RESEARCH ARTICLE

The Outcomes of Distraction Osteogenesis over an Intramedullary Nail for the Treatment of Bone Defects in Infectious Nonunions

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Abstract

Objectives: The concurrent utilization of an external fixator and intramedullary nail (IMN) for segment transportation may potentially decrease the duration of external fixator implementation and reduce associated complications. This study aimed to report the outcomes of bone transport utilizing a combination of IMN and Ilizarov frame in a cohort of individuals who had tibia or femur critical-sized bone deficiency resulting from nonunion.

Methods: The present research used a single-arm clinical trial design to enroll a series of patients presenting with critical-sized bone defects resulting from infectious nonunion of the tibia or femur. The study was conducted during the period of 2017-2020 in a referral Orthopedic Surgery Center located in Tehran, Iran. The management of patients with infectious nonunion was carried out through two main stages, including infection eradication and bone transportation. The process of bone healing and segment transportation was evaluated by radiographic assessment throughout the follow-up period.

Results: A total of 39 patients with bone defects in the tibia (19 cases) or femur (20 cases) with a mean age of 31.44 (±11.95, range=18-60) were included in this study. Twenty-nine (74.3%) patients had open fractures. The bone defect exhibited an average size of 6.31 ± 1.95 cm. The mean of the consolidation index (CI) was 0.97 (range=0.51–1.32) mo/cm, and the mean of the external fixator index was 0.67 (range=0.41-1.10). Although the CI was longer in patients with open fracture compared to those with closed fracture, the difference was not statistically significant (P=0.353). After the end of the two-year follow-up, complete union was observed in 35 patients (89.7%).

Conclusion: Intercalary segmental bone transportation using the Ilizarov technique over an IMN, as well as preserving the advantages of the conventional callotasis method, reduces the complications of long-term use of the Ilizarov frame and increases patient adherence to treatment.

Level of evidence: IV

Keywords: Bone defect, Ilizarov technique, Infectious nonunion, Intramedullary nail, Segment transport

Introduction

In the case of long bone fractures, nonunion is defined as the absence of radiological evidence of healing for a period of three months or the lack of complete union for an interval of six to nine months. Nonunion is classified into hypertrophic, atrophic, and infectious types based on radiological and laboratory characteristics.[1]

The management of infectious nonunion involves an integrated strategy that combines both medical and surgical interventions. It is now widely accepted that in the case of an infectious union, the priority is to eliminate the infection before proceeding with the union; therefore, debridement and complete removal of necrotic tissue and devitalized bone constitute an essential component in the

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management of this injury. Hence, bone defect is a frequently occurring complication during the management of infectious nonunions.[2]

Bone defects may arise from a multitude of factors, including but not limited to tumors, traumatic injuries, and osteomyelitis. However, the most common cause of bone defects in long bones is trauma and its complications, such as nonunion.[3] The reconstruction of critical-sized diaphyseal bone defects has consistently posed a formidable challenge for orthopedic surgeons. In 1987, a novel technique was introduced by Dr. Ilizarov that relied on distraction osteogenesis caused by transporting a bone segment.[4] The mentioned technique is a crucial approach for addressing bone deficiencies exceeding about 4 cm in length that are beyond the scope of bone grafting reconstruction.[2] The present method of bone reconstruction operates through callotasis, which refers to the elongation of the callus formation phase of secondary bone healing. One of the drawbacks of this treatment method is the prolonged utilization of an external circular fixator that may result in various complications, including pin tract infection, joint stiffness, and limb deformities.[5]

In recent years, a modification of the conventional bone transport technique has been introduced, which involves the utilization of an intramedullary nail (IMN) in conjunction with Ilizarov. Studies have demonstrated that this modification presents certain benefits over the conventional method, rendering it a more desirable option for both the surgeon and the patient.[6,7]

This study aimed to present the results of our modification of bone transport using a combination of IMN and Ilizarov in a series of patients with tibia and femur bone defects due to infected nonunion.

Materials and Methods

Study design and population

We designed a single-arm clinical trial study to include patients referred to Imam Hossein Hospital, a referral Orthopedic Surgery Center affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran, during a period of four years (2017-2020). The study's inclusion criteria necessitated the presence of either femur or tibia infectious nonunion. The diagnosis of this condition is based on radiological evidence of nonunion with either a concomitant fistula or discharge or laboratory evidence of elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, and white blood cell (WBC) count.

Additionally, patients were required to provide informed consent to undergo orthopedic surgery, which involved the concurrent application of an IMN and an Ilizarov fixator. This surgical intervention was intended to reconstruct the bone defect in the long bones of the lower limbs. Exclusion from the study happened if the patient was not willing to participate in surgery or study, inadequate data, presence of pathologic fractures, metabolic bone diseases, long-term corticosteroid consumption, bone malignancy, metastatic lesion in bone, or bone defects less than 4 cm after sequestrectomy.

Surgical technique

According to the presence of infection at the fracture site, patients underwent multiple surgeries for radical debridement, sequestrectomy, hybrid fixator (IMN and Ilizarov) application, and corticotomy. Bone transport was performed using the Ilizarov method, and we used two rings to transport the intercalary bone segment.

The management of infectious nonunion cases involved two primary stages, which were infection eradication and bone reconstruction, respectively. During the initial stage, all retained implants were extracted. The "Paprika sign" was utilized to establish the border between viable bone tissue and sequestrum on both sides of nonunion during radical debridement. The edges of the defect on either side have been cut to be planar and orthogonal to the longitudinal axis of the bone to reduce the chances of soft tissue interposing during docking. These osteotomies were executed utilizing multiple drill holes. Then, antibiotic-loaded polymethylmethacrylate (PMMA) intramedullary rods were utilized to fill the bone defect and the intramedullary canal. Temporary braces were utilized to stabilize the extremity. The infected bone and/or soft tissues underwent culture and antibiogram tests.

After administering parenteral antibiotics for a period of approximately six weeks, and confirmation of infection eradication through laboratory assessments, the patient was prepared for the second stage of treatment, which involved the application of the hybrid fixation using Ilizarov frame and IMN, corticotomy, and bone transportation [Figure 1]. After extracting the antibiotic-loaded cement rod, the tissue samples were sent for a frozen section, and after confirming the presence of less than 5 neutrophils in each high-power field, the canal was over-reamed to a diameter 0.5-1 mm greater than the previous IMN or canal diameter. Subsequently, the bone's standard rotation, alignment, and length were obtained and secured using an IMN. It is recommended to utilize the IMN with a 2 mm narrower diameter compared to the preceding reamer employed, as this promotes friction-free movement of the intercalary segment around it. Thereafter, Sub-periosteal corticotomy was performed preferably on the healthy diaphysis-metaphysis junction using a small incision under C-arm visualization. Two Ilizarov rings were subsequently applied, one being applied on the docking side and the other being used for transporting the intercalary segment. Each ring was attached to the bone using two pins that were sufficiently tightened (110–130 Newton) and secured to the bone in an oblique manner (60–90 degrees). Subsequently, the rings were interconnected utilizing 3-4 rods. The process of distraction was initiated following a latency phase of 5 days to facilitate preliminary callus formation. It is recommended to maintain a velocity of bone segment transportation directed towards the docking site at a rate of one millimeter per day, with a frequency of every six hours. The patients were provided with education regarding pin site care and the appropriate technique for turning the Ilizarov nut, which involved a quarter turn four times a day. Patients were discharged with antibiotics to address the organisms responsible for their infection and advised to seek follow-up care.

Upon completion of transportation and docking, the compression of the docking site was sustained at a daily rate of 0.25 mm until docking site union was attained or until the patient experienced discomfort at the compression site. After that, the Ilizarov frame was removed. In cases of docking site nonunion following compression by Ilizarov, the patient underwent a subsequent surgical procedure. This procedure involved the removal of interposed soft tissue, followed by bone grafting for the patient.

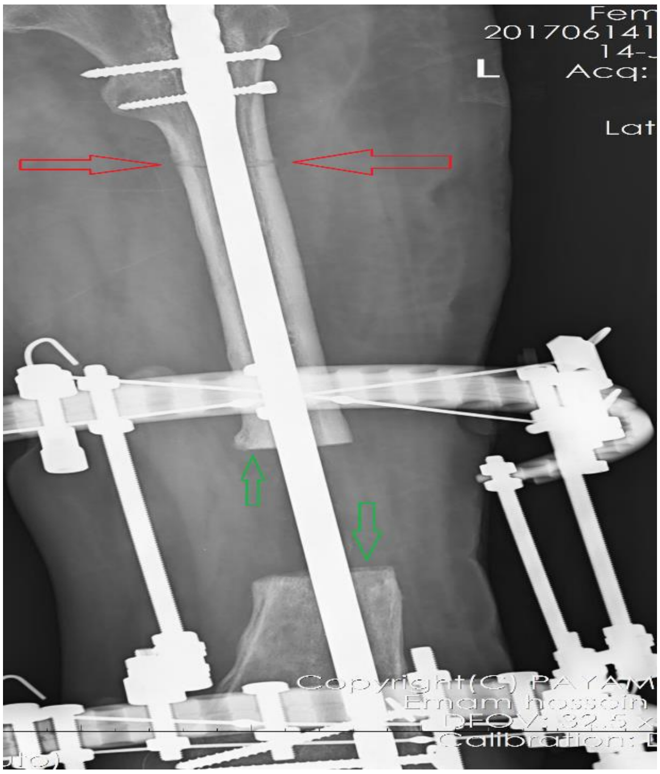

Figure 1. Anteroposterior (AP) Femur Radiograph after the Second Stage In this radiograph, the red arrows point to the subperiosteal corticotomy performed at the junction of the metaphysis and the diaphysis. Additionally, the green arrows highlight the planar and orthogonal endpoints of the sequestrectomy

Patient follow-up

The post-discharge patient follow-up occurred on a biweekly basis for three months, followed by monthly follow-ups during the second trimester and bimonthly follow-ups until the end of the one-year postoperative. Then, follow-up sessions were scheduled every three months until the end of the second postoperative year. Radiographic imaging was utilized to assess the condition of bone union, coverage of defects, the process of distraction osteogenesis, and the development of callus. A physical assessment of the surgical site was conducted to evaluate the pin tract infection and potential pin loosening. Furthermore, the range of motion of the lower limb was assessed during subsequent assessments.

Following Ilizarov's removal, patients with restricted joint range of motion underwent 10-20 sessions of physical rehabilitation administered by an experienced physiotherapist.

Data collection and study variables

Data in this study was collected in two phases, namely pre-operation interview and post-operation follow-up. Patients enrolled in the study were first assessed for demographic details through an interview. Variables assessed before surgery were the patient's age, sex, and type of fracture (open/closed). Outcomes assessed post-operatively were the presence of infection, time of bone segment transport, and bone healing-related complications.

In this study, we used parameters such as consolidation index (CI), which is calculated by calculating the elapsed time from Ilizarov application to the time of consolidation in the distraction zone, divided by the length of the bone defect, and external fixator index (EFI), which is calculated by the elapsed time from Ilizarov application to the time of its removal divided by the length of the bone defect, to determine the clinical outcome of this approach in these patients.

Statistical analysis

Quantitative variables were summarized by mean with standard deviation (±SD) and range. Qualitative variables were summarized in frequency and percentages. Chi-squared test and t-test were used to evaluate associations between different categorical and quantitative variables. Spearman correlation coefficient was used to examine the correlation between quantitative variables. Two-tailed P-value < 0.05 was set as the significance level for reporting the results of comparisons. IBM SPSS Statistics (version 21) was used to analyze the collected data.

Ethical considerations

This study received Ethical Approval from the Ethical Committee at Shahid Beheshti University of Medical Sciences (Code: IR.SBMU.RETECH.REC.1398.078). All patients provided informed consent prior to participation in the study and were free to leave the study at any stage. Study investigators were committed to keeping patients' data private and using them only for the conducted study. Patients confirmed the publication of results by informed consent.

Results

The study included 39 patients with bone defects in the tibia or femur, with a mean age of 31.44 (±11.95, range=18-60). The majority of patients were male (95%). The primary mechanism of bone fracture was motor vehicle collision (94.8%), with a smaller proportion attributed to gunshots (5.1%). Among the patients, 74.3% had open fractures, and the remaining 25.6% had closed fractures.

The distribution of nonunion locations revealed that the mid-shaft of the femur (28.2%) and the distal-shaft of the tibia (23%) were the most common sites. The direction of bone segment transport was retrograde in 53.8% of cases and ante-grade in 46.1% of cases [Figure 2]. Notably, soft-tissue reconstruction was not required in any patient, and the neurological status remained intact before and after bone transportation [Table 1].

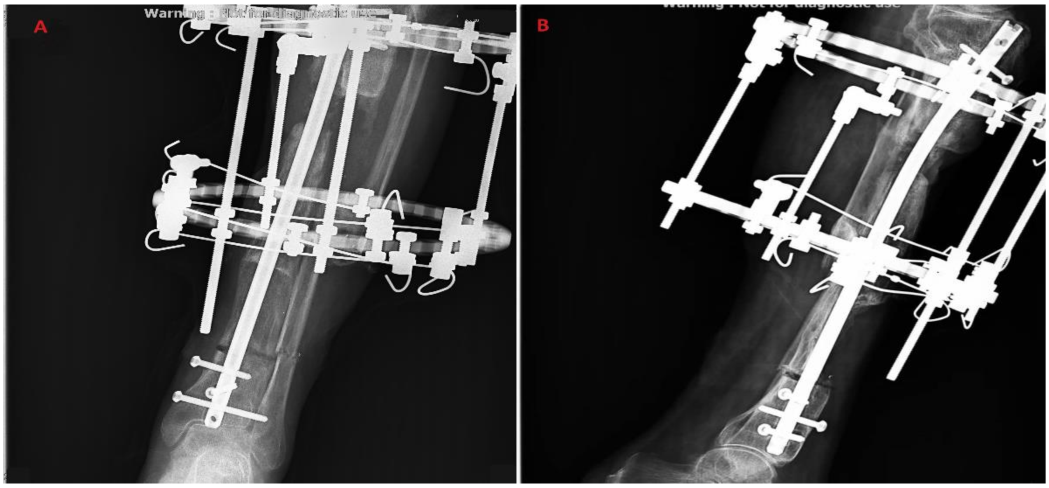

Figure 2. Proximal Tibial Shaft Bone Defect (A) Anteroposterior and (B) lateral views showcase the defect in the proximal tibial shaft. Corticotomy, performed at the diaphysis-distal metaphysis junction, precedes the proximal transport of the intercalary segment

Table 1. Fracture Characteristics

PARAMETER	Value
MECHANISM OF FRACTURE	
- MOTOR VEHICLE COLLISION	37 (94.8%)
- GUNSHOT	2 (5.1%)
FRACTURE TYPE	
- OPEN	29 (74.3%)
- CLOSED	10 (25.6%)
NONUNION LOCATION	
- MID-SHAFT FEMUR	11 (28.2%)
- DISTAL-SHAFT TIBIA	9 (23%)
- DISTAL-SHAFT FEMUR	9 (23%)
- PROXIMAL-SHAFT TIBIA	5 (12.8%)
- MID-SHAFT TIBIA	5 (12.8%)
BONE SEGMENT TRANSPORT	
- RETROGRADE	21 (53.8%)
- ANTE-GRADE	18 (46.1%)

The majority of patients (87.1%) underwent more than one surgery for the complete eradication of infection. Regarding bone grafts, 25.6% of patients did not require grafting, while others needed grafts one to three times. At the end of the follow-up period, 89.7% of patients achieved complete union; however, complications such as docking site nonunion and transportation site nonunion were observed in a few cases [Table 2].

Following Ilizarov's removal, 12.8% of patients exhibited ankle dorsiflexion restriction exceeding 5 degrees, and 84.6% demonstrated knee flexion restriction exceeding 15 degrees compared to the contralateral limb. Physiotherapy effectively addressed these motion limitations, with only 7.7% of patients retaining knee movement restrictions.

Table 2. Treatment Details

PARAMETER	Value
SOFT-TISSUE RECONSTRUCTION	Not needed in any patient
NEUROLOGICAL STATUS	Intact before and after bone transportation
BONE GRAFT	
- NOT NEEDED	10 (25.6%)
- NEEDED ONCE	10 (25.6%)
- NEEDED TWICE	14 (35.8%)
- NEEDED THRICE	5 (12.8%)

Notably, none of the operated patients experienced limb length discrepancy more than 2 cm. The mean bone defect size was 6.31 ± 1.95 cm, and consolidation was achieved in 224 (88–376) days. The CI was 0.97 (0.51–1.32) mo/cm. The mean Ilizarov frame time was 5.2 months (range=3.3-6.8), and the Ilizarov frame index was 0.67 (0.41-1.10). While CI was longer in patients with open fractures, the difference was not statistically significant (P=0.353) [Table 3].

The pre- and post-operative plain radiographs are depicted in [Figure 3].

Table 3. Treatment Outcomes

PARAMETER	Value
UNION STATUS	35 (89.7%) achieved complete union
COMPLICATIONS	
- DOCKING SITE NONUNION	3 cases
- TRANSPORTATION SITE NONUNION	1 case
FOLLOW-UP PERIOD	
- MEAN CONSOLIDATION TIME	224 days (88–376 days)
- CONSOLIDATION INDEX (CI)	0.97 (0.51–1.32) mo/cm
- ILIZAROV FRAME TIME	Mean: 5.2 months (3.3-6.8 months)
- ILIZAROV FRAME INDEX	0.67 (0.41-1.10)

Figure 3. Treatment Progression in Femoral Shaft Infection (A) Initial plain radiograph of infectious nonunion development in the femoral shaft. (B) Following radical debridement and nail extraction for infection eradication, a new nail is implanted, and corticotomy at the proximal metaphyseal-diaphyseal junction is performed. The Ilizarov frame is utilized, spanning both sides of the bone defect for distal transportation. (C) Complete union is attained in both the transportation and docking zones following the application of maximum compression at the docking site and subsequent removal of the Ilizarov frame

Discussion

In general, there are two categories of treatment approaches for long bone defects, including prostheses replacement and biological reconstruction. The biological reconstruction consists of bone transport and bone graft. Choosing the optimal technique poses a significant challenge for treating patients with critical-size bone defects where limb salvage is the selected therapeutic approach.[8,9] The process of bone reconstruction is typically deferred until the primary pathology (e.g., tumor and infection) and soft tissue reconstruction have been addressed. Therefore, in infected nonunions, the appropriate treatment strategy should be chosen after radical debridement and complete eradication of the infection, according to the length of the subsequent bone defect and the status of covering soft tissue.[10]

The utilization of bone grafting is applicable in scenarios where the bone deficiency is limited in size, typically measuring less than 4 cm in length. However, in cases with infected critical-size bone defects, bone transportation is the treatment choice. In cases of infected nonunions of long bones with extensive bone defects necessitating soft tissue reconstruction, the strategy of shortening and re-lengthening may be considered appropriate. This is because shortening can potentially obviate the need for soft tissue reconstruction.[11]

In cases where a significant bone defect exists and soft tissue reconstruction is considered unnecessary, intercalary bone segment transportation may be employed as a viable alternative. Several modifications can be employed to transport an intercalary bone segment. The conventional approach for executing this strategy involves the exclusive utilization of an external fixator. Despite the revolutionary nature of this approach to biological reconstruction, the extended duration of external fixator usage has been associated with patient complications. The mean EFI in the conventional approach of utilizing the external fixator exclusively is 1.85 months/cm. In contrast, transportation over the IMN technique yields an average index of 0.55 months/cm. Our study reveals that the index is further reduced to 0.51 month/cm.[12]

The employment of both locking plates and external fixators concurrently is an additional technique for bone transportation. Although this approach results in a reduced duration of external fixator usage (EFI=0.45 month/cm) compared to the previous method and a decrease in associated complications, it is not without drawbacks. These include the inability to bear weight until the end of the treatment period, as well as the potential for malunion and limb deformities. This technique is particularly suitable for situations where the insertion of IMNs is impractical, such as cases where the defect's borders are in close proximity to the joint.[13]

Transferring bone segments over an IMN is a highly recommended technique. This method entails transferring the bone segment along an IMN, which reduces deformities and malunion resulting from callotasis in the path of the nail [Figure 4]. In addition, it permits early weight-bearing and reduces the time required to use an external fixator. The absence of necessity for splints and casts is an additional advantage of this method over using an external fixator and plate.

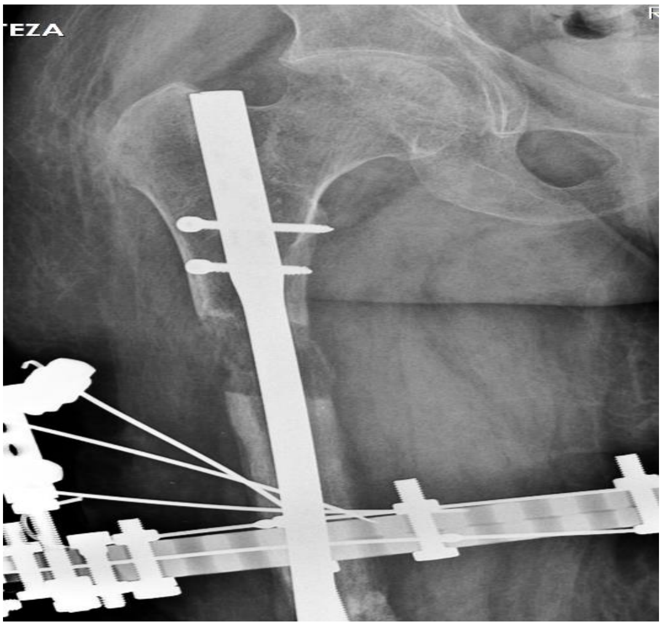

Figure 4. Callotasis Pathway along the Nail In this image, the phenomenon of callotasis, marked by callus elongation along the nail, is depicted. This technique serves as a crucial preventive measure against deformities and malalignments during distraction osteogenesis

Docking site nonunion is a commonly observed complication in this procedure and acts as the limiting-rate factor in the overall duration of treatment. Our study findings indicate that a considerable percentage of the patient cohort, specifically 74%, demonstrated no union at the docking site, even with the implementation of maximum compression through Ilizarov. As a result, another surgical procedure was required to remove the fibrocartilage tissue that had been interposed and perform an autologous bone graft. Despite undergoing multiple bone grafting procedures, three patients were observed to have failed to achieve union at the end of the follow-up period. While it is common practice to perform segmental resection by cutting flat uniplanar surfaces, certain surgeons have proposed using a plunger and mortise configuration to enhance contact and promote the removal of interposed fibrous tissue through compression. In some studies, due to the high probability of docking site nonunion, after the completion of transportation and simultaneously with the removal of the external fixator, bone graft was performed for all patients.[6,14]

Infection represents a significant complication among this cohort of individuals. The etiology of infection in these patients can be attributed to two primary sources. The first is the failure to completely eradicate the initial infection, resulting in residual hidden foci of infection at the surgical site. The second factor is the occurrence of pin tract infection, which can spread throughout the bone medulla via the nail. To prevent these potential complications, it is generally accepted to conduct transportation only after confirming the complete elimination of the infection by observing the normal ESR, CRP, WBC count, and negative frozen section. The utilization of antibiotic-impregnated PMMA prior to IMN presents a potentially promising option to address this widely recognized concern. Furthermore, all patients were instructed on proper pin-site care and advised of the need to seek medical attention in the event of discharge or erythema at the pin-entry site.[15]

The limitations of this study were the small size of the patients' cohort and the lack of a control group. Since surgeries were performed by two surgeons (F.A.O and S.A), assessor bias was possible. Studies with a higher sample size and comparative studies can provide more reliable results.

Conclusion

The obtained results indicated that utilizing bone transportation over an IMN can effectively decrease the duration of external fixator usage while retaining the benefits of the conventional external fixator approach, including a high rate of union for critical-size bone defects. Furthermore, this technique may significantly reduce the occurrence of complications associated with this biological reconstruction method, such as pin tract infection. Moreover, the utilization of IMN facilitates early weight bearing, which enhances patients' adherence to their treatment plan. Early removal of the external fixator could prevent the occurrence of significant joint mobility restrictions through enhanced physical therapy interventions. An additional benefit of utilizing this approach in contrast to the concurrent utilization of an external fixator and plate is the absence of necessity for splinting and casting.

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