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Induced membrane technique for acute bone loss and nonunion management of the tibia

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Abstract

Objectives: To report our experience and clinical results of using the Masquelet technique for the treatment of tibial nonunions and acute traumatic tibial bone defects.

Design: Retrospective study of prospectively collected data (Level IV).

Setting: Level I trauma center in the UK.

Patients/Participants: Consecutive patients with tibial nonunions and open fractures associated with bone loss.

Intervention: Two-stage Masquelet Procedure for the tibia.

Main Outcome Measurements: Clinical and imaging assessment at 6 weeks, 3,6,9,12 months, or until pain-free mobilization and union.

Results: There were 17 eligible patients, with a mean size of bone defect of 6 cm (range, 4–8 cm) and an 88.2% union rate at a mean of 8 months (range 5–18 months). Mean range of motion was 95 degrees of knee flexion (range 80°–130°). All patients but 2 returned to their previous occupation.

Conclusions: The Masquelet technique is simple, effective, and has a high rate of success for the management of a variety of situations including acute bone loss or infected nonunions and is associated with a low incidence of complications.

Keywords: bone defect, infection, masquelet technique, nonunion, RIA graft, tibia

1. Introduction

Long bone nonunion may become a devastating complication after fracture, with its management being chronic, and associated with tremendous impact on the patient's life, healthcare system, and society.[1,2] Its incidence ranges from 5% to 10%, and the tibia is the most common anatomical site of nonunion secondary to its compromised soft tissue envelope compared with other long bones.[2,3] Interestingly, the chronic health impact of fracture nonunion may be worse compared with important medical comorbidities including congestive heart failure, myocardial infraction, diabetes, and others.[4] The development of fracture nonunion is multifactorial and depends on patient and injury characteristics, local biological conditions, and the quality of surgery carried out. Several factors have been implicated in the pathogenesis of nonunions, and a recent meta-analysis of tibial nonunions[3] has identified several potential factors including age >60years, male gender, tobacco smoker, body mass index>40, diabetes, middle or distal third fracture compared with proximal third, high-energy injury, open fracture grade, Arbeitsgemein-schaft für Osteosynthesefragen (AO) type C fracture, requirement for open reduction, fixation other than minimally invasive percutaneous plate osteosynthesis, opioid use, non-steroidal anti-inflammatory drug use, and the presence of infection.[5] Other contributing factors may include patient nutritional status and alcohol consumption, vitamin D deficiency, reduced bone mineral density, renal, and peripheral vascular disease, significant bone loss and soft-tissue compromise including compartment syndrome.[5,6] Surgeon-related factors may also play a role as respecting the principles of the diamond concept of fracture healing is paramount for a successful bone repair response.[7] Taking into consideration all of the above, treatment of fracture nonunion depends on the type of nonunion (septic vs aseptic), state of the osteosynthesis, biology, and individual patient profile.

The Masquelet (or Induced Membrane) technique, invented in the 1980 s,[8] consists of 2 stages: During the first stage, thorough debridement of the bone and soft tissue is carried out, and a cement spacer (with or without antibiotics) is put in place to fill the resultant cavity, with the construct being stabilized either temporarily or permanently. A subsequent period of 6 to 8 weeks is enough for the cement to induce around it an inflammatory, richly vascularized "foreign body" membrane containing

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important molecular mediators. A closed cavity then forms which during the second stage is opened and after the removal of the cement spacer is filled in with bone graft and enhanced with adjuncts, for example bone marrow aspirate concentrate (BMAC) or bone-morphogenetic protein-2 (BMP-2). The affected extremity is then stabilized definitively as indicated with the appropriate selection of suitable implants. The thorough debridements and antibiotic cement presence aid in establishing an aseptic environment which will be favorable for the eradication of contamination (acute fractures) or infection (infected nonunions) and subsequent healing and integration of the bone graft during the second stage. Hence, the technique may be used for: infected nonunions; suspected infections in which lab investigations may be normal, which may be the case in up to 26% of cases[9]; aseptic bone defects or nonunions (for example, post open fracture debridement), to promote healing and to restore limb function. The purpose of this study is to report our experience and clinical results of using the Masquelet technique for the treatment of tibial nonunions and acute traumatic tibial bone defects.

2. Patients and methods

Between 2016 and 2020, the records of all consecutive patients with tibial nonunions and open tibial fractures associated with bone loss were available for review. Inclusion criteria were patients which their nonunion and/or acute bone defect was managed with the Masquelet technique. Exclusion criteria were patients in which their nonunion was managed with a different reconstruction treatment method as well as acute traumatic tibial bone loss that was managed with bone transport. Patients who were referred for initial treatment but then their care was transferred to a different institution were also excluded. The institutional affiliation of the Institutional Review Board (IRB) provided consent for the research (application number – LTH 8195). The research was conducted in accordance with the Declaration of the World Medical Association (www.wma.net).

Data extracted and analyzed included: Patient demographics and comorbidities, type of fracture or nonunion (aseptic vs septic), original method of fixation, time from original fixation to nonunion, defect size, definitive method of fixation, graft material used, complications, time to union, range of motion of the affected extremity, and return to the previous occupation. Besides the US Food and Drug Administration definition of a fracture that is at least 9 months old without any signs of healing for 3 consecutive months,[10] there is no universally accepted definition of "non-union," and we define nonunion as "a fracture, that in the opinion of the treating physician has no possibility of healing without further intervention."[11] Radiographically, union was defined as the presence of bridging callous in at least 3 out of 4 cortices. The minimum follow-up was 1 year (range 12–36 months).

3. Management

All patients were managed as per our Institution's previously developed standardized protocol, summarized in Supplemental Digital Content Figure 1, http://links.lww.com/OTAI/A26.[12] As far as a surgical management, this consists of 2 stages, as previously described.[13] During the first stage: careful debridement of either the acute open fracture, or of the chronic infection including excision of the dead/infected bone; insertion of a gentamycin-impregnated polymethyl methacrylate cement spacer; appropriate method for soft tissue envelope reconstruction (e.g., flap or skin grafting); bone stabilization (temporary or permanent) based on the personality of the fracture; 6-week minimum systemic antibiotic treatment in infected cases according to microbiology guidelines. The first stage lasts between 6 and 8 weeks and is then followed by the second stage: autologous bone graft is harvested from the contralateral or ipsilateral femur using the reamer irrigator aspirator device (RIA) (Depuy-Synthes, West Chester, Pennsylvania). Adjuncts to this autograft include BMAC from the iliac crest, platelet-rich plasma, Synthetic Bone Graft Substitute (e.g., Vitoss, Stryker or BonAlive) or xenograft; external fixator removal including pin site irrigation/debridement (when it has been used during the first stage as a temporary fixation device); exposure of the induced membrane, which is carefully incised to allow cement spacer removal while preserving the membrane; inspection of the area and debridement of any nonviable tissue (tissues sent to microbiology for culture); definite osteosynthesis with either plate or intramedullary nail as appropriate; implantation of the composite bone graft inside the membrane and careful closure; avoidance of using surgical drains. Our postoperative protocol includes thromboprophylaxis for 6 weeks, mode of weightbearing mobilization as indicated with progression to full weightbearing after a period of 6 to 8 weeks. Outpatient follow-up includes clinical assessment at 2 weeks for wound inspection and clinical/imaging assessment at 6 weeks, 3, 6, 9, 12months, or until pain-free mobilization and union. Of note, antibiotics are given at the time of debridement and the initial empirical antibiotic therapy is modified as well as the length depending on the patient systemic and local wound response according to the culture results and microbiology guidelines.

4. Results

Overall, based on the inclusion criteria, 17 of 21 patients were eligible to participate (4 were excluded, 2 moved to other institutions, and 2 were lost to follow-up). There were 13 males, 4 females with mean age of 39.5 years (range, 22–67years). There were 4 smokers, while 1 patient was diabetic and another 1 was hypertensive. Patient characteristics are shown in Supplemental Digital Content Table 1, http://links.lww.com/OTAI/A27. There were 5 aseptic nonunions, 7 cases with acute traumatic bone loss, and 5 septic nonunions. Anatomical segment of the affected tibia included 6 proximal, 5 midshaft, and 6 distal tibial cases. The initial method of fixation (stage 1) was intramedullary nailing (IMN) in 8, locking plate in 5, frame in 3, and external fixation in 1 patient. Mean time from the original injury to nonunion was 8.7months (range, 5–14months). The final stage 2 method of fixation was IMN in 8 (including 1 external fixator converted to retrograde IMN, 1 original nail retained, 1 plate converted to IMN), locking plate in 8 (including 1 original plate retained, 2 frames converted to plate), and frame (1 patient). Mean size of the bone defect was 6.0 cm (range, 4–8 cm). In all patients, the graft material consisted of RIA enhanced with various adjuncts as described in the Methods section (Supplemental Table 1, http://links.lww.com/OTAI/A27).

Mean time to union was 8months (range, 5–18months). Fifteen of the 17 patients healed uneventfully with no complications. In the 2 remaining patients (11.8%) additional procedures needed to be carried out; however, all of them finally healed (see Supplemental Table 1, http://links.lww.com/OTAI/A27, patients 16, 17).

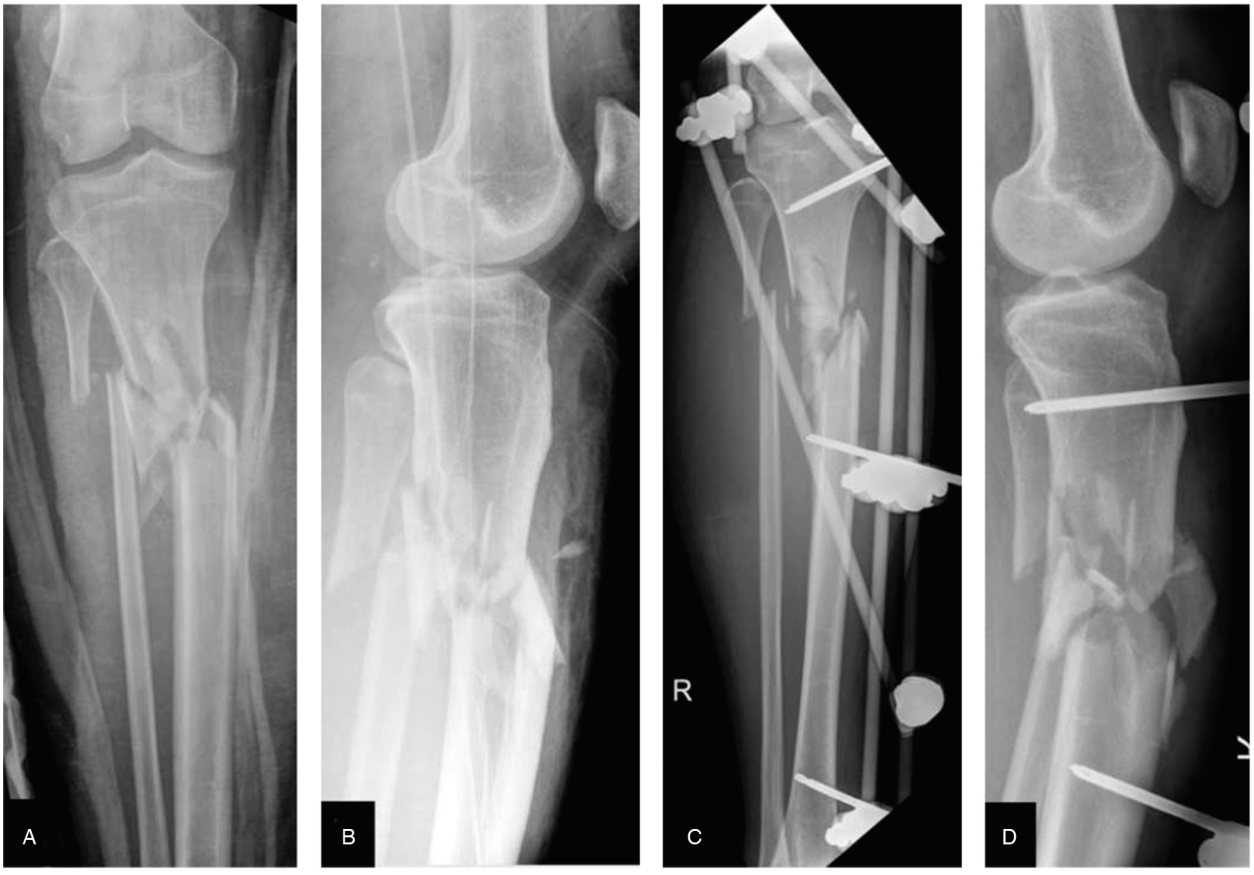

Figure 1. Example from patient 1 (of table 1, http://links.lww.com/OTAI/A27): AP and lateral (A, B) of the original closed injury initially stabilized with an external fixator (C, D). AP = anteroposterior.

The mean range of motion of the affected extremity at the knee was 95 degrees of flexion (range 80–130) whilst the ipsilateral ankle range of motion was full in the plantar and dorsiflexion plane of movement. An illustrative case example is shownin Figures 1 to 5 (patient lfrom Supplemental Table 1, http://links.lww.com/OTAI/A27). All patients but 2 returned to the previous occupation. Two of them changed to a sedentary type of vocation (1 was a roofer while the other patient was a lorry driver).

5. Discussion

The surgeon may be faced with several challenging situations in which a bone defect has to be addressed: infected nonunions, suspected infections with normal laboratory parameters (9), or aseptic/avascular situations. The common denominator in all situations is to establish an infection-free environment and a vascular bed providing the necessary conditions for bone regeneration and healing according to the "diamond concept" (7): osteoconduction, osteoinduction, osteogenesis, vascularity, and mechanical stability.

Several techniques have been used to address bone defects with the 2 most popular ones being the Masquelet (induced membrane) [12,13] and bone transport (Ilizarov) techniques.[14] The Ilizarov technique is a well-established method of reconstituting bone defects with good results in the literature, with a recent review reporting excellent and good rates in both bony union and function.[14] However, there have been concerns and a recent analysis of 282 patients[15] showed that there were 189 problems, 166 obstacles, and 406 (257 minor and 149 major) complications including pin-site infection in 66%, axial deviation in 41%, joint stiffness in 24%, soft-tissue incarceration in 22%, and delayed union of the docking site in 13.5%. Furthermore, there can be negative psychological effects of maintaining a frame with significant impact to the patient's mental well-being even after discontinuation of the device.[16] A recent cost-analysis paper comparing the Ilizarov vs the Masquelet technique highlighted the increased overall cost of the former (40% higher cost), related to increased number of surgical procedures, admissions, intraoperative cost, and outpatient clinic follow-up.[17]

The Masquelet technique has several advantages, including the local delivery of antibiotics, the creation of a favorable biologic chamber for bone regeneration, and healing time regardless ofthe defect length.[18] Its success rate is very high, around 86% to 89% for mean bone defect size of 6.32 cm (range 2–25 cm),[19,20] with the main complication being deep infection (8%), most likely due to suboptimal surgical debridement.[21]

In cases of acute bone loss in a contaminated environment such as in the setting of open fractures, the cement occupies a space allowing the injured soft tissue envelope around the bone defect to heal supporting resolution of inflammation and re-establishment of vascularity and local immune function, while at the same time restoring the alignment of the limb and delivering local antibiotics to prevent contamination becoming infection. In those cases, following appropriate debridement, soft-tissue

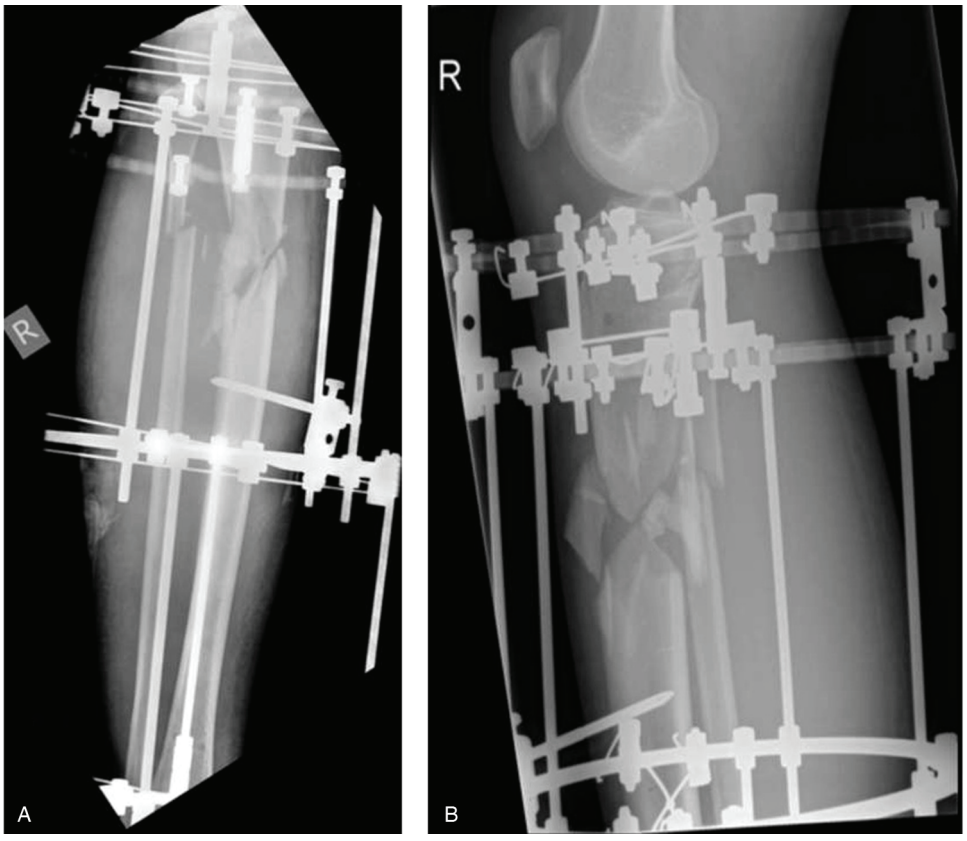

Figure 2. AP and lateral (A, B) showing conversion of the external fixator into a frame. AP = anteroposterior.

procedures are carried out to convert the open space into a closed space which will allow induction of the membrane in anticipation of the second stage.[12]

The management of aseptic/avascular conditions remains challenging as bone grafting without refreshing of the edges to healthy bleeding margins can be associated with increased risk of

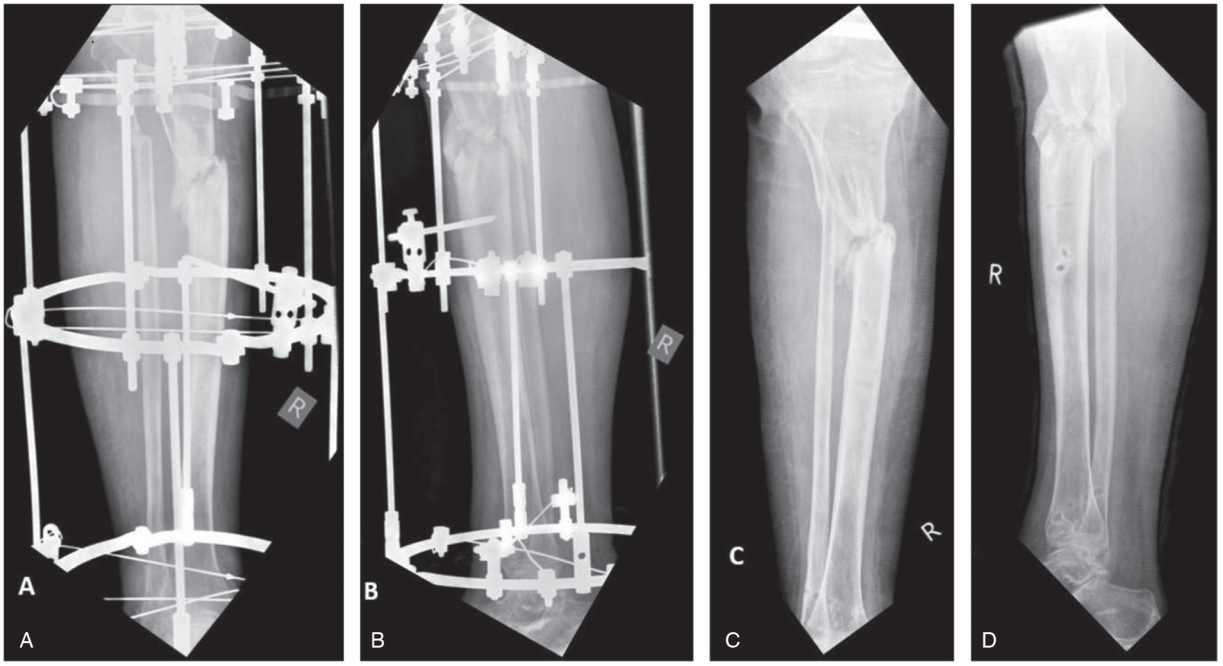

Figure 3. AP and lateral (A, B) showing that the fracture has not yet healed at 12 months, and therefore, the frame was removed (C, D). AP = anteroposterior.

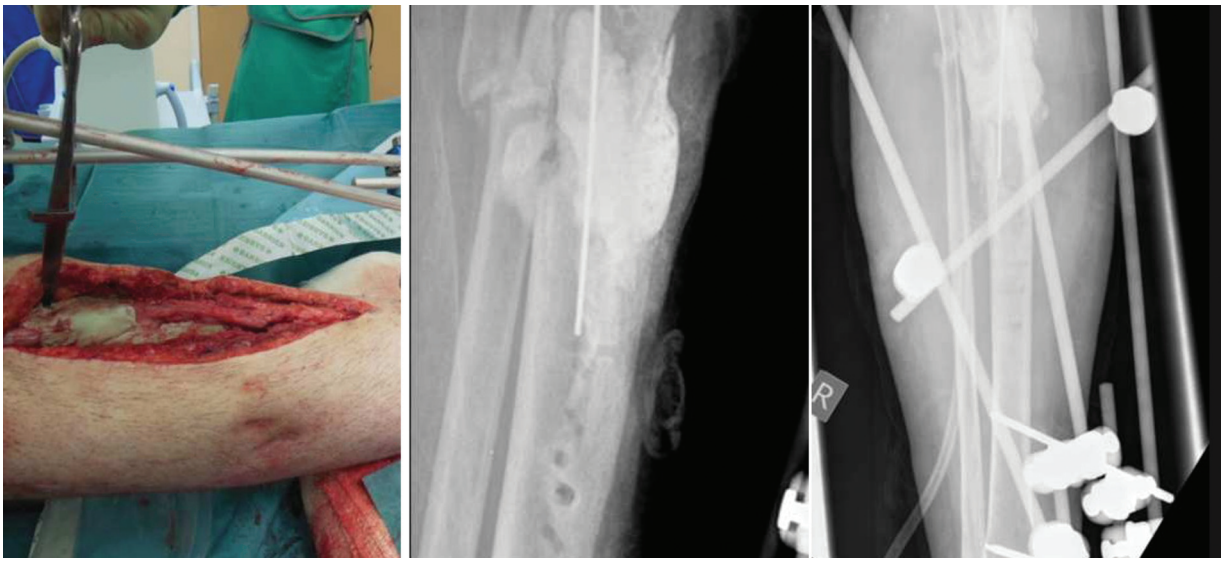

Figure 4. First-stage Masquelet procedure showing the insertion of the cement following appropriate debridement of the nonunion site (A). Corresponding AP and lateral radiographs (B, C). AP = anteroposterior.

failure. It is also very important to overlap the bone ends with cement in order for the induced membrane to incorporate them during the second stage. In the herein case series 5 cases required extensive debridement to reach a healthy vascular margin, leading to a mean defect of 4.4 cm. Three of the cases were open fractures whereas the other 2 were closed high energy injuries with associated comminution and extensive soft tissue degloving. In such cases options of treatment include bone grafting, bone transport, or titanium cage implantation.[22] We opted to use the Masquelet technique due its simplicity and user-friendly approach. Moreover, it was also the technique preferred by the patients.

In the infected situation, a radical bone debridement is vital, and the cement spacer also helps establish and maintain an aseptic environment. This also holds true during the second stage; if there are any concerns about the vascularity of the bone or its aseptic state, further debridement is of utmost importance at this point to decrease incidence of reinfection and graft failure. Routine microbiology specimens should be sent during the second stage as well, and if there is ongoing infection then antibiotics and/or repeat of stage 1 (cement implantation) may be warranted.[12] In one of the cases (patient 16, Supplemental Table 1, http://links.lww.com/OTAI/A27) due to infection the Masquelet technique was abandoned, and the defect was

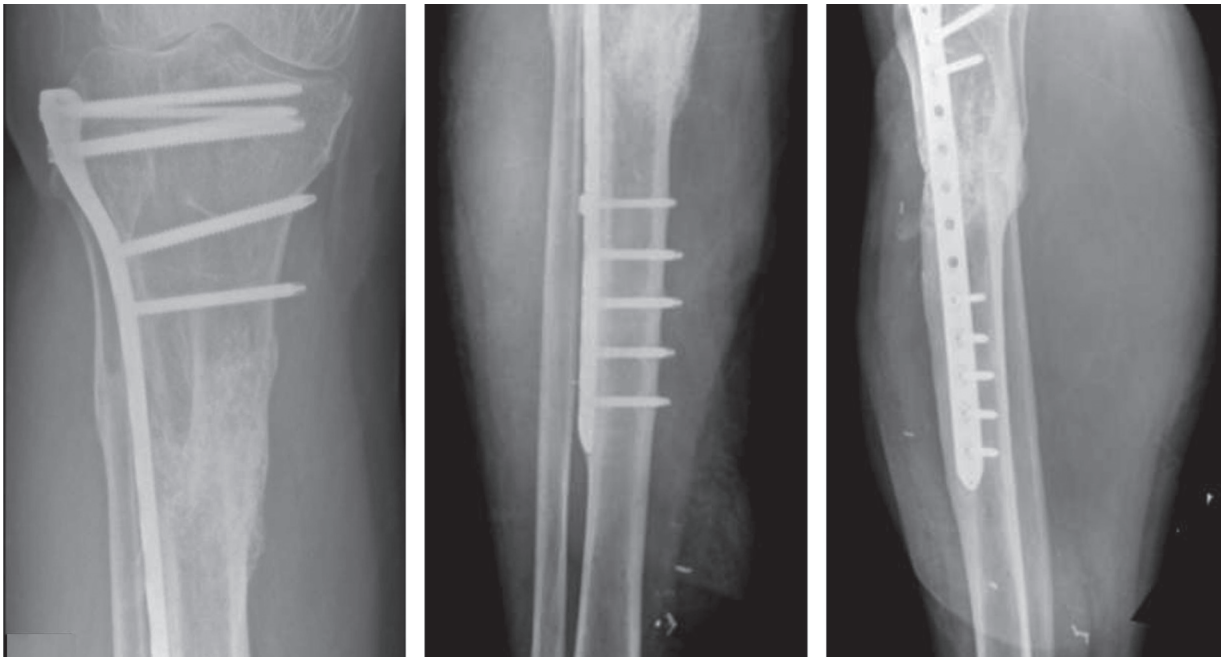

Figure 5. After 6 to 8 weeks, a second-stage Masquelet procedure was performed and at final follow-up 14 months radiographs (A–C) demonstrate complete incorporation of the graft and osseous union. AP = anteroposterior.

reconstructed with bone transport. In this case series we did not observe the need of frequent reinterventions as it has been previously reported with the bone transport method. However, in 1 patient (patient 14, Supplemental Table 1, http://links.lww.com/OTAI/A27) one of the proximal locking nail screws had to be removed as it was causing soft tissue irritation.

Although the practice of cement loading with antibiotics has been controversial,[23] in the herein study the cement spacer was loaded with gentamycininallpatients and ina recentmeta-analysis it was found that it decreased the need for revision.[24] We do not add methylene blue to the cement during the first stage as we have found no issues with cement identification during the second stage. As far as membrane quality is concerned, there were no problems encountered. In all patients, the membrane was handled in a very delicate manner to ensure that it is not damaged and that when closed it provided a sealed biological chamber for the graft. Regarding graft choice, we find that harvesting of the RIA gives consistently a large volume of graft. When more graft is required, especially for defects of more than 6 cm, addition of further synthetic bone graft, allograft, or xenograft has been useful. To increase osteogenic potential according to the diamond concept,[7] BMAC or BMP-2 are also routinely used in those cases.

The union rate of this series was 88.2% (15/17 patients), as 2 patients required additional procedures; however, they all finally healed. Patient 17 who failed to heal distally required an additional grafting procedure using BMAC and BMP-2 after 6 months and conversion of his IMN to a lateral locking plate secondary to patellar tendon irritation. He went on to unite at 18 months after the injury, which was the longest of all the patients who apart from him were all united by 12months.

There are several limitations to this study: small sample size, absence of control group, lack of randomization, outcomes are not reported using standardized instruments. All of these limitations may be difficult to avoid, as those cases are complex and heterogeneous. However, the authors feel that this report adds to the already growing body of literature in favor of the Masquelet technique for nonunion and acute bone defect management.

In conclusion, the Masquelet technique is a simple, safe, and effective method of addressing bone defects in a variety of situations including acute bone loss or infected nonunions and is associated with a low incidence of complications.

References

1. Chloros GD, Kanakaris NK, Vun JSH, et al. Scoring systems for early prediction of tibial fracture non-union: an update. Int Orthop. 2021; 45:2081–2091.
2. Mills LA, Aitken SA, Simpson AHRW. The risk of non-union per fracture: current myths and revised figures from a population of over 4 million adults. Acta Orthopaedica. 2017; 88:434–439.
3. Tian R, Zheng F, Zhao W, et al. Prevalence and influencing factors of nonunion in patients with tibial fracture: systematic review and meta-analysis. J Orthop Surg Res. 2020; 15:377.
4. Brinker MR, Hanus BD, Sen M, et al. The devastating effects of tibial nonunion on health-related quality of life. J Bone Joint Surg. 2013; 95:2170–2176.
5. Chloros GD, Howard A, Giordano V, et al. Radiographic long bone fracture healing scores: can they predict non-union? Injury. 2020; 51:1693–1695.
6. Andrzejowski P, Giannoudis PV. The 'diamond concept' for long bone non-union management. J Orthop Traumatol. 2019; 20:1–13.
7. Giannoudis PV, Einhorn TA, Marsh D. Fracture healing: the diamond concept. Injury. 2007; 38:S3–S6.
8. Masquelet A, Fitoussi F, Begue T, et al. Reconstruction des os longs par membrane induite et autogreffe spongieuse. Ann Chir Plast Esthet. 2000; 45:346–353.
9. Tosounidis TH, Holton C, Giannoudis VP, et al. Can CRP levels predict infection in presumptive aseptic long bone non-unions? A prospective cohort study. J Clin Med. 2021; 10:425.
10. Giannoudis PV, Chloros GD, Ho YS. A historical review and bibliometric analysis of research on fracture nonunion in the last three decades. Int Orthop. 2021; 45:1663–1676.
11. Brinker MR, O'Connor DP, Browner BD, Jupiter JB, Levine AM, Trafton P, Krettek C. Nonunions: evaluation and treatment. Skeletal Trauma: Basic Science, Management, and Reconstruction. 2009; WB Saunders, Philadelphia, PA:637–718.
12. Giannoudis PV, Harwood PJ, Tosounidis T, et al. Restoration of long bone defects treated with the induced membrane technique: protocol and outcomes. Injury. 2016; 47:S53–S61.
13. Giannoudis PV, Faour O, Goff T, et al. Masquelet technique for the treatment of bone defects: tips-tricks and future directions. Injury. 2011; 42:591–598.
14. Aktuglu K, Erol K, Vahabi A. Ilizarov bone transport and treatment of critical-sized tibial bone defects: a narrative review. J Orthop Traumatol. 2019; 20:22.
15. Liu Y, Yushan M, Liu Z, et al. Complications of bone transport technique using the Ilizarov method in the lower extremity: a retrospective analysis of 282 consecutive cases over 10years. BMC Musculoskel Dis. 2020; 21:1–9.
16. Abulaiti A, Yilihamu Y, Yasheng T, et al. The psychological impact of external fixation using the Ilizarov or Orthofix LRS method to treat tibial osteomyelitis with a bone defect. Injury. 2017; 48:2842–2846.
17. Kanakaris NK, Mohrir G, Chloros G, et al. Tibial bone defects: analysis of time to union and direct medical costs using distraction osteogenesis with an ilizarov frame or the masquelet technique. Free Paper 1121 presented in EFORT (European Federation of National Associations of Orthopaedics and Traumatology) Annual Meeting, 30 June to 02 July 2021; Vienna, Austria 2021.
18. Morelli I, Drago L, George DA, et al. Masquelet technique: myth or reality? A systematic review and meta-analysis. Injury. 2016; 47:S68–S76.
19. Masquelet A, Kanakaris NK, Obert L, et al. Bone repair using the Masquelet technique. J Bone Joint Surg. 2019; 101:1024–1036.
20. Mi M, Papakostidis C, Wu X, et al. Mixed results with the Masquelet technique: a fact or a myth? Injury. 2020; 51:132–135.
21. Papakostidis C, Bhandari M, Giannoudis P. Distraction osteogenesis in the treatment of long bone defects of the lower limbs: effectiveness, complications and clinical results; a systematic review and meta-analysis. Bone Joint J. 2013; 95:1673–1680.
22. Tetsworth K, Woloszyk A, Glatt V. 3D printed titanium cages combined with the Masquelet technique for the reconstruction of segmental femoral defects: preliminary clinical results and molecular analysis of the biological activity of human-induced membranes. OTA Int. 2019; 2: e016.
23. Mathieu L, Durand M, Collombet J-M, et al. Induced membrane technique: a critical literature analysis and proposal for a failure classification scheme. Eur J Trauma Emerg Surg. 2020; 47:1373–1380.
24. Hsu C-A, Chen S-H, Chan S-Y, et al. The induced membrane technique for the management of segmental tibial defect or nonunion: a systematic review and meta-analysis. Biomed Res Int. 2020; 2020:5893642.