 2015;81:523–529.
3. Yıldırım A, Kapukaya A, Atıcı R, et al. The use of an “internal fixator technique” to stabilize pathologic fractures developing secondary to osteomyelitis. J Pediatr Orthop. 2017;37:222–226. https://doi.org/10.1097/BPO.0000000000000619.
4. Chen CE, Ko JY, Pan CC. Results of vancomycin-impregnated cancellous bone grafting for infected tibial nonunion. Arch Orthop Trauma Surg. 2005;125:369–375. https://doi.org/10.1007/s00402-005-0794-6.
5. Oh CW, Song HR, Roh JY, et al. Bone transport over an intramedullary nailing for reconstruction of long bone defects in tibia. Arch Orthop Trauma Surg. 2008;128:801–808. https://doi.org/10.1007/s00402-007-0691-8.
6. Oh CW, Song HR, Kim JW, et al. Limb lengthening with a submuscular locking plate. J Bone Joint Surg Br. 2009;91:1394–1399. https://doi.org/10.1302/0301-620X.91B10.22325.
7. Paley D, Maer DC. Ilizarov bone transport treatment for tibial defects. J Orthop Trauma. 2000;14:76–85. https://doi.org/10.1097/01.blo.000005131-200020000-00002.
8. Eralp L, Kocaoglu M, Polat G, et al. A comparison of external fixation alone or combined with intramedullary nailing in the treatment of segmental tibial defects. Acta Orthop Belg. 2012;78:652–656.
9. Chan YS, Ueng SW, Wang CJ, et al. Management of small infected tibial defects with antibiotic-impregnated autogenic cancellous bone grafting. J Trauma. 1998;45:758–764. https://doi.org/10.1097/00005373-199810000-00023.
10. Bodde EW, De Visser E, Duyiens JE, et al. Donor-site morbidity after free vascularized autogenous fibular transfer: subjective and quantitative analyses. Plast Reconstr Surg. 2003;111:2237–2242. https://doi.org/10.1097/01.PRS.0000060086.95242.F1.
11. Halim AS, Chai SC, Ismail WF, et al. Long-term outcome of free fibula osteocutaneous flap and massive allograft in the reconstruction of long bone defect. J Plast Reconstr Aesthetic Surg. 2015;68:1755–1762. https://doi.org/10.1016/j.bjps.2015.08.013.
12. Blum A, BongioVanni J, Morgan S, et al. Complications associated with distraction osteogenesis for infected nonunion of the femoral shaft in the presence of a bone defect: a retrospective series. J Bone Joint Surg Br. 2010;92:565–570. https://doi.org/10.1302/0301-620X.92B4.23475.
13. Kapukaya A, Subasi M, Arslan H, et al. Technique and complications of callus distraction in the treatment of bone tumors. Arch Orthop Trauma Surg. 2006;126:157–163. https://doi.org/10.1007/s00402-006-0123-8.
14. Leckenby JL, Grobbleaar AO, Aston W. The use of a free vascularised fibula to reconstruct the radius following the resection of an osteosarcoma in a paediatric patient. J Plast Reconstr Aesthetic Surg. 2013;66:427–429. https://doi.org/10.1016/j.bjps.2012.08.007.
15. Chang Y, Goldberg VM, Caplan AI. Toxic effects of gentamicin on marrow-derived human mesenchymal stem cells. Clin Orthop Relat Res. 2006;452:242–249. https://doi.org/10.1097/01.blo.0000229324.75911.c7.
16. Holton PD, Pavkovic SA, Bravos PD, et al. Inhibitory effects of the quinolone antibiotics trovafloxacin, ciprofloxacin, and levofloxacin on osteoblastic cells in vitro. J Orthop Res. 2000;18:721–727. https://doi.org/10.1002/jort.1100180507.
17. Van de Belt H, Neut D, Schenk W, et al. Staphylococcus aureus biofilm formation on different gentamicin-loaded polymethylmethacrylate bone cements. Biomaterials. 2001;22:1607–1611. https://doi.org/10.1016/S0142-9612(00)00313-6.
18. Hendriks JC, Neut D, van Horn JR, et al. Bacterial survival in the interfacial gap in gentamicin-loaded acrylic bone cements. J Bone Joint Surg Br. 2005;87:272–276. https://doi.org/10.1302/0301-620X.87B2.14781.
19. Corona PS, Espinal J, Rodriguez-Pardo D, et al. Antibiotic susceptibility in gram-positive chronic joint arthroplasty infections: increased aminoglycoside resistance rate in patients with prior aminoglycoside-impregnated cement spacer use. J Arthroplasty. 2014;29:1617–1621. https://doi.org/10.1016/j.arth.2014.03.028.
20. Granchi D, Capietti G, Savarino L, et al. Effects of bone cement extracts on the cell-mediated immune response. Biomaterials. 2002;23:1033–1041. https://doi.org/10.1016/S0142-9612(01)00215-0.
21. Kendall RW, Duncan OP, Smith JA, et al. Persistence of bacteria on antibiotic-loaded acrylic deports. A reason for caution. Clin Orthop Relat Res. 1996;329:273–280. https://doi.org/10.1097/00003086-199608000-00034.
22. Nwokike OC, Esezobor EE, Olomu DO, et al. Tibialization of fibula to reconstruct the radius following the resection of an osteosarcoma in a paediatric patient. Arch Orthop Trauma Surg. 2015;135:2265–2270. https://doi.org/10.1007/s00402-015-2803-2.
23. Tuli SM. Tibialization of the fibula: a viable option to salvage limbs with extensive scarring and gap nonunions of the tibia. Clin Orthop Relat Res. 2005;431:80–84.
24. Kassab M, Samaha C, Saillant G. Ipsilateral fibular transposition in tibial nonunion using Huntington procedure: a 12-year follow-up study. Injury. 2003;34:770–775. https://doi.org/10.1016/S0020-1383(03)00666-4.
25. Cierney 3rd G, Mader JF, Penninck J. A clinical staging system for adult osteomyelitis. Clin Orthop Relat Res. 2003;414:7–24. https://doi.org/10.1097/01.blo.0000088564.81746.62.