



HAL
open science

Restoring the Anatomy of Long Bones with Large Septic Non-Union Defects with the Masquelet Technique

Vasileios Giovanoulis, Christos Koutserimpas, Nikolaos Lepidas, Angelo V Vasiliadis, Cécile Batailler, Tristan Ferry, Sébastien Lustig

► To cite this version:

Vasileios Giovanoulis, Christos Koutserimpas, Nikolaos Lepidas, Angelo V Vasiliadis, Cécile Batailler, et al.. Restoring the Anatomy of Long Bones with Large Septic Non-Union Defects with the Masquelet Technique. *Maedica - A Journal of Clinical Medicine*, 2023, 18 (3), 10.26574/maedica.2023.18.3.413 . hal-04465623

HAL Id: hal-04465623

<https://hal.science/hal-04465623>

Submitted on 19 Feb 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Restoring the Anatomy of Long Bones with Large Septic Non-Union Defects with the Masquelet Technique

Vasileios GIOVANOULIS^a, Christos KOUTSERIMPAS^b, Nikolaos LEPIDAS^c,
Angelo V. VASILADIS^a, Cécile BATAILLER^{a, d}, Tristan FERRY^{e, f, g}, Sébastien LUSTIG^{a, d}

^aOrthopaedic Surgery and Sports Medicine Department, Croix-Rousse Hospital, Lyon University Hospital, Lyon, France

^bDepartment of Orthopaedics and Traumatology, “251” Hellenic Air Force General Hospital of Athens, 11525 Athina, Greece

^cSecond Orthopedic Department, Panagiotis & Aglaia Kyriakou Children Hospital, Athens, Greece

^dUniv Lyon, Claude Bernard Lyon 1 University, IFSTTAR, LBMC UMR_T9406, 69622 Lyon, France

^eDepartment of Infectious Diseases, Groupement Hospitalier Nord, Hospices Civils de Lyon, 69004 Lyon, France

^fRegional Reference Center for the Management of Complex Bone and Joint Infections, Hospices Civils de Lyon, 69004 Lyon, France

^gCentre International de Recherche en Infectiologie (CIRI), Inserm, U1111, Université Claude Bernard Lyon 1, CNRS, UMR5308, Ecole Normale Supérieure de Lyon, 69007 Lyon, France

ABSTRACT

Objectives: Septic non-union in long-bone fractures represents a challenging clinical entity. Management of lower extremity segmental bone defects, aiming to restore functional anatomy, remains extremely difficult and controversial. Masquelet technique is a reconstruction method for large diaphyseal bone defects, based on the notion of the induced membrane. The principle of the induced membrane is to create a foreign body reaction by placing cement spacer in the bone defect. The purpose of this study was to assess the success rate of induced membrane technique (IMT) in treating lower extremity large bone defects due to septic non-union.

Address for correspondence:

C Koutserimpas, MD, PhD

Department of Orthopaedics and Traumatology, “251” Hellenic Air Force General Hospital of Athens, 11525 Athina, Greece

Mailing address: Kanellopoulou Av 3, 11525, Athens, Greece

Tel: +306948712130; email: chrisku91@hotmail.com; ORCID: 0000-0002-1398-9626

Article received on the 4th of August 2023 and accepted for publication on the 19th of September 2023

Methods: This is a retrospective observational study performed in a single referral center in France, Europe, which is specialized in complex bone and joint infections. All patients operated for septic non-union were identified from a prospectively maintained database. Patients treated with the IMT for septic femoral or tibial non-union between 2013 and 2017 were enrolled in this study. Exclusion criteria were infection of a continuous bone, aseptic non-union, or patients with less than one year of follow-up after antibiotic treatment ending.

Results: Twenty-three cases (19 patients) with an average age of 41.3 years were included in the present study. There were 19 tibial and four femoral fractures. The mean bone defect was 65.3 mm. The mean time interval from initial trauma to the first surgical phase was 17 months, while that between the two surgical phases was 77.7 days. After the first surgical phase, samples were positive in 13 cases (68.5%), isolating *Staphylococcus* (26%) and more than one pathogen in 22% of cases. Bone union was successful in 16 of 23 cases (69.6%, 14 patients). There were seven failures: five amputations due to mechanical and/or infection-related failure and two failed unions.

Conclusion: This study found that 69% of cases with septic non-union of tibial or femoral fracture treated with the two-step surgical protocol achieved bone union and infection eradication within about 13.2 months after the second stage of the procedure. The study revealed promising results in patients suffering large-size bone defect; hence, the IMT may prove beneficial in the management of such cases.

Keywords: septic non-union, surgical anatomy, osseous infection, bone defects, referral center for bone and joint complex infection.

INTRODUCTION

The Masquelet technique or induced membrane technique (IMT) was described in 1986 and represents a two-step procedure for treating non-unions, especially in long-bones, and the concomitant osseous defects (1). It is a relatively new approach for reconstructing segmental bone defects, caused by resection of infectious, tumorous and/ or traumatic injured bone tissue (2).

The general steps of IMT have been documented and are well established. Nevertheless, the details of the procedure are highly variable and dictated more by surgeon preference and patient conditions, rather than evidence (1-3). During the first stage of the procedure, the affected bone is resected and polymethyl methacrylate (PMMA) cement is placed to fill the defect. Internal or external fixation could be performed, according to surgeon preference and the patient's condition (3). Following the first step of the technique, a period of at least 4-8 weeks is given, so that the autologous foreign-body "induced" membrane around the cement spacer may be formed. The second stage of the procedure includes the cement spacer removal and bone graft placement in the cavity (1, 2).

Septic non-union represents a major complication for long bone fractures. Large osseous de-

fects may be present, complicating bone healing and the patient's quality of life (4). Therapeutic interventions in these cases require medical and surgical treatment and multidisciplinary approach is of utmost importance.

There are scarce data regarding the IMT, especially in treating septic non-union and the concomitant bone defects in long bones. Many issues, including the time-interval between the two stages, the factors that affect infection's eradication and bone union, remain vague in the literature so far. There is only a few small series describing the outcomes of this technique in septic union of long bones. Furthermore, many variants are depended on surgeon's preference, such as the use and type of fixation, the impregnation of cement with antibiotics and type of bone graft.

The purpose of the present study was to evaluate the efficacy of the IMT in treating femoral and/or tibial large bone defects and restoring the functional anatomy due to septic non-union as well as in eradicating the infection. □

METHODS

This is an observational retrospective study of a prospectively collected database. From January 2013 to December 2017, all femoral and tibial septic non-union cases treated with two-stage IMT were enrolled in research.

TABLE 1. Paley-Maar bone score

Excellent	Consolidation, absence of infection, absence of > 5 axial defect, < 2.5 cm limb-length discrepancy, docking site and osteogenesis zone consolidation solid enough not to require protection
Good	Consolidation without infection, with one of the following criteria: > 5 axial defect, > 2.5 cm limb-length discrepancy
Moderate	Consolidation without infection, with both of the following criteria: > 5 axial defect, > 2.5 cm limb-length discrepancy OR Insufficient docking site or osteogenesis zone consolidation
Poor	Non-union and/or bone infection

Data of patients' age, comorbidities and history of trauma were recorded. Risk factors were evaluated using the Non-Union Scoring System (NUSS) on 100 points, including bone (54 points), soft tissue (12 points) and patient-specific factors (34 points). The NUSS score has been useful when assessing patients with fracture non-union. It takes into consideration the bone quality, bone involvement, soft tissue management and patients' risk factors, while higher scores imply a higher difficulty to procure union. This score categorizes patients into four groups, including group 1 (0-25), group 2 (26-50), group 3 (51-75) and group 4 (76-100), with group 4 having the highest severity.

Meticulous assessment was performed prior to treatment initiation at the end of antimicrobial treatment and then at least 12 months after the final surgical intervention. Bone consolidation was assessed with orthogonal X-rays, defined by bringing callus of two cortices on the two X-ray views (antero-posterior and lateral). Functional results and bone quality were evaluated with the Paley-Maar score. Table 1 summarizes the values of this score, which was initially described for the segmental transport used by the Ilizarov technique and fixator.

All patients underwent the same rigorous surgical and medical protocol. Their medical history was reviewed during a multidisciplinary meeting, involving orthopaedic and plastic surgeons, infectious disease specialists as well as microbiologists.

The procedure was performed in two steps: initially, resection of the infectious site and PMMA cement spacer loaded with Gentamicin (PALACOS R+G®, Heraeus, Germany) was placed. During this step, at least five separate samples were sent for microbiological and histological examination. Stabilization with external fixator could be used, according to surgeon's preference, while skin closure was performed with direct suture when it



FIGURE 1. A: anteroposterior (AP) view of the right distal tibia; screw breakdown and sequestrum due to *Staphylococcus epidermidis* are shown. B: AP view of the first stage of Masquelet technique, plates removal, external fixation and spacer with Gentamicin. C: AP view, second stage, infection eradication, fixation with locking plate. D: AP view, bone union after three months

was permitted by soft tissue quality. If not, a pedicle flap or a free flap was performed by plastic surgeon. Then, patients received intravenous (iv) antimicrobial treatment for 15 days, including, initially, empirical treatment with vancomycin and piperacillin/tazobactam, while treatment was adapted according to microbiological and histological results. Following hospital discharge, patients were commenced on *per os* appropriate antimicrobial treatment for at least 30 days. Infection eradication was assessed according to patient's signs and symptoms, laboratory examination and imaging results.

Following infection eradication, the reconstruction phase was initiated. The second stage of the surgical intervention was performed, including careful incision of the induced membrane, removal of the cement spacer and placement of autologous cancellous bone combined with bone

graft substitute [Cerament® (bioresorbable hydroxyapatite/calcium sulphate cement)]. Finally, definitive osteosynthesis with locking plate was performed (Figure 1).

The time interval between the two surgical phases was at least six weeks, while it related to the microbiological diagnosis, the chronicity of the infection and the healing of soft tissues.

The study has been approved from the scientific committee of Hospices Civils de Lyon. This study has also been included in the registry of clinical trials as NCT02817711. □

RESULTS

A total of 19 patients with 23 septic non-union tibial and/or femoral cases were included in this cohort.

The studied population’s main characteristics are highlighted in Table 2. Most patients were males (13; 68.4%). Patients’ mean age was 42.7 years [standard deviation (SD) 13.6], while their mean body mass index (BMI) was 25.4 kg/m² (SD 5.1). The mean follow-up, after the second stage of the operation, was 44.6 months (SD 21.01). Fourteen patients (73.6%) were heavy smokers.

Most cases referred to tibial (19; 82,6%), followed by femoral fractures (4; 17.4%), while the majority of the cases (17; 74%) were related to open fractures.

The mean number of surgical interventions prior to IMT was 2.8 procedures (SD 1.7), while

the mean bone defect was 65.3 mm (SD 15.2). At the time of inclusion to the protocol, the mean NUSS score was 54.6 (SD 13.4). According to NUSS groups, one patient (4.3%) was in group 1, seven subjects (30.4%) in group 2, 15 patients (65.2%) in group 3 and none in group 4.

The first surgical phase was performed after 17 months (SD 14.1) from the initial trauma. During the first stage, external fixation was performed in 16 (69.6%) of cases. In five cases (21.7%) during the first step, a musculocutaneous flap was also required for wound coverage. After the first surgical phase samples were positive in 13 cases (68.5%), isolating in six cases (31.6%), followed by methicillin resistant *Staphylococcus aureus* (MRSA) and *Propionibacterium acnes* in three cases each (15.8%). In five cases (26.3%), more than one organism was isolated.

Dual or triple appropriate antimicrobial therapy was administrated awaiting the second phase, according to multidisciplinary team discussion considering the microbiological and histological results. After the second surgical phase, samples were positive in four cases, isolating the same organism as in first phase in one case (4.3%).

In the second phase, bone autograft was harvested from the anterior iliac crest in two patients (10.5%) and from both anterior and/or posterior iliac crests in 17 subjects (89.5%), while allograft (bone bank) was additionally used in 18 patients (94.7%). Bone stabilization was achieved by internal fixation with locking plates. The mean period

	Mean	Standard deviation	Extremes (Min-Max)
23 septic non-union cure (n=19 patients)			
Age (years)	41.3	13.3	16-74
BMI (kg/m ²)	25.4	5.1	17-35
Localization	Tibia: 19 (82.6%) Femur: 4 (17.4%)		
Bone localization	Diaphysis: 16 (69.6%) Metaphysis: 7 (30.4%)		
Open fractures	Open fractures: 17 (74%)		
Surgery after initial trauma	External fixation: 9 (39%) Intramedullary nail: 6 (26%) Plate OS: 7 (30%) Percutaneous OS: 4 (4.3%)		
Bone defect (cm ³)	65.3	15.2	35-106
Bone defect (cm ³)	<60: 9 (39.1%) >60: 14 (60.9%)		
NUSS score	49.8	20.2	0-71

TABLE 2. Patients’ main characteristics

between the two surgical steps was 77.7 days (SD 46.2).

Bone union was achieved in 16 of 23 cases (14 patients, 69.6%) at a mean of 13.2 months (SD 7.77) after the second stage of the procedure. According to the Paley-Maar Bone Score, five patients (21.7%) had an excellent score, eight subjects (34.8%) a good score and three patients (13%) a poor score. There were two recurrences of sepsis, which were treated with below-knee amputation. In terms of mechanical-related failure (loosening of the hardware or plate breakage) there were five cases leading to three amputations and two non-unions. □

DISCUSSION

The treatment of large septic femoral or tibial non-union is challenging and frequently requires multidisciplinary approach. In France, specialized team treatment of these infections is the norm with the creation of referral centers for bone and joint complex infections, eg, “Centres de référence des infections ostéo-articulaires complexes” (CRIOAc) in 2008. These centers permit a multidisciplinary team treatment associating orthopedic surgeons, infectious disease specialists, microbiologists and plastic surgeons.

The main finding of the present study is that the IMT achieved 69.5% union rate at a mean follow-up of 13.2 months in patients suffering large bone defects due to long-bone septic non-unions. Siboni *et al* evaluated 19 cases of septic non-union of the tibia, with a mean size of bone defect at 52.4 mm after the first stage, having 89% successful bone union in a period of 16 months (7). Pesciallo *et al* (8) studied 21 cases of infected femoral and tibial bone defects with a median bone defect size at 45 mm and found union rate at 95.23% over a median time of 7 (range 6-12) months. In the present study, 23 cases with mean bone defect of 65.3 mm were evaluated.

The present cohort showed that the majority of patients (14; 73.6%) with large septic tibial or femoral non-union were heavy smokers. Furthermore, there were two recurrences of sepsis, which were treated with below-knee amputation, while in terms of mechanical-related failure there were five cases leading to three amputations and two non-unions. It should be noted that these “failed” cases were all among the heavy smokers group.

This has been already documented. Siboni *et al* reported that only one of the eight patients achieving union after the second phase without any supplementary procedure was an active smoker (7). In addition, Bauer *et al* showed that most patients with infected non-union of the tibia or the femur were active smokers (9). Nevertheless, in a retrospective study of 36 patients evaluating the vascularity of the induced membrane, Niikura *et al* found that smoking did not affect the IM vascularity and suggested a relationship between vascularity and osteogenesis inside the IM (10).

In the present study, after the first stage, the most commonly isolated organism was *Staphylococcus epidermitis* (six cases; 31.6%), followed by methicillin-resistant *Staphylococcus aureus* (MRSA) (3; 15.8%). Similarly, Scholz *et al* (11) identified the types of organisms in a series of 13 cases of diaphyseal bone defects treated with the IMT. They also isolated *Staphylococcus* (69%) as the primary pathogen and 23% of those was MRSA, followed by *Enterococci* (30.8%). *S. epidermitis* has also been associated with orthopaedic implant related infections. In the present study, only one case with multi-bacterial infection which led to amputation was recorded. However, due to the small number of cases, a correlation between infection with multiple organisms and failure of the technique could not be made.

The type of fixation used for limb stabilization also represents an understudied issue. In this study, external fixation was used in most of cases (69.6%) in the first stage of the procedure. As for the second stage, internal fixation by locking plate was the only stabilization method used by us. Overall, five mechanical failures (21.7%) and 69.5% union rate were recorded. In a retrospective multicenter cohort study, Morwood *et al* (12) found 85.9% union rate in a series of 64 cases sustaining significant femur and/or tibial bone loss where stabilization was assured by plate. However, in contrast with the present study, the bone defects in those patients were not due only to septic non-union. Therefore, it could be assumed that infection, as cause of osseous defect, could lead to less favorable outcomes. In a systematic review evaluating the results of IMT in the management of critical size bone defects in children, Aurégan *et al* (13) found no difference in favor of a certain type of fixation used for the second stage. However, it was noted that osteosyntheses deemed “unstable” by the surgeon were more

likely to fail. Different fixation methods based on the stage of the procedure have been recommended. Initially, rigid stabilization is favored immediately after the second stage to promote revascularization. Subsequently, a shift towards more flexible stabilization – even with an external fixation – is preferred to enhance corticalization by adjusting the fixation rigidity and introducing dynamization by gradually removing the rods (14).

Reconstruction of long bone defects and restoration of the anatomy and function of the lower extremity remains a major challenge for an orthopedic surgeon. Commonly, these large bone defects are associated with damage or loss of the surrounding wound tissues. In the literature, in most series the bone defects were classified into four types, according to the Karger's classification (2): type I less than 20 mm, type II between 20-50 mm, type III 50-100 mm and type IV more than 100 mm. Very few studies have provided detailed information regarding the use of IMT for large bone defects. The herein study showed encouraging results of IMT patients with bone defects among class 3 and above.

Generally, the Ilizarov technique and the vascularized fibular autograft represented the most commonly used procedures for the reconstruction of large bone defects (15). These techniques are associated with an increased risk of fracture and are highly demanding in terms of micro-surgical approach. Masquelet technique may provide potential advantages in these challenging cases, creating the favorable biologic cavity to improve bone regeneration and its osteoconductivity regardless of the defect size (16). Bone graft substi-

tute may also be used to complete the insufficient amount of autograft (17, 18). In the present cohort this was necessary for almost all patients (18 subjects; 94.7%).

The present study has some limitations. It is a retrospective single center study which does not comprise a control group. Furthermore, it is a relatively small cohort. Nevertheless, only few such small cohorts exist so far in the literature – hence, it is important to report the outcomes of IMT technique to provide evidence-based data for treatment options of an extremely challenging osseous infection. □

CONCLUSION

The present study reported that 69% of patients treated at a referral center for bone and joint complex infections using the IMT achieved bone union and infection eradication within about 13.2 months after the second stage of the procedure. A polymicrobial infection may have an impact on the resolution of the infection and the bacterial profile should be investigated, while smoking seems to lead to non-favorable outcomes. A multidisciplinary approach is of utmost importance for the management of these challenging cases for achieved desired outcomes. □

Conflicts of interest: none declared.

Financial support: none declared.

Institutional review board statement: The study has been approved by the scientific committee of Hospices Civils de Lyon, France, and has also been included in the registry of clinical trials as NCT02817711.

REFERENCES

1. Masquelet AC, Fitoussi F, Begue T, Muller GP. (Reconstruction of the long bones by the induced membrane and spongy autograft). *Ann Chir Plast Esthet* 2000;45:346-353.
2. Karger C, Kishi T, Schneider L, et al. French Society of Orthopaedic S, et al. Treatment of posttraumatic bone defects by the induced membrane technique. *Orthop Traumatol Surg Res* 2012;98:97-102.
3. Aparid T, Bigorre N, Cronier P, et al. Two-stage reconstruction of post-traumatic segmental tibia bone loss with nailing. *Orthop Traumatol Surg Res* 2010;96:549-553.
4. Calori GM, Phillips M, Jeetle S, et al. Classification of non-union: need for a new scoring system? *Injury* 2008;39 Suppl 2:S59-S63.
5. 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.
6. Paley D, Maar DC. Ilizarov bone transport treatment for tibial defects. *J Orthop Trauma* 2000;14:76-85.
7. Siboni R, Joseph E, Blasco L, et al. Management of septic non-union of the tibia by the induced membrane technique. What factors could improve results? *Orthop Traumatol Surg Res*

- 2018;104:911-915.
8. **Pesciallo CA, Garabano G, Dainotto T, Ernst G.** Masquelet technique in post-traumatic infected femoral and tibial segmental bone defects. Union and reoperation rates with high proportions (up to 64%) of allograft in the second stage. *Injury* 2021;52:3471-3477.
 9. **Bauer T, Klouche S, Grimaud O, et al.** Treatment of infected non-unions of the femur and tibia in a French referral center for complex bone and joint infections: Outcomes of 55 patients after 2 to 11 years. *Orthop Traumatol Surg Res* 2018;104:137-145.
 10. **Niikura T, Jimbo N, Komatsu M, et al.** Histological analysis of induced membranes in patients whose bone defects were treated with the Masquelet technique to identify factors affecting the vascularity of induced membranes. *J Orthop Surg* 2021;16:248.
 11. **Scholz AO, Gehrman S, Glombitza M, et al.** Reconstruction of septic diaphyseal bone defects with the induced membrane technique. *Injury* 2015;46(Suppl 4):S121-S124.
 12. **Morwood MP, Streufert BD, Bauer A, et al.** Intramedullary Nails Yield Superior Results Compared With Plate Fixation When Using the Masquelet Technique in the Femur and Tibia. *J Orthop Trauma* 2019;33:547-552.
 13. **Aurégan JC, Bégué T, Rigoulot G, et al.** Success rate and risk factors of failure of the induced membrane technique in children: a systematic review. *Injury* 2016;47:S62-S67.
 14. **Masquelet AC.** Induced Membrane Technique: Pearls and Pitfalls. *J Orthop Trauma* 2017;31:S36-S38.
 15. **Pederson WC, Person DW.** Long bone reconstruction with vascularised bone grafts. *Orthop Clin North Am* 2007;38:23-35.
 16. **Chloros GD, Kanakaris NK, Harwood PJ, Giannoudis PV.** Induced membrane technique for acute bone loss and non-union management of the tibia. *OTA Int* 2022;5(2 Suppl):e170.
 17. **Piacentini F, Ceglia MJ, Bettini L, et al.** Induced membrane technique using enriched bone grafts for treatment of posttraumatic segmental long bone defects. *J Orthop Traumatol* 2019;20:13-18.
 18. **Jäger M, Herten M, Fochtman U, et al.** Bridging the gap: bone marrow aspiration concentrate reduces autologous bone grafting in osseous defects. *J Orthop Res* 2011;29:173-180.

