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Clinical outcomes of the induced membrane technique for ultra-large (>12 cm) segmental bone defects caused by osteomyelitis: a retrospective cohort study

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Clinical outcomes of the induced membrane technique for ultra-large (>12 cm) segmental bone defects caused by osteomyelitis: a retrospective cohort study

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Abstract

Background: The length of the bone defect is an important factor affecting surgical methods and treatment strategies for osteomyelitis. However, specialized research on the induced membrane technique (IMT) for the treatment of ultra-large bone segmental defects >12.0 cm is still lacking. This study aims to evaluate clinical outcomes of ultra-large bone defects due to osteomyelitis treated using IMT.

Methods: This retrospective observational study included patients with ultra-large bone segmental defects (>12.0 cm) due to osteomyelitis who underwent staged treatment with IMT at our hospital between January 2018 and March 2024. Data were collected for subsequent analyses, including the Self-rated Anxiety Scale (SAS) score, radiographic bone healing time, full weight-bearing time, Hospital for Special Surgery (HSS) Knee Score, and American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hind Foot Score.

Results: Thirty-eight patients were included in the study (30 men and 8 women; age, 52.6±12.9 years). They had an average bone defect length of 16.0±4.1 cm. The mean radiological healing and full weight-bearing times were 4.8±2.1 and 5.2±1.8 months, respectively. The radiographic union rates were 57.8% at 4 months and 86.8% at 6 months. The mean AOFAS and HSS scores were 85.2±7.7 and 85.1±6.3, respectively. A total of six complications were observed in four cases, and good outcomes were obtained with proper intervention.

Conclusions: IMT demonstrated reliable clinical efficacy in treating ultra-large bone segmental defects >12.0 cm, consistently achieving both bone healing and functional joint recovery.

Trial registration: This retrospective study has been registered with the Chinese Clinical Trial Registry (registration number: ChiCTR2500109019; registration date: 2025-09-10).

Level of Evidence: Therapeutic Level IV.

Key words: Ultra-large bone defect, induced membrane technique, osteomyelitis, outcome

Introduction

Treatment of osteomyelitis is a bone infection that leads to considerable challenges for orthopedic surgeons. The complexity of these infections, which often involve biofilm formation on implants, necessitates multifaceted treatment strategies. Surgical debridement may create bone defects [1]; thus, treatment aims to eliminate the infection and reconstruct the bone defects [2]. Current therapeutic strategies for large bone defects include surgical modalities such as bone transport (Ilizarov technique), free-vascularized fibular graft, and the induced membrane technique (IMT) [3-5].

Schmitz and Hollinger defined a critical bone defect as one in which the defect length is >1.5 × the bone diameter [6]. The range of critical bone defects in clinical practice is 1.5–3.0 cm. Biomechanical requirements (fixation strength), bone grafting strategies, and prognostic outcomes differ substantially across bone defects of different lengths.

The IMT was first reported by Masquelet et al.[7] IMT is an effective strategy for managing complex segmental bone defects. The process is divided into two stages. First, the bone defect is filled with bone cement for 6–8 weeks after radical debridement. The bone cement is then removed, and bone reconstruction is performed by bone grafting in the induced membrane [3]. Previous studies have reported mixed outcomes with IMT [8, 9]. Although IMT has been used for many years, the bone defect length in most studies is relatively limited [9, 10]. Its use for treating ultra-long segmental bone defects >12.0 cm has been reported [11-13]; however, no specific research has focused solely on ultra-long bone segmental defects.

In this study, we aimed to evaluate the clinical effectiveness and functional outcomes of IMT when used for ultra-large bone defects.

Materials and Methods

Study design and setting

This retrospective cohort study was conducted at our hospital between January 2018 and March 2024. All surgeries were performed by a high-volume subspecialist in osteomyelitis and nonunion. Ethical approval was obtained from our institutional review board, and the study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [14].

Participants

This study included patients with osteomyelitis who underwent staged IMT treatment.

The inclusion criteria were as follows: (1) osteomyelitis in the diaphysis or metaphyseal regions, (2) treatment with IMT, (3) a segmental bone defect length >12.0 cm before bone grafting, and (4) anatomical Cierny–Mader type IV osteomyelitis. The exclusion criteria were intra-articular infections and incomplete clinical data.

Patient flow and baseline data

Thirty-eight patients were included in this study (Fig. 1). The preoperative data and baseline patient characteristics are shown in Table 1.

Surgical procedure

The surgery was divided into two stages. In stage I, radical debridement was performed first. At least three independent deep tissue specimens were obtained for bacterial culture; pathological examination confirmed infection if there were more than five neutrophils/high-power field (×400) in more than five high-power fields. The bone defect was filled with antibiotic-loaded bone cement (Palacos® R+G, Heraeus Medical, Germany), which wrapped the broken bone ends and extended at least 1 cm beyond them. Palalos® R+G bone cement contained 0.5g of gentamicin per 40.0g; additionally, 4.0g of vancomycin (Vancocin, Italia

S.R.L.) and/or 4.0g of imipenem (Merck Sharp & Dohme Corp.) were mixed into every 40.0g of bone cement during the surgery according to the antimicrobial susceptibility test (AST) results. It is generally recommended to place a central core of plain bone cement (without added antibiotics) surrounded by a 2.0–3.0 mm outer layer of antibiotic-loaded cement, which can be described as a "bamboo-like" bone cement filling configuration. The cement was extended 2.0 cm beyond the fracture edges (Fig. 2).

In stage II, internal fixation and autologous iliac/allogeneic bone grafts were used. If external fixation was used in stage I, then it was removed 1 week before the second operation and replaced with a plaster cast. In this surgery, the induced membrane was carefully incised, and the bone cement was removed. Internal fixation was performed to stabilize bone defects.

Bilateral autogenous iliac bone, bone morphogenetic protein-loaded artificial bone, and allogeneic fibula were used to perform sufficient bone grafting. Allografting or a demineralized bone substitute was used at a ratio of ≤1:3 (allograft: autograft) to achieve sufficient graft volume or strength [15]. The bone grafting method used a "Swiss roll" technique, consisting of inner (allogeneic fibula or intramedullary nail), middle (allogeneic cancellous bone and/or antibiotic-loaded calcium phosphate cement), and an outer (autologous cancellous bone combined with thin cortical bone strips trimmed to 2.0 mm in width) layers (Fig. 2).

Postoperative care

Stage I: Partial weight-bearing was allowed on the affected limb within 1.5 months, and functional exercises were performed under the guidance of the doctors. Antibiotics were continued until stage II according to the AST, and intravenous antibiotics were administered for at least 2–4 weeks.

Stage II: No weight bearing was allowed on the affected limb within 1 week after the

operation. Subsequently, partial weight-bearing was allowed, and functional exercises were performed under the guidance of doctors. At the 3-month follow-up, full weight-bearing was allowed based on the fracture-healing shown on the computed tomography (CT) scan. At least 2–4 weeks of intravenous antibiotics were administered postoperatively according to the AST, followed by oral antibiotics, with a total treatment duration of at least 12 weeks.

Outcome assessments

X-rays and CT images of the affected limbs, white blood cell count, erythrocyte sedimentation rate, and C-reactive protein levels were evaluated at 1.5, 3, 6, and 12 months postoperatively, and then every 3–6 months. If no radiographic healing was observed at the 3-month follow-up, the patient was instructed to undergo radiography/three-dimensional CT every 1–2 months thereafter to assess bone healing.

Data were collected, including recurrence of infection, Self-rated Anxiety Scale score, radiographic bone healing, full weight-bearing time, Hospital for Special Surgery Knee Score, and American Orthopaedic Foot and Ankle Society Ankle-Hind Foot Score. The criteria for the recurrence of infection were local redness and swelling; purulent secretion or sinus tract; or elevated white blood cell count, C-reactive protein level, and erythrocyte sedimentation rate. Radiographic bone healing was defined as three or more sides of cortical bridging on anteroposterior and lateral radiographs and three-dimensional CT. Excellent outcomes were defined as bone union, absence of infection, deformity <7, and leg-length discrepancy <2.5 cm [16].

Statistical analysis

SPSS 25.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The normally distributed continuous data are expressed as means ± standard deviation.

Results

Baseline characteristics of patients are presented in Table 1. The rate of microbial infection was 71.1% (Table 2). Postoperative characteristics of the patients after stage II are presented in Table 3.

Outcomes of osseous union and functional recovery

The radiographic union rates were 57.8% at 4 months and 86.8% at 6 months. Table 3 shows the postoperative healing and recovery of patients. Follow-up results are shown in Table 4.

Complications and subsequent treatments

Three patients required a second debridement before bone grafting because of recurrent infections. One patient required a third debridement before grafting. Details of complications are provided in Table 5. One patient experienced nonunion with subsequent internal fixation failure 10 months postoperatively. The patient underwent revision fixation with autologous bone grafting and achieved good healing after 3 months of follow-up. One patient developed redness, swelling, and exudation at the incision site 1 month after bone grafting. The wound healed well after debridement and intravenous administration of antibiotics, with no recurrence of infection in >1-year follow-up. Four patients had limited knee and ankle joint functions, which improved through functional exercises under the guidance of rehabilitation doctors.

Typical case 1

A 44-year-old man with tibial and fibular fractures underwent open reduction and internal fixation with an intramedullary nail at a local hospital. Six months after the surgery, the

patient visited our hospital because of the formation of a sinus tract, and the microbial culture result showed *Enterobacter cloacae*. Debridement was performed, and the tibial intramedullary nail was removed. The infected bone (7.0 cm) was resected, and the bone defect was filled with bone cement loaded with imipenem and vancomycin. Eight weeks after the first debridement, localized redness and swelling appeared, requiring repeated debridement. During the second debridement, bone corrosion associated with inflammatory changes in the surrounding soft tissue was observed. Therefore, 11.0 cm of the infected bone was resected. The total length of the bone defect was 18.0 cm (Fig. 3). Twelve weeks after the second debridement surgery, when inflammatory indicators were normal, the bone defect was fixed using a plate combined with external fixation and filled with a bone graft. Radiological bone union was observed 5 months after bone grafting, and the limb achieved full weight-bearing 5 months after surgery. At the last follow-up, function was excellent, and the patient could walk and work without pain (Fig. 4).

Typical case 2

A 39-year-old man had a femoral fracture and underwent open reduction and internal fixation with a plate at a local hospital. Eight months after the surgery, the patient visited our hospital because of incision dehiscence and exudation, and the microbial culture result showed *Staphylococcus aureus*. Subsequently, debridement surgery was performed. A large segment of femur corrosion was observed during debridement, and a 22.5 cm infected bone was resected. The bone defect was fixed using external fixation and filled with bone cement loaded with vancomycin (Fig. 5). After 7 weeks, when the patient's inflammatory indicators were normal, the bone defect was fixed using an intramedullary nail combined with a locking plate and filled with a bone graft. Radiological bone union was observed 4 months after bone grafting, and the limb achieved full weight-bearing at 4 months after bone grafting. At the last

follow-up, there were no recurrences of infection (Fig. 5).

Discussion

The standardized fracture classification by the Arbeitsgemeinschaft fur Osteosynthesefragen (AO) and Orthopaedic Trauma Association (OTA) [17] is limited in its definition of bone defects [18], with classifications such as “none,” “some,” or “segmental” [19]. Tetsworth et al.[20] built on the AO/OTA fracture classification system and introduced a fourth category, labeled "D"[19, 20]. According to Ferreira and Tanwar [21], bone defect lengths are divided into <2.0 cm, 2.0–6.0 cm, 6.0–12.0 cm, and >12.0 cm. The cases included in this study belonged to type D3C according to Tetsworth et al.’s classification and type IV according to Ferreira and Tanwar’s classification. Research suggests that larger defect sizes were associated with higher odds of nonunion[22, 23]. When the bone defect size is greater than 62 mm, the success rate of Masquelet technique decreases[24]. However, there is almost no research on ultra long segmental bone defects, so this study focuses on exploring the effectiveness of Masquelet technique in treating these cases.

The current mainstay treatments for critical-sized bone defects include the Ilizarov technique, free vascularized fibular graft, and IMT [25, 26]. The principal advantage of the Ilizarov technique is its capacity for simultaneous tissue regeneration, which effectively resolves both bone and soft tissue defects in a single procedure. However, the mineralization time per cm of bone defect using the Ilizarov technique was approximately 1.5–2.5 months [27]. For ultra-large bone defects >12.0 cm, the bone healing time for the Ilizarov technique tends to be >18–30 months, and the prolonged use of the external frame can result in more severe complications such as mobility impairment and pin-tract infection [28-30]. Free vascularized fibular grafting demonstrates proven efficacy in massive bone defect reconstruction, with the added advantage of the osteocutaneous flap capability for simultaneous bone and soft tissue

restoration [31, 32]. However, this technique presents significant challenges, including surgical complexity, demanding microsurgical expertise, and potential donor-site morbidity [33].

Mi et al. [9] described the effect of IMT as “mixed” because some previous studies have observed good clinical results of IMT, accompanied by some complications [34]. However, the authors believe that complications, particularly infections, do not occur due to IMT but rather due to the debridement surgery [9]. IMT requires adequate soft tissue coverage, and flap reconstruction is necessary in cases of soft tissue defects. IMT offers distinct advantages for massive bone-defect management, including technical simplicity relative to microsurgical methods, reliable infection control via staged protocols, and a markedly shorter healing duration. Although a previous study reported a linear increase in healing time with IMT [35], recent research has found no significant correlation between defect length and healing time [36]. Our study revealed no definitive linear relationship between the defect length and healing time, with union rates of 57.8% at 4 months and 86.8% at 6 months. The observed outcome variations may be correlated with grafting techniques.

In the first stage of the Masquelet technique, complete resection of the infected tissue is important during debridement. The entire infected bone area is regarded as a cystic structure containing sequestrum, pus, and implant, whereas the junction between the infected and normal tissues is regarded as the cyst wall [37]. Complete resection involves removing all cystic structures, including bacterial biofilm, such as implants, sequestrum, sinus tract, scars, granulation, and non-vital tissues [38]. The preoperative plan requires determination of the extent of bone and soft tissue debridement based on imaging. Surgical management demands radical excision continued until visualization of the characteristic "paprika sign" (viable bone punctate hemorrhage) [39]. When it is difficult to determine the extent of infection intraoperatively, intraoperative frozen section pathology should be performed, with

consideration given to more extensive resection if indicated, and the findings should be confirmed by postoperative pathological examination [40].

Multiplanar three-dimensional stabilization is essential for ultra-large bone defects requiring greater fixation strength and longer-span external fixation. Occasionally, multiple unilateral external fixators can be used. This method enhances the structural integrity while promoting fracture site stability and infection management. Clinically available spacers include polymethylmethacrylate, calcium sulfate, calcium phosphate, and bioglass. Polymethylmethacrylate can be molded intraoperatively, allowing for more flexible placement while providing mechanical stability, making it a more suitable spacer for extensive segmental bone defects [41]. Schurman et al. indicated that antibiotic release occurs primarily within the superficial 100-micron layer, with few antibiotics released from the deeper layer [42]. Therefore, the "bamboo-like" bone cement proposed in this study reduces the total intraoperative local antibiotic dosage while increasing the antibiotic concentration on the cement surface.

The need for sufficient autogenous bone graft volume is a major disadvantage in the management of ultra-large segmental bone defects in the second stage of IMT [43]. This necessitates comprehensive bone harvesting, including bilateral anterior/posterior iliac crest autografts, Reamer-Irrigator-Aspirator technique, and augmentation with structural allografts, synthetic bone substitutes and allogeneic fibula. We recommend a "Swiss-roll" bone grafting technique, which provides structural support through the inner layer of allogeneic fibula or intramedullary nails, while the middle layer of allogeneic cancellous bone compensates for the limited availability of autologous bone. The outer layer, which is composed of highly osteogenic autologous bone, promotes optimal bone healing. In a retrospective study of 203 patients, the average healing time was 9.3 months[22]. In another study using IMT to treat an average 5.9cm defect, the average healing time was 6.6 months[44]. The mean bone healing

time in this study was 4.8±2.1 months, demonstrating the reliability and effectiveness of this technique in facilitating bone regeneration.

Ultra-large segmental bone defects require reinforced fixation to achieve sufficient stability for bone healing. Compared with routine fracture fixation, the reconstruction of ultra-large bone defects requires stronger internal fixation. Therefore, multiple locking compression plates (LCPs), the ortho-bridge system, LCP combined with external fixation, or an intramedullary nail combined with LCP are used to fix the fracture ends. Fixing should be done outside the induced membrane to avoid occupying the bone graft space and damaging the blood supply. Additionally, attention should be focused on restoring limb length and alignment during fracture reduction. Adequate postoperative drainage combined with a compressive dressing effectively prevents hematoma formation and subsequent infection. Strict follow-ups, functional exercises, and postoperative antibiotic management are important. In this study, all the patients achieved bone union with satisfactory joint function.

Limitations

The main limitations of the study are the small number of patients and the lack of a control group. Owing to personal privacy concerns, their race is not included in this study, which may affect the generalizability of the study. Further randomized controlled trials with larger sample sizes are required.

Conclusion

IMT demonstrates reliable clinical efficacy in treating ultra-large bone segmental defects >12.0 cm, consistently achieving both bone healing and functional joint recovery. In particular, it has distinct advantages in controlling infections and bone healing.

List of abbreviations

IMT: induced membrane technique; AST: antimicrobial susceptibility test; CT: computed tomography; AO: Arbeitsgemeinschaft fur Osteosynthesefragen; OTA: Orthopaedic Trauma Association; LCP: locking compression plates; AOFAS:American Orthopaedic Foot and Ankle Society; HSS: Hospital for Special Surgery; SAS: Self-rated Anxiety Scale.

Declarations

Ethics approval and consent to participate

This study adhered to the principles outlined in the Declaration of Helsinki and ethical approval was obtained from the Medical Ethics Committee of the Second Hospital of Jilin University, Changchun, China (No. 2025-194; approval date: 2025-05-23). The requirement for informed consent was waived by the Medical Ethics Committee of the Second Hospital of Jilin University owing to the retrospective nature of the study.

The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting observational cohorts. This retrospective study has been registered with the Chinese Clinical Trial Registry (registration number: ChiCTR2500109019; registration date: 2025-09-10).

Consent for publication was obtained from the subject. No identifying information is contained in the report. The patient had given written informed consent for their personal and clinical details along with identifying images to be published in this study.

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Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials. Further data that support the findings of this study are available from the corresponding authors, upon reasonable request.

Conflicts of interest statement: All the authors declare no competing interests. Consent for publication was obtained from the subject. No identifying information is contained in the report. The patient had given written informed consent for their personal and clinical details along with identifying images to be published in this study.

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476 **Tables**

477 **Table 1. Preoperative data and baseline characteristics**

Items	n=38
Sex	
Male	30 (78.9%)
Female	8 (21.1%)
Tibia	23 (60.5%)
Femur	15 (39.5%)
Ages (years)	Mean: 52.6±12.9 (range, 15–77)
Type of injury	
Closed injury	18 (47.4%)
Open injury	20 (52.6%)
Type of Host (C-M classification)	
A-Host	13 (34.2%)
B-Host	25 (65.8%)
Initial injury mechanism	
Traffic accident	14 (36.8%)
Falling	24 (63.2%)
Number of previous operations	2.6±0.8 (range, 2.0–4.0)
Previous fixation	
Plate fixation	28 (73.7%)
Intramedullary nail fixation	3 (7.9%)
External fixation	7 (18.4%)
Location	
Proximal	9 (23.7%)

Medial	25 (65.8%)
Distal	4 (10.5%)
Soft tissue defect	13 (34.2%)
Follow-up period (months)	Mean: 20.4±10.2 (range, 12.0–60.0)
Sinus tract	20 (52.6%)

Table 2. Details of pathogens

Pathogen	n=38
Staphylococcus aureus	10 (26.3 %)
Methicillin-Resistant *Staphylococcus aureus*	4 (10.5%)
Staphylococcus epidermidis	4 (10.5%)
Enterobacter cloacae	4 (10.5%)
Klebsiella pneumoniae	2 (5.3%)
Escherichia coli	1 (2.6%)
Proteus mirabilis	1 (2.6%)
Mixed consortium	1 (2.6%)
N/A	11 (28.9%)

N/A, not available

Table 3. Postoperative data after stage II

Items	n=38
Bone defect size (cm)	Mean: 16.0±4.1 (range, 12.2–28.0)
Flap coverage	13 (34.2%)
Duration of spacer (weeks)	Mean: 15.7±7.6 (range, 6.0–40.0)
Self-rated Anxiety Scale (no/mild/moderate/sever)	37/1/0/0
Time to radiological healing (months)	Mean: 4.8±2.1 (range, 3.0–13.0)
Time to full weight-bearing (months)	Mean: 5.2±1.8 (range, 3.0–13.0)
AOFAS score	Mean: 85.2±7.7 (range, 58–98)
HSS score	Mean: 85.1±6.3 (range, 71–95)
Complications [cases (times)]	4 (6)

AOFAS, American Orthopedic Foot and Ankle Society; HSS, Hospital for Special Surgery

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494 **Table 4. Evaluation of the results**

Results	Tibia	Femur	Total	Criteria
Excellent	21	12	33	Union, no infection, deformity < 7°, limb length discrepancy (LLD) < 2.5 cm
Good	2	3	5	Union plus any two of the following: absence of infection, deformity <7°, LLD < 2.5 cm
Fair	0	0	0	Union plus any one of the following: absence of infection, deformity < 7°, LLD < 2.5 cm
Poor	0	0	0	Nonunion/refracture/union plus infection plus deformity >7° plus LLD > 2.5 cm

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496 **Table 5. Details of complications**

Complications	Times
Internal fixation failure	1
Nonunion	1
Ankylosis of the joints	3
Infection recurrence	1
Total	6

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Figure Legends

Fig. 1 Patient flow chart. IMT, induced membrane technique

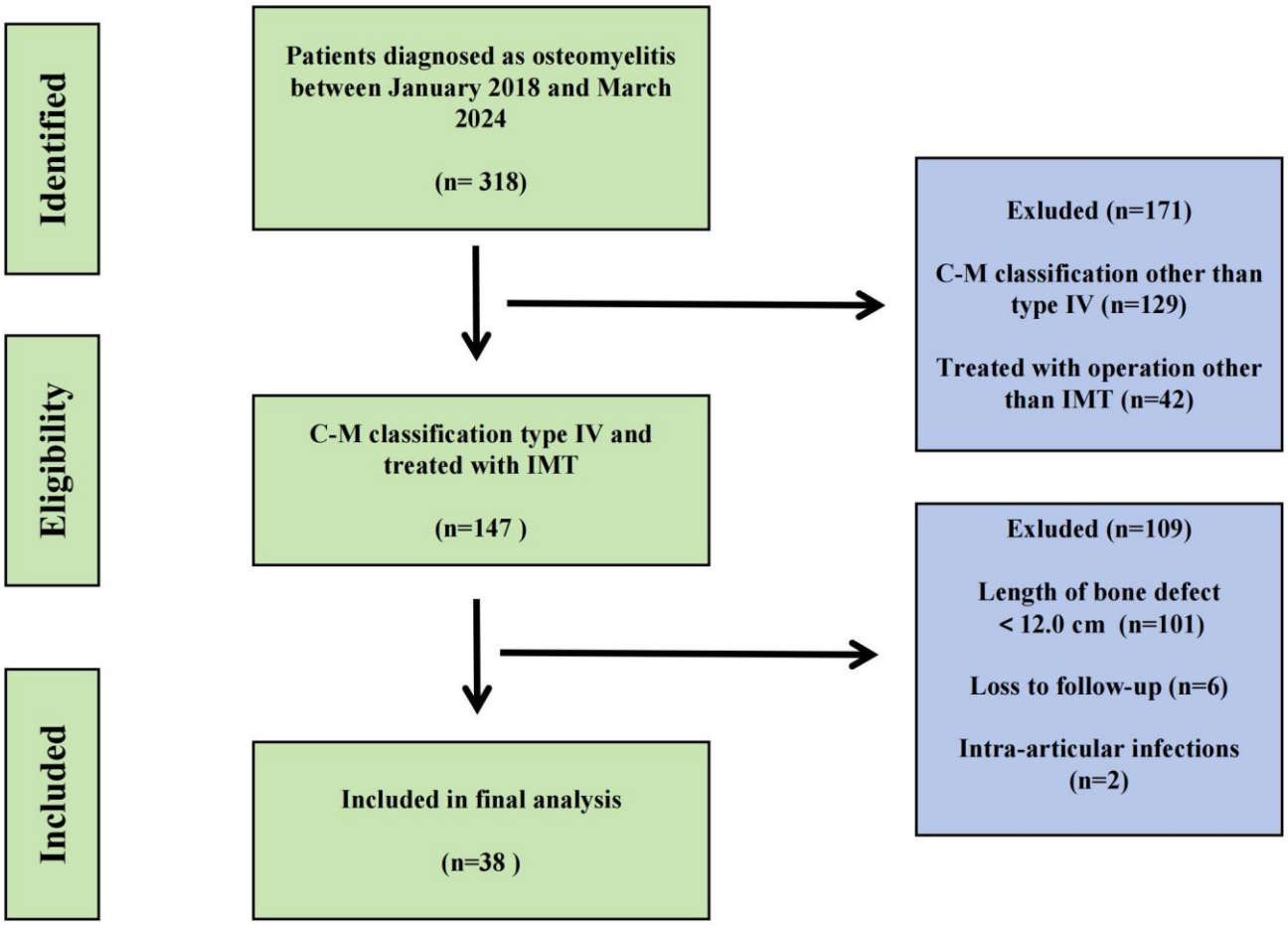


Fig. 2 Technical description of bone cement and bone grafting. (A) “Bamboo like” bone cement: a. bone cement column without additional antibiotics; b. expandable antibiotic-loaded bone cement; (B) “Swiss roll” bone grafting: a. allogeneic fibula; b. calcium phosphate cement; c. induced membrane; d. allogeneic cancellous bone; e. autogenous iliac bone.

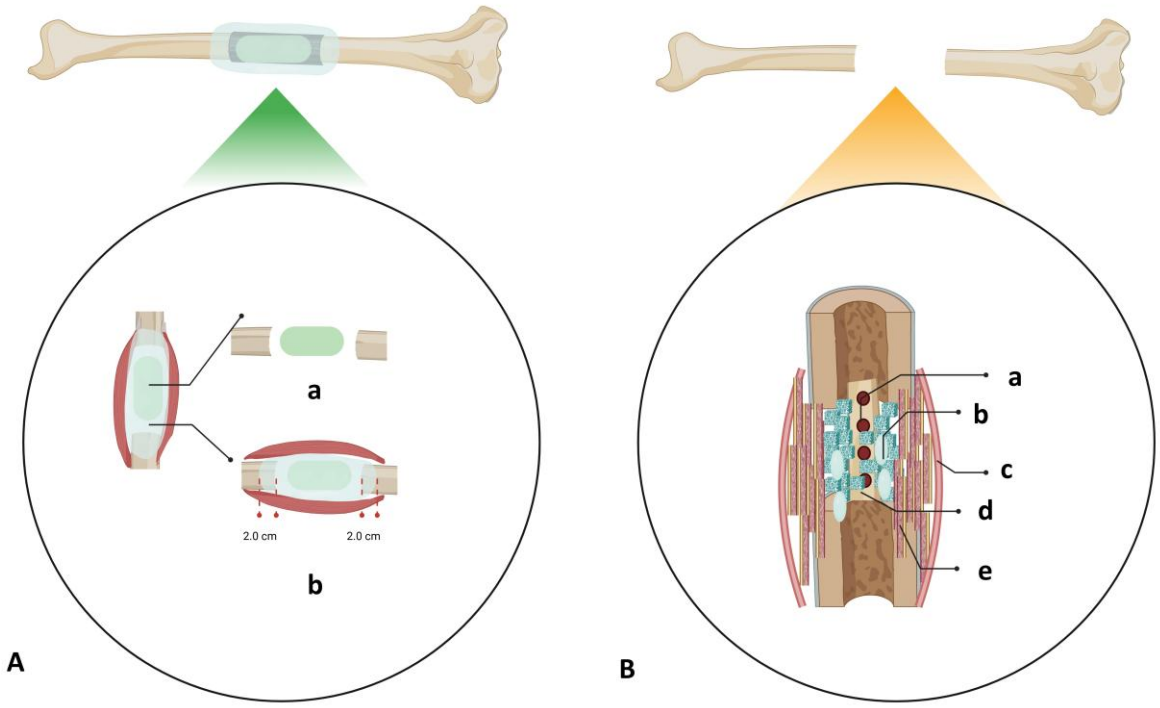


Fig. 3 Typical case 1 (stage I). (A) Preoperative radiograph before the first debridement; (B) preoperative appearance of the affected limb (the sinus tract is marked by a blue arrow); (C) intraoperative images of debridement; (D) postoperative radiographs; (E) appearance of the affected limb before second debridement; (F) intraoperative images of the second debridement surgery; and (G) radiographs after the second debridement.

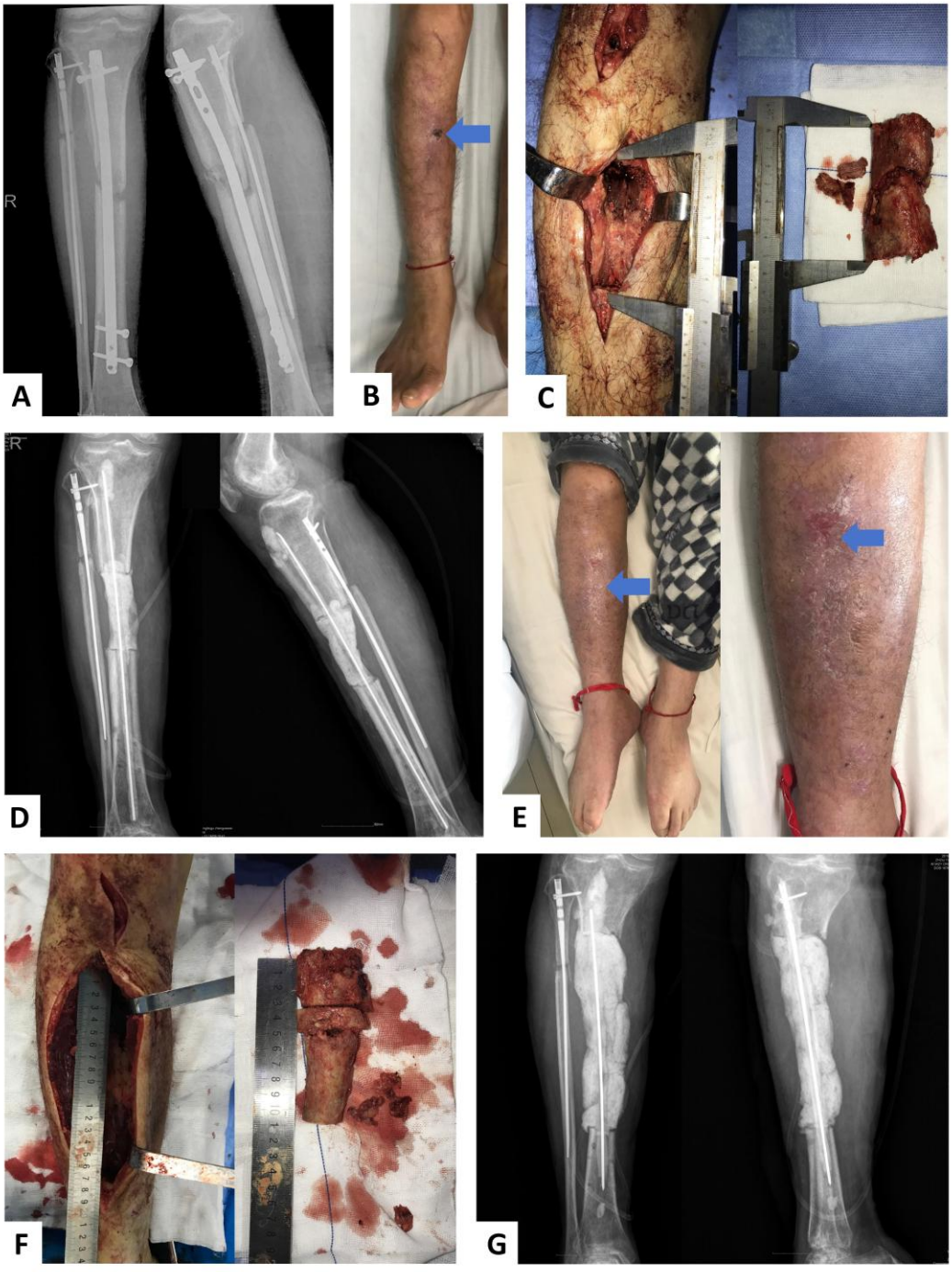


Fig. 4 Typical case 1 (stage II) and follow-up results. (A) Intraoperative imaging during bone grafting; (B–G) radiographs 3 days and 1.5, 3, 5, 12, and 18 months postoperatively; and (H) functional imaging 18 months postoperatively.

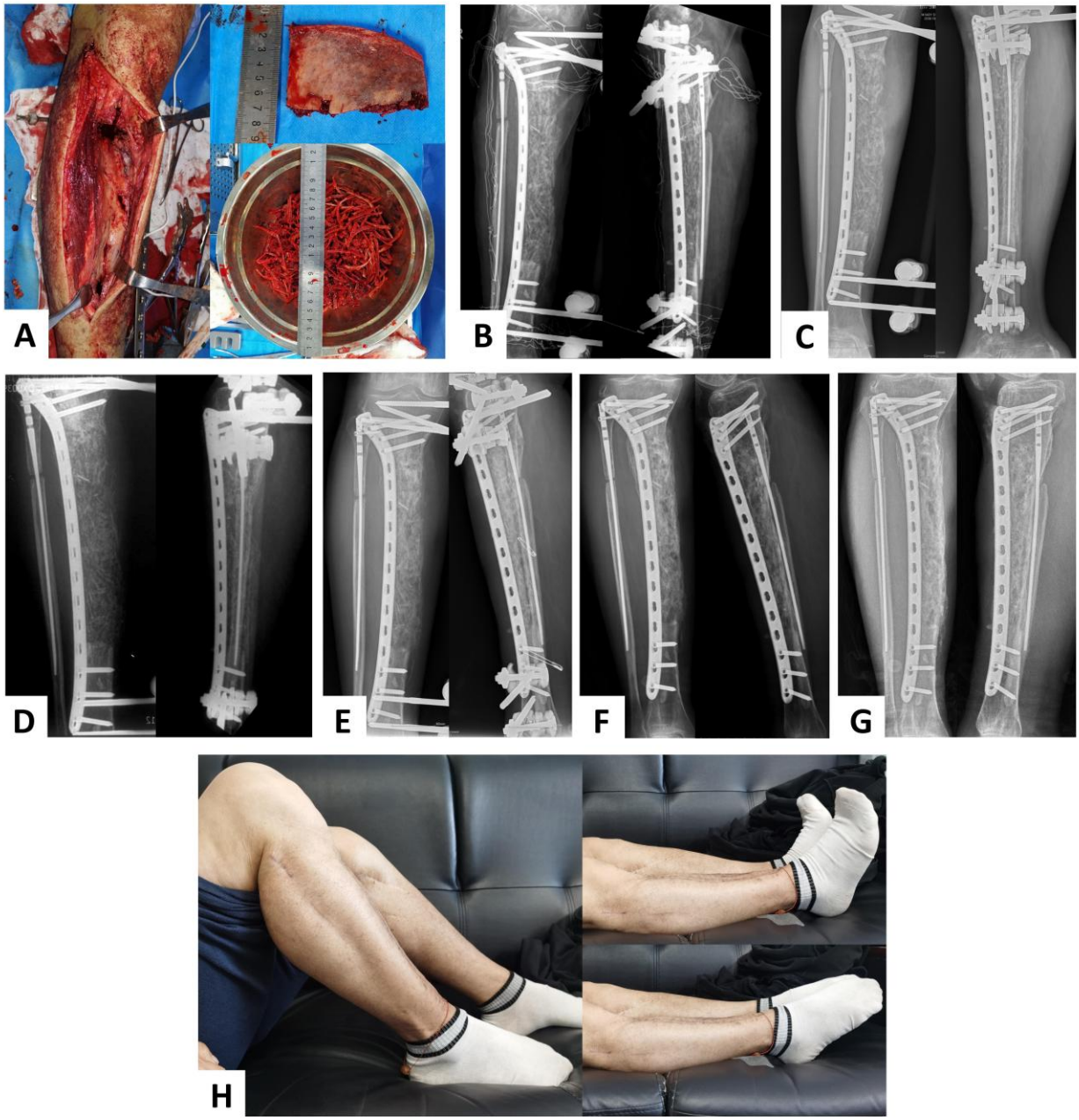


Fig. 5 Typical case 2. (A) Preoperative radiograph and appearance of the affected limb (the sinus tract is marked by blue arrows); (B) intraoperative imaging; (C) postoperative radiographs after debridement; (D) intraoperative imaging during bone grafting; (E–I) radiographs 3 days and 2, 4, 12, and 30 months postoperatively; and (J) functional imaging 30 months postoperatively.

