Wang *et al. BMC Surgery* (2025) 25:137
https://doi.org/10.1186/s12893-025-02865-1

BMC Surgery

RESEARCH

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Clinical outcome of chronic haematogenous osteomyelitis of the femur or tibia in adults using selective segmental osteotomy and induced membrane technique

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Abstract
Identification of infected lesions in chronic haematogenous osteomyelitis (CHOM) is challenging due to no distinct boundary. The optimal methods of debridement and bone reconstruction remain controversial. The aim of this study was to evaluate the clinical efficacy of selective segmental osteotomy with induced membrane technique in adult CHOM patients of the femur or tibia. The patients who underwent a staged surgery of induced membrane technique were include. In the first stage. the patients were treated by selective segmental osteotomy for debridement according to imaging result preoperatively. In the second stage, spacer removing, fixation and bone grafting were performed sequentially. 16 patients were included. The mean age was 34.7 years. After debridement, the mean bone defects length was 7.9 cm. At a mean followed-up of 30.5 months, no infection recurrence in all patients. At the last follow-up, all patients achieved bone union on average at 6.9 months. Visual Analogue Scale (VAS) score, Self-rated Anxiety Scale (SAS) score, and Hospital for Special Surgery (HSS) score improved at 3 months after the second stage of surgery and at the final follow-up compared with initial admission ($P < 0.05$). For adult patients with CHOM of femur and tibia, selective segmental osteotomy with induced membrane technique is a feasible and effective treatment method.

Keywords Chronic osteomyelitis, Femur, Tibia, Induced membrane technique, Internal fixation

Introduction

Haematogenous osteomyelitis is may result from hematogenous bacterial emboli from a distant source lodging in the bone, the contiguous spread of an adjoining soft-tissue infection [1]. In high-income countries, acute haematogenous osteomyelitis has an estimated incidence about 8 of 100,000 children per year [1, 2]. In the United States, patients with haematogenous osteomyelitis account for approximately 19% of the total of osteomyelitis [3]. Children typically have good outcomes with accurate diagnosis, appropriate antimicrobial therapy and radical surgical debridement [3]. Nevertheless, with a lack of care during the initial episode, up to 9% of paediatric patients with acute haematogenous osteomyelitis experience serious long-term sequelae [4], can delay recurrence in adulthood and develop into chronic haematogenous osteomyelitis (CHOM). In southern China, chronic haematogenous osteomyelitis accounts for approximately 16.0–17.9% of the total number of chronic

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osteomyelitis [5, 6].Due to the lesion on the bone and soft tissues of the affected limb, the majority of patients suffer from a poor quality of life and the loss of labor skills because pain, drainage, fistula or abscess.

The treatment of chronic osteomyelitis often depends on surgery with radical debridement and resection of lesion bone, and the result of treatment is the forming of critical-size infected bone defect. Masquelet et al. [7, 8]. reported a two-stage surgical treatment of bone defects, namely the induced membrane technique. This technique has been successfully applied to the treatment of bone defects caused by various reasons (including infected bone defects), and long-term follow-up has also confirmed the reliability of this method [9–11]. However, unlike post-traumatic osteomyelitis, adult haematogenous osteomyelitis is often accompanied by long segments of bone cortex thickening and periosteal reaction due to perennial infection stimuli, and bone morphology is markedly altered, making it a challenge to determine the site and extent of the infected lesion.

The purpose of this study was to evaluate the clinical efficacy and feasibility of a surgery using selective segmental osteotomy with the induced membrane technique in patients with CHOM of the femur or tibia in adults.

Materials and methods

Subjects

This case series study protocol was approved by the Institutional Ethics Committee of the 920th Hospital. All study participants provided written informed consent prior to the start of the study. We retrospectively analyzed data from patients with CHOM of the femur and tibia who underwent surgery by our surgical team between January 2016 and January 2021. Inclusion criteria were as follows: (i) patients who had haematogenous osteomyelitis of the femur and tibia in childhood and did not recover or relapsed in adulthood; (ii) with local manifestations such as pain, swelling, draining fistula, fever and sepsis e tc.; (iii) a segmental bone defect after debridement with the length of the defect exceeding 4 cm; (iv) patients who underwent two-stage surgery using the Masquelet technique; (v) patients aged 16–60 years. Exclusion criteria were: (i) Patients with physiological Cierny-Mader class C; (ii) History of open trauma or fracture in the affected limb; (iii) Incomplete follow-up data.

Surgical technique

Pre-operative Preparation

All patients were confirmed by a combination of history, clinical examination, X-ray, CT scan, magnetic resonance imaging (MRI) and radionuclide bone scintigraphy. The infected focus and the extent of the osteotomy were determined according to the clinical presentation, local symptoms and preoperative imaging finding, including MRI, CT, and radionuclide bone scintigraphy. MRI detects bone marrow edema and abscess formation, CT identifies sequestra, and radionuclide scans localize areas of increased tracer uptake. Since most patients with chronic hematogenous osteomyelitis do not present with fractures or other confounding factors, areas of radionuclide uptake typically indicate infection sites.

Surgical procedure

The first stage surgery

The sinus tract, necrotic tissue and sequestrum were removed. According to the debridement range determined preoperatively, the infected bone was resected segmentally until punctate bleeding appeared at the bone ends ("Paprika sign"). Then medullary cavity was grinded with a hard reamer inserted from the broken ends until the necrotic soft tissue in medullary cavity was completely removed. The infected soft tissue and bone were harvested for bacterial culture and pathological examination. After rinsed with 3000 mL normal saline, a locking compression plate (LCP; Ausmai, China) was used to stabilized the both ends of bone defect. Meanwhile, Antibiotic-loaded Polymethyl methacrylate (PMMA) bone cement (Heraeus, Hanau, Germany) was prepared by assistant, the routine is to add vancomycin (Eli Lilly, Tokyo, Japan) 2 g to every 40 g of bone cement. 2 Kirschner wires were wrapped with antibiotic bone cement to make 2 bone cement rods with a diameter of 6 ~ 8 mm. After debridement, the solidified rods were inserted into proximal and distal medullary cavities, respectively. The remaining vancomycin bone cement was utilized to fill in the bone defect, wrapped the bone ends and LCP. The ice water was used to cool down the bone cement spacer. 2 drainage tubes were placed and the wound was sutured layer-by-layer. If there would be a soft tissue defect, the flap technique was used to cover the wound.

Management of interval

The drainage tube was placed for 7 to 14 days, and the drainage fluid was less than 30 ml for 3 consecutive days before being pulled out. According to the bacterial culture, sensitive antibiotics were utilized for continuous antibiotic treatment for 2 weeks, and a third-generation cephalosporin (ceftazidime) was administered if no bacteria were isolated. This was followed by 4 weeks of oral antibiotics (levofloxacin 400 mg + rifampicin 450 mg per day). In case of recurrence of infection, debridement was repeated until the infection is controlled. The white blood cells (WBCs), C-reactive protein (CRP) level, and erythrocyte sedimentation rate (ESR), were measured every two weeks. The second-stage surgery was performed until the results of WBCs, CRP and ESR were normal for at least 2 times. During this interval, the involved limb was allowed to exercise, but no weight-bearing was conducted.

The second stage surgery

The second-stage surgery was conducted more than 6 ~ 8 weeks after the first-stage surgery. Before the surgery, the volume of the bone defect was estimated according to the CT scanning [12]. The induced membrane was incised sharply and exposed the bone cement. The bone cement, internal fixation, and bone cement rods were removed. After reamed medullary cavity and rinsed, the bone defect was fixed with intramedullary nail (IMN) and/or LCP in accordance with the location of involved bone. The graft harvested from both side posterior superior iliac spine was cut to a size of 8 ~ 10mm^3, and filled in the bone defect. The induced membrane was sutured. Sensitive antibiotics were administered for 2 weeks postoperatively, and suction drainages were applied for 7–14 days.

Postoperative follow-up and data collection

All patients were followed up regularly at 1, 2, 3, 6, 9, 12, 18 and 24 months after the stage II surgery, the anteroposterior (AP) and lateral radiographs of the affected limb, WBCs, CRP and ESR were obtained to assess bone defects union and infection control at routine follow-up intervals. The radiographs were independently assessed by two authors in an unblinded fashion. Another author would intervene to assess the radiograph if there was disagreement. CT scans were performed if radiographs did not clearly show bone union. The time of weight-bearing was determined according to the results of these images.

These data were collected to assess the clinical outcome: (1) Visual Analogue Scale(VAS), hospital for special surgery(HSS) knee score and Self-rated Anxiety Scale (SAS) score of initial admission, three months after stage II and at the last time follow-up; (2) WBCs, CRP and ESR of initial admission, three months after stage II and at the last time follow-up; (3) Radiographic bone healing time and total weight-bearing time; (4) Complications.

We defined radiographic bone union as the presence of bridging callus on three out of four cortices on the AP and lateral radiographs. Infection recurrence refers to the recurrence of pain, redness, sinus tract and other local manifestations, as well as WBCs, ESR and CRP increased continuously. The complications included the presence of Infection recurrence, nonunion of bone defect, bone resorption, and re-fracture etc. Efficacy assessment included infection control, bone union, and complications. Complications were assessed by the surgeons involved in the treatment of the patients. At the last follow-up (at least 24 months), the treatment outcome was considered "healing" if the patient had no symptoms of recurrent infection such as local redness, swelling, pain, or sinus in the affected limb, radiological imaging showed good bone healing without deformity, and there were no other complications.

Statistical analysis

SPSS 25.0 software (SPSS Chicago, IL, USA) was used for statistical analysis. The patients' VAS, HSS knee score and SAS score at baseline, three months after stage II surgery and at the last follow-up were tested for normality of data using the Shapiro-Wilk test. Continuous data conforming to the normal distribution were expressed as mean ± standard deviation ($\bar{X} \pm S$). Student's t-test was used to compare them between two groups. The value was taken as 0.05 on both sides. $P < 0.05$ was defined as a statistically significant difference.

Results

Demographics of subjects

A total of 16 patients (14 males) were included in this study. The patients with a mean age of 34.7 years (range 17–56 years), and the mean duration of osteomyelitis ranged 20.0 years (range 0.6–40 years). The infection was located in the tibia in 9 cases, followed by femur in 7 cases. Besides, 10 cases had sinus tract or local redness, swelling, as well as fever of the affected limbs. The Cierny-Mader classification showed 4 cases of type III, and 12 cases of type IV. In addition, 12 cases had been operated on between 1 and 5 times in other hospitals (Table 1).

Surgical-related parameters

The deep tissue culture was positive in 9 patients, including 5 strains of *Staphylococcus aureus*, 2 Methicillin-resistant Staphylococcus aureus (MRSA), 1 *Escherichia coli*, and 1 *Pseudomonas aeruginosa* (Table 1). After the first stage surgery, 15 patients were fixed with an LCP as internal fixation, a patient with external fixation. Skin flaps were used to cover wounds in 5 patients, including 4 calf fasciocutaneous flaps and 1 thigh fasciocutaneous flaps. 3 patients required re-debridement due to infection recurrence, all patients were relieved after once or twice re-debridement. 2 patients performed skin grafting due to partial necrosis of the flap tips (Table 2).

The mean interval time between two stages was 10.4 weeks (range, 6–38 weeks). The mean length of the bone defects was 7.9 cm (range, 5 ~ 12 cm) (Table 1). After the stage II, 8 patients were fixed with IMN plus LCP, 5 LCP and 2 IMN alone. All patients were followed up for 30.5 (range from 22 to 47) months. The radiological bone union time was 6.9 (range from 4 to 11) months, and the full weight-bearing time of the affected limb was 8.4 (range from 5 to 14) months. 1 patient developed infection of donor site, and the wounds were healed after repeated debridement; 1 patient had local graft

Table 1 Demographics and clinical outcomes of patients

Patient	Age (years)	Sex	Location	Cierny-Mader types	Duration of infection (years)	Sinus tract	Times of prior surgeries	Types of Bacteria	Interval of stage I & II (weeks)	Bone defect size (cm)	Follow-up period (months)	Radiological union (months)	Full-weight bearing (months)
1	29	M	Tibia	III	15	Yes	2	No growth	6	5	47	9	9
2	56	M	Femur	IV	38	None	0	MRSA	38	9	36	8	10
3	27	M	Femur	IV	13	Yes	2	No growth	8	6	34	5	5
4	44	F	Femur	IV	32	Yes	4	No growth	8	8	22	9	12
5	31	M	Femur	IV	18	None	0	S. aureus	9	7	34	5	5
6	47	M	Tibia	IV	33	Yes	0	MRSA	9	12	44	10	10
7	33	M	Femur	IV	24	Yes	0	S. aureus	12	9	24	7	7
8	16	M	Tibia	IV	0.6	Yes	2	No growth	7	8	27	5	8
9	18	M	Tibia	IV	0.9	Yes	2	P. aeruginosa	7	9	28	5	6
10	29	M	Femur	IV	17	Yes	5	No growth	12	11	26	11	14
11	24	M	Tibia	III	3	Yes	3	S. aureus	6	5	32	4	5
12	26	M	Femur	III	9	None	3	No growth	6	6	23	6	7
13	48	M	Tibia	III	27	None	4	No growth	6	4	26	7	9
14	42	M	Tibia	IV	31	None	2	*E. coli*	16	9	22	7	10
15	33	F	Tibia	IV	19	None	5	S. aureus	8	11	25	7	11
16	51	M	Tibia	IV	40	Yes	1	S. aureus	9	8	38	6	7

Note: MRSA: Methicillin-resistant Staphylococcus aureus; *S. aureus*: Staphylococcus aureus; *S. epidermidis*: Staphylococcus epidermidis; *P. aeruginosa*: Pseudomonas aeruginosa; *E. coli*: Escherichia coli

Table 2 Complications of soft tissue coverage after debridement

Patient	Method of soft tissue coverage	Complication	Manage-ment
1	Tension-reducing suture	Delayed healing	Repeated dressing
2	Thigh fasciocutaneous flap	None	None
3	Primary closure	None	None
4	Primary closure	None	None
5	Primary closure	None	None
6	Calf fasciocutaneous flap	Partial Necrosis	Re-debride-ment and skin grafting
7	Primary closure	None	None
8	Primary closure	None	None
9	Primary closure	None	None
10	Primary closure	None	None
11	Calf fasciocutaneous flap	None	None
12	Primary closure	None	None
13	Tension-reducing suture	None	None
14	Primary closure	None	None
15	Calf fasciocutaneous flap	Partial necrosis	Re-debride-ment and Skin grafting
16	Calf fasciocutaneous flap	None	None

resorption, which was by re-grafting. 1 patient with IMN and LCP had a non-healing postoperative wound due to rejection of the implanted allograft bone, which was re-debridement and healed after removal of the LCP and some of the allograft bone. At the last follow-up, no infection recurrence was found. All patients reached bone union and there were no complications such as loosening or breakage of internal fixation (Fig. 1). WBC, ESR, CRP, VAS score, SA score, and HSS score improved at 3 months after the second stage of surgery and at the final follow-up compared with those at the time of admission, and the differences were statistically significant ($P<0.05$); except for ESR and HSS scores, the differences between the final follow-up and 3 months after the second stage of surgery were not statistically significant ($P>0.05$)(Table 3).

Discussion

The present study suggested that the combination of selective segmental osteotomy and the induced membrane technique in adult patients with CHOM of the femur or tibia could effectively control infection, relieve patients' symptoms, achieve bone union and reduce the incidence of complications.

The identification of infected lesions in CHOM is a dilemma due to there is no distinct boundary between a non-infected and infected bone [12]. The extent of the lesion is accurately localized preoperatively by imaging such as radiography, CT, radionuclide bone scintigraphy, and MRI [13]. Compared to radiography, CT provides more detail of the bone structure and evidence of infection: reactive cortical bone, sequestrum and intraosseous fistulae [14]. Magnetic resonance imaging (MRI) accurately reflects the extent of soft tissue involvement and provides the extent of intramedullary lesions, but edema may have an impact on the determination of infection [15]. Radionuclide bone scintigraphy uses radiopharmaceuticals to visually track pathophysiological changes in bone tissue, such as fracture healing, bone reconstruction, and inflammatory response following infection, and combines functional imaging with morphological imaging, to precisely localise suspected infected lesions and help differentiate between bone and soft tissue infection [16]. However, fracture union occurs with similar pathophysiological changes, so Radionuclide bone scintigraphy needs to be combined with history, physical examination, and MRI to more accurately determine the extent of the infected lesion and the location of the dead bone [17].

Treatment of CHOM involves surgery and antibiotic therapy. Surgery is the most important method for controlling bone infection. An aggressive debridement is essential to prevent infection recurrence [18]. Eckardt et al. [18]were the first to apply segmental osteotomy (*en bloc*) to manage the chronic bone infection. This method had previously been used to treat giant cell tumors of bone. All patients were followed up for an average of 58 months with no infection recurrence. Ozan et al. [19] demonstrated that radical resection combined with the induced membrane technique achieved an 85% treatment success rate in cases of Cierny-Mader type III/IV post-traumatic osteomyelitis. A clinical randomised controlled study by Simpson et al. demonstrated that, in patients with Cierny-Mader physiological classification of class A or B, the resection of more than 5 mm of normal bone and 2 mm of normal soft tissue significantly reduced the rate of recurrence of infection [20]. In this study, all adult CHOM patients had extensive bone and soft tissue involvement, and the lesions could not be completely removed by opening or irrigation, so bone debridement was performed by segmental resection and turning infected wounds into contaminated. There was no recurrence of infection after debridement in all patients, confirming t segmental Osteotomy is a reliable method for debridement.

After radical debridement at the first stage, the broken ends of the bone defect must be stabilized to maintain the limb length and alignment, provide a stable environment for induced membrane formation, and is also beneficial to the control of infection [21, 22].The method of fixation must ensure the following requirements: the overall structure is stable and does not increase the risk of infection recurrence. Types of fixation include external fixation and internal fixation. Zhang et al. [23]. compared

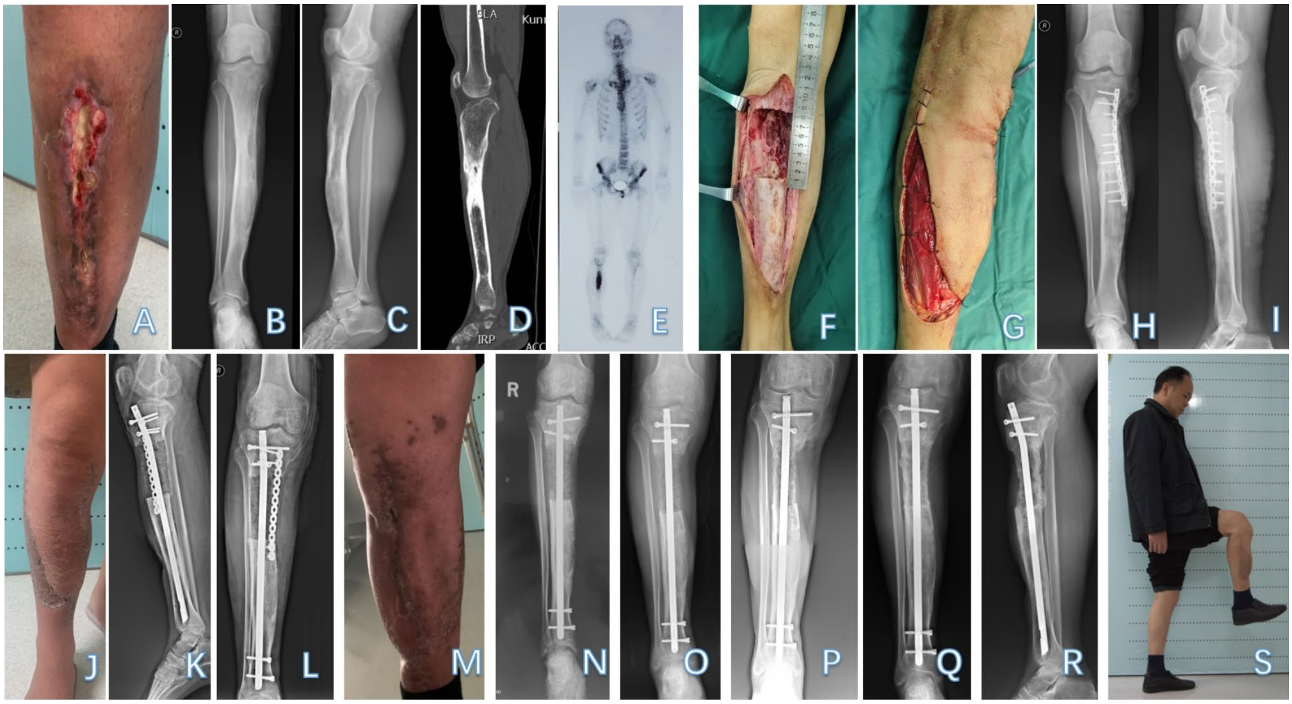

Fig. 1 Patient #16, Cierny-Mader type IV osteomyelitis in the right tibial shaft. **A**: preoperative appearance of the right leg; **B**: preoperative anteroposterior (AP) radiograph of the right leg; **C**: preoperative lateral radiograph of the right leg, there was a kyphosis deformity at the middle of the affected limb; **D**: preoperative CT image of right leg; **E**: preoperative whole body radionuclide scanning; **F**: after selective osteotomy according to preoperative imaging results, there was an 8 cm long bone defect in the right tibia; **G**: Skin defect formed after soft tissue debridement, which was covered with a calf fasciocutaneous flap; **H**: AP radiograph of the right leg after the first stage surgery; **I**: lateral radiograph of the right leg after the first stage surgery, the deformity was corrected; **J**: the appearance of the right leg before the second stage surgery; **K**&**L** AP and lateral radiographs of the right leg after the second stage surgery; **M**: 1 month after the second stage surgery, the incision did not heal and there was a small amount of drainage; **N**: AP radiograph 3 months after the second stage surgery, the plate and part of allograft were removed; **O**: AP radiograph 6 months after the second stage surgery, bone defect achieved radiographic union; **P&R**: AP and lateral radiographs 23 months after the second stage surgery. **S**: the appearance of the right leg, the knee function is good

Table 3 Comparison of clinical data between initial admission and post-operation ($n = 16$)

Index	Initial admission	Three months after stage II surgery	The last follow-up	*P* value	P1 (Initial admission vs. Three months after stage II surgery	P2 (Initial admission vs. The last follow-up	P3 (Three months after stage II surgery vs.The last follow-up)
WBC ($\bar{x} \pm s$, $\times 10^9$)	12.85 ± 3.83	6.99 ± 1.79	6.28 ± 1.76	< 0.001	< 0.001	< 0.001	0.266
ESR ($\bar{x} \pm s$, mm/H)	63.84 ± 20.87	12.25 ± 3.51	7.49 ± 2.53	< 0.001	< 0.001	< 0.001	0.001
CRP ($\bar{x} \pm s$, mg/L)	66.44 ± 20.79	15.06 ± 4.91	14.19 ± 4.55	< 0.001	< 0.001	< 0.001	0.633
VAS score ($\bar{x} \pm s$)	6.19 ± 1.11	2.06 ± 0.68	1.94 ± 0.68	< 0.001	< 0.001	< 0.001	0.609
SAS score ($\bar{x} \pm s$)	55.69 ± 12.21	47.94 ± 7.59	42.00 ± 7.63	0.001	0.002	0.002	0.017
HSS knee score ($\bar{x} \pm s$)	67.25 ± 13.67	83.06 ± 6.17	88.38 ± 6.39	< 0.001	< 0.001	< 0.001	< 0.001

*Compared with preoperative value, $P < 0.05$; # compared with the value at 3 months after stage II surgery, $P < 0.05$

WBC, white blood cell; ESR, erythrocyte sedimentation rate; CRP, C-reaction protein; VAS, visual analogue scale; SAS, self-rating anxiety scale; HSS, Hospital for Special Surgery

internal and external fixation after debridement in the induced membrane technique for tibial post-traumatic osteomyelitis with segmental osteotomy, then concluded that there were no differences between the two fixation methods after debridement in the first stage of the induced membrane technique for tibia osteomyelitis. The choice of fixation method is based on the location of the defect. Early studies and the latest meta-analysis results showed that the use of IMN in the first stage will increase the recurrence rate of infection after bone reconstruction of the second stage surgery, IMN is not recommended for the first stage surgery [24]. For metaphyseal defects, external fixation is the first choice [25], but it is difficult to avoid some inherent complications (pin tract infection, loosening, poor stability et al.), and it cannot reduce infection [26–28]. In this study, we performed internal fixation coated with antibiotic-loaded bone cement (Chongqing technique) as methods of stability in most patients at the first stage, and the fixation was replaced by a definitive internal fixation method at the second stage, the method of stability has achieved satisfactory clinical results and better comfort for patients. Because of the higher stability requirements of the second stage and to avoid small amounts of bacteria in biofilm colonising on the internal fixation surface, the internal fixation must be replaced during the second surgery.

In recent years, bone defect reconstruction techniques have advanced rapidly. Classic bone transporting techniques, vascularized fibula grafting and open bone grafting are often associated with long treatment time, high complications, or high technical requirements [29, 30]. However, due to simple operation, rapid bone union and the bone union duration is independent of the length of the bone defect. the induced membrane technique has gradually become the "gold standard" for the treatment of reconstruction of bone defects [31]. Fung et al. [28]. systematically reviewed and meta-analysed of 1,386 cases of outcomes and predictive variables for the management of long bone defects using the induced membrane technique, and showed that 82.3% of cases achieved bone union after grafting by one time, and the mean time was 6.6 months (1.4 to 58.7). Furthermore, 10% of cases were positive for a deep infection recurrence and 18.2% of cases required further procedures. This technique was shown to be an effective management strategy for critical segmental bone defects. Raven et al. [11]. used the induced membrane technique to treat bone nonunion with a mean time to bone union of 12.1 months, 72% of patients had infection controlled and bone union achieved and most importantly 46.7% of patients had no complications. Jia et al. [32]. used an antibiotic bone cement-coated locking steel plate for internal fixation to temporarily stabilize fracture ends after stage I debridement in 183 patients with infected lower limb bone defects, and only 8.7% of patients experienced recurrent infection. Wang et al. [33]. used the induced membrane technique to treat 15 patients with CHOM of the tibia. No infection recurred, the radiological bone healing time was 3 to 8 months. Our previous studies have confirmed that early debridement combined with the induced membrane technique is an effective treatment for paediatric patients with CHOM, but there are significant different between children and adults in the pathological features, and the reconstruction strategy needs to be adapted accordingly [34, 35].In this study, all cases were adult CHOM, the bone defect was union within an average 6.9 months, and the patient's pain sensation and anxiety were significantly improved, increasing the health-related quality of life. This result confirms that the induced membrane technique is equally effective in the treatment of adult CHOM.

The limitations of the present study should be noted. First, this is a single-center retrospective study, which is subject to selection and indication bias. Second, the follow-up period was also short. Thirdly, there is no control group to compare the results with. Therefore, further multicenter studies with large sample sizes are needed to address these limitations and verify the results of the present study.

Conclusions

In conclusion, selective segmental osteotomy with the induced membrane technique is a feasible and effective treatment for adulthood patients with CHOM. It can reduce surgical trauma, decrease the difficulty of bone defect reconstruction, and does not increase the recurrence rate of infection. However, an experienced surgeon is required to accurately determine the site and extent of the infection based on preoperative imaging.

Abbreviations

CHOM	Chronic haematogenous osteomyelitis
PMMA	Polymethyl methacrylate
LCP	Locking compression plate
MRI	Magnetic resonance imaging
CT	Computed tomography
WBC	White blood cells
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
VAS	Visual analogue scale
HSS	Hospital for special surgery
SAS	Self-rated anxiety scale
MRSA	Methicillin-resistant *Staphylococcus aureus*
IMN	Intramedullary nail
AP	Anteroposterior

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12893-025-02865-1.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

Conception and design, JS and YW; Material preparation and data collection: JYL, XJZ, XYY and MGS; Funding acquisition: JS and YQX; Statistical analyses: YW, JYL, and XJZ; Methodology: JS and YW; Writing-original draft: YW; All authors have read and agreed to the published version of the manuscript.

Funding

This study was funded by the Applied Basic Research Joint Project of Yunnan Science and Technology Department and Kunming Medical University (202101AY070001-294), the grants from Yunnan Orthopaedics and Sports Rehabilitation Clinical Medicine Research Centre (202102AA310068) and Clinical Key Subject Construction Project of PLA.

Data availability

Data is provided within the manuscript or supplementary information files. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All procedures were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. This study was approved by the institutional review board with approval No. 2024-072-01 from the 920th Hospital of the Joint Logistics Support Force of the PLA. Informed consent was obtained from all individual participants included in the study. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 21 October 2024 / Accepted: 21 March 2025
Published online: 05 April 2025

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