Study of Nonunion Closed Fracture Shaft Femur in Cases Treated by Intramedullary Nailing in Adults

Mohamed Abdelhamed Romeih[a]*
[a]Department of Orthopedic Surgery, Faculty of Medicine, Tanta University, Tanta, Egypt

Abstract
Background: Reduction and internal fixation by the interlocking intramedullary nail (IMN) are the gold standard in managing femoral shaft fractures with excellent union and a high success rate. although, the reported associated nonunion up to 12.5%.
Objective: To assess the determinants of nonunion fractures shaft femur in adults undergoing IMN treatment.
Patients and methods: This retrospective observational study included 200 adult patients, both sexes, with diaphyseal closed fractures shaft femur previously treated by IMN, who were admitted to the author's institution from April 2018 to April 2022. All patients were subjected to history taking, clinical examination, and radiographic imaging.
Results: The incidence of nonunion of the femoral shaft following IMN was 8%. Body mass index (BMI), diabetes mellitus (DM), non-steroidal anti-inflammatory drugs (NSAIDs), unreamed and delayed weight bearing were significantly higher in the nonunion group than in the union group (P = 0.037. 0.004, 0.002, <0.001 respectively). The type of fracture was significantly different between both groups (P <0.001). Multiple fractures, and nail insertion were insignificantly different between both groups. Reamed was significantly lower in the nonunion group than in the union group (P <0.001).
Conclusion: The incidence of nonunion of the femoral shaft following IMN was 8%. The substantial risk factors leading to nonunion in femoral shaft fractures treated by IMN include higher BMI, the presence of DM, the use of NSAIDs, certain types of fractures, the use of unreamed nails, and delayed initiation of weight bearing.
Keywords: Femoral Shaft Fractures; Intramedullary Nailing; Nonunion Complication; Trauma
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***Correspondence**: romeih@med.tanta.edu.eg
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Introduction

Femur is essential for supporting weight in the lower limbs. Fractures along the femoral shaft are frequently encountered injuries **(Bianco Prevot et al., 2023)**. Annually, worldwide femur shaft fractures occur at a rate of 10 to 37 cases per 100,000 individuals, predominantly affecting young men around the age of 27 and elderly women around the age of 80. These fractures often result from high-impact incidents, including automobile collisions and falls, which exert significant force **(Wu et al., 2019)**.

The AO-Müller/orthopedic trauma association (AO/OTA) system is widely employed to classify femur shaft fractures, as well as all long bone fractures. This system categorizes fractures of the femur shaft (diaphyseal) into three primary types: simple fractures, wedge fractures, and complex fractures, based on the pattern of the break **(Garnavos et al., 2012)**.

Intramedullary nailing (IMN) is the preferred remedy for femoral shaft fractures, demonstrating low complication rates of approximately 4.9%. It is also highly regarded as an effective treatment for aseptic nonunions in cases of noncomminuted femoral shaft fractures, with reported success rates of bone healing varying between 72% and 100% **(Bell et al., 2016)**. Nevertheless, the occurrence of nonunion continues to be an obstacle for orthopedic surgeons, presenting considerable socioeconomic loads for patients. The frequency of nonunion following IMN can be as high as 8% **(Rupp et al., 2018)**. Recognized risk factors for nonunion of femoral shaft fractures include open fractures, use of tobacco, postponed initiation of weight bearing, fragmentation at fracture location, fracture reduction instability, nonsteroidal anti-inflammatory (NSAIDs) medication use, and selecting an inappropriate nail diameter for the procedure **(Donohue et al., 2016)**.

To extend our knowledge regarding certain risk factors for nonunion fractures shaft of femur, this work aimed to assess the determinants of nonunion fractures shaft femur in adults undergoing IMN treatment.

Patients and methods

This retrospective observational study involved 200 adult patients of both sexes with diaphyseal closed femur shaft fractures, previously treated with IMN (comprising 15 cases with unreamed IMN and 185 cases with reamed IMN. The time between trauma and surgery varied from 2 to 7 days with a mean of 4 days. These patients were admitted to the author's institution between April 2018 and April 2022. Patients were divided according to the fracture union into 16 patients in the nonunion group and 184 in the union group.

Patients' data obtained from the hospital's patient administration system database. The research was conducted with the approval of the Ethical Committee of the author's institution (Approval code: 36264PR75/2/23). Informed written consent from the patient or their guardians was obtained.

Exclusion criteria were patients younger than 18 years old, intra-articular fractures of the femur, pathological fractures, and open fractures shaft femur.

The patients' data, including medical history, clinical examination details, and radiographic imaging (both preoperative and postoperative X-rays, as well as postoperative CT scans showing femoral shaft fractures), were recorded.

Antegrade nailing

On a fracture table, the patient was positioned supine. Foot skin traction was administered on the boot secured foot. The non-injured leg was in the hemilithotomy position, widely abducted and flexed. Betadine scraping of the wounded limb. To identify the skin incision location, the greater trochanter was palpated. A 3-5 cm incision was made proximal to the tip of the greater trochanter, and the fascia was then opened using scissors. The gluteus muscle was subsequently sectioned along its natural fibers. The dissection extended down to the bone. To palpate the greater trochanter, a finger was inserted. Using an image intensifier, the entrance points of the greater trochanter were identified in both anteroposterior (AP) and lateral views. The track started with an awl. Insertion of a rigid reamer widened the medullary canal. With the aid of an image intensifier, a guide wire was introduced to the medullary canal. It was inserted until it was approximately 5 mm proximal to the intercondylar notch into the distal major fragment. To mitigate the risk of eccentric reaming and subsequent nail malposition, which may lead to varus, valgus, antecurvatum, and retrocurvatum malalignment, it was essential that the guide wire be centered. Once the tissue protector had been positioned, the initial reamer head was connected to the reaming shaft, and it was passed over the guide wire. Implementing the reaming process with a 9mm medullary reamer.

Unreamed nails were used for fractures with undisplaced butterfly fragments, with a nail size of 10mm. For reamed nails, the size was determined by the last reamer used, minus 1mm, (**Fig.1**).

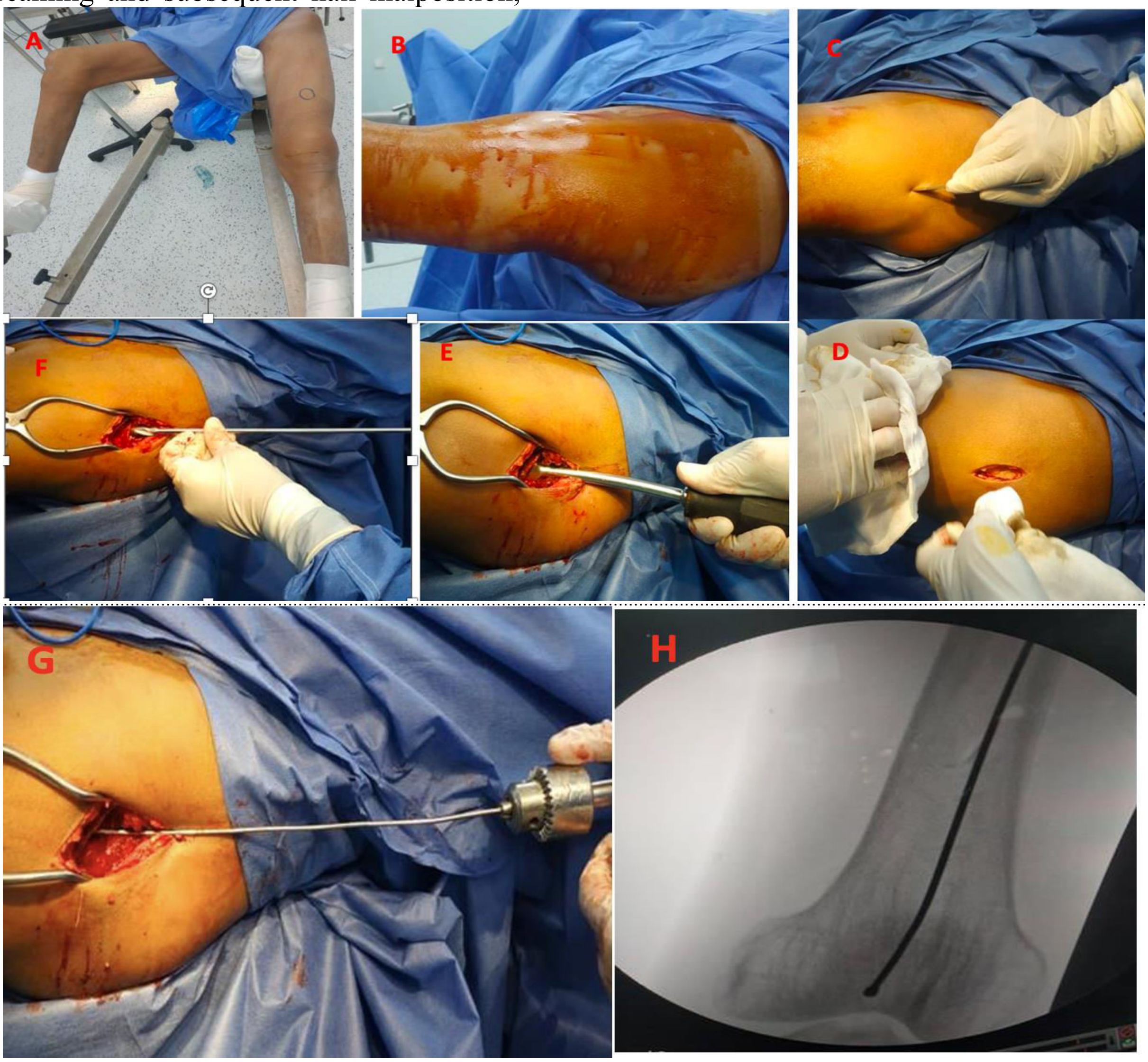

Fig.1. Antegrade nailing insertion techniques; (A) supine position, (B) scraping with betadine, (C) site of skin incision (D)deep fascia dissection, (E) insertion of awl, (F) rigid reamer, (G) guide wire and (H) X-ray of guide wire

Reaming proceeded in incremental steps, with each step increasing by 0.5mm to ensure adequate preparation for smooth nail insertion. Determination of the correct nail length was achieved using a radiographic ruler, with its tip placed at the center of the distal femur. Nail length was determined based on the position of the piriformis fossa rather than the tip of the greater trochanter. Subsequently, the insertion handle was attached to the nail using the corresponding connecting screw. Manual nail insertion followed with a 90° rotation from its entry point to its final orientation. With guidance from the image intensifier, the nail was carefully pushed down to the fracture zone and fully inserted. Finally, locking screws were introduced to ensure rotational stability and maintain the desired length, (**Fig.1**).

Postoperatively, mobilization typically began on the first day, unless contraindicated by other injuries or complications. Weight-bearing was initiated using crutches or a walker unless early weight-bearing was compromised by other fractures. In these cases, early active exercises of the knee and hip were initiated as tolerated. Wound healing was closely monitored in the short term, up to two weeks, and then radiographic assessments were conducted every four weeks up to six months, followed by every six weeks thereafter. Additionally, computed tomography (CT) scans were performed every three months to ensure maintenance of reduction and monitor healing progress. All patients were followed up for at least two years.

Statistical analysis

SPSS v27 (IBM2, Armonk, NY, USA) was used for statistical analysis. Histograms and the Shapiro-Wilks test were used to assess the normality of the data distribution. Mean and standard deviation (SD) were used to provide parametric quantitative data, which were then evaluated using the unpaired student t-test. The frequency and percentage (%) were used to provide qualitative variables. The Chi-square test or Fisher's exact test was used where appropriate. P values less than 0.05 with two tails were deemed to be statistically significant.

Results

Age, sex, and smoking were comparable between both groups. Body mass index (BMI), diabetes mellitus (DM), and non-steroidal anti-inflammatory drugs (NSAIDs) were significantly higher in the non-union group than in the union group (P = 0.037, 0.004 and 0.002 respectively). (**Table.1**).

Table 1. Demographic data and NSAIDs of the studied groups

Variables		Nonunion group (n=16)	Union group (n=184)	P value
Age (years)		31.69 ± 8.84	35.95 ± 10.79	0.127
Sex	**Male**	10 (62.5%)	131 (71.2%)	0.464
	Female	6 (37.5%)	53 (28.8%)	
BMI (kg/m^2)		32.09 ± 4.24	29.2 ± 5.37	**0.037***
DM		7 (43.75%)	28 (15.22%)	**0.004***
Smoking	**Ex-smoker**	0 (0%)	18 (9.78%)	0.222
	Smoker	9 (56.25%)	70 (38.04%)	
	Non-smoker	7 (43.75%)	96 (52.17%)	
NSAIDs		10 (62.5%)	48 (26.09%)	**0.002***

Data are presented as mean ± SD or frequency (%), * significantly different as P value <0.05, BMI: body mass index, DM: Diabetes mellitus, NSAIDs: Non-steroidal anti-inflammatory drugs.

Multiple fractures (9 cases involved fractures to both bones in the leg, 3 cases of cases of forearm fractures, 3 proximal humerus fractures and one case of a contralateral patella fracture was treated with tension band fixation) were comparable between both groups. The type of fracture was significantly different between both groups (P <0.001) with high incidence of bending wedge fracture (6 cases (37.5%)) in nonunion groups. Delayed weight bearing due to multiple fractures were significantly higher in the nonunion group than in the union group (P <0.001). Nail insertion was antegrade in all patients in both groups, (**Table.2**).

In this study, 223 patients were assessed for eligibility, 17 patients did not meet the criteria and 6 patients refused to participate in the study. The remaining 200 patients were allocated into two groups, nonunion group (n=16) and Union group (n=184). All allocated patients were followed-up and analyzed statistically, (**Fig.2**).

Table 2. Type of fracture, multiple fractures, nail insertion, nail size, and delayed weight bearing of the studied groups

Variables		Nonunion group (n=16)	Union group (n=184)	P value
Type of fracture	**Transverse**	3 (18.75%)	130 (70.65%)	**<0.001***
	Oblique	0 (0%)	21 (11.41%)	
	Bending wedge	6 (37.5%)	11 (5.98%)	
	Spiral wedge	4 (25%)	7 (3.8%)	
	Simple spiral	0 (0%)	9 (4.89%)	
	Complex irregular	2 (12.5%)	4 (2.17%)	
	Fragmented wedge	1 (6.25%)	2 (1.09%)	
Multiple fractures		3 (18.75%)	20 (10.87%)	0.343
Delayed weight bearing		9 (56.25%)	26 (14.13%)	**<0.001***

Data are presented as frequency (%). *: Significantly different as P value <0.05.

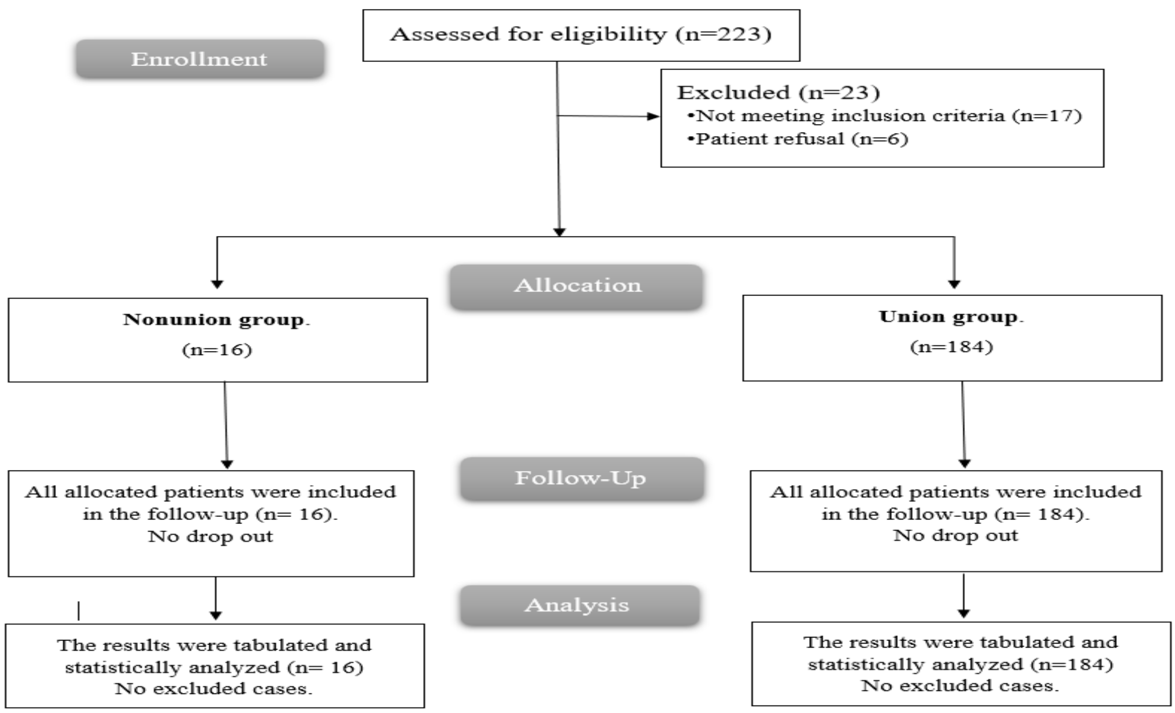

Fig.2. STROPE flowchart of the enrolled patients

Case presentation: A 26-year-old male patient with a BMI of 24.6 presented following a road traffic accident with a closed spiral wedge fracture shaft femur (AO 32B1). The fracture was treated using a unreamed intramedullary nail. Risk factors for nonunion in this case are smoking, patient on NSAIDs, type of fracture (AO 32B1), unreaming, (**Fig.3**).

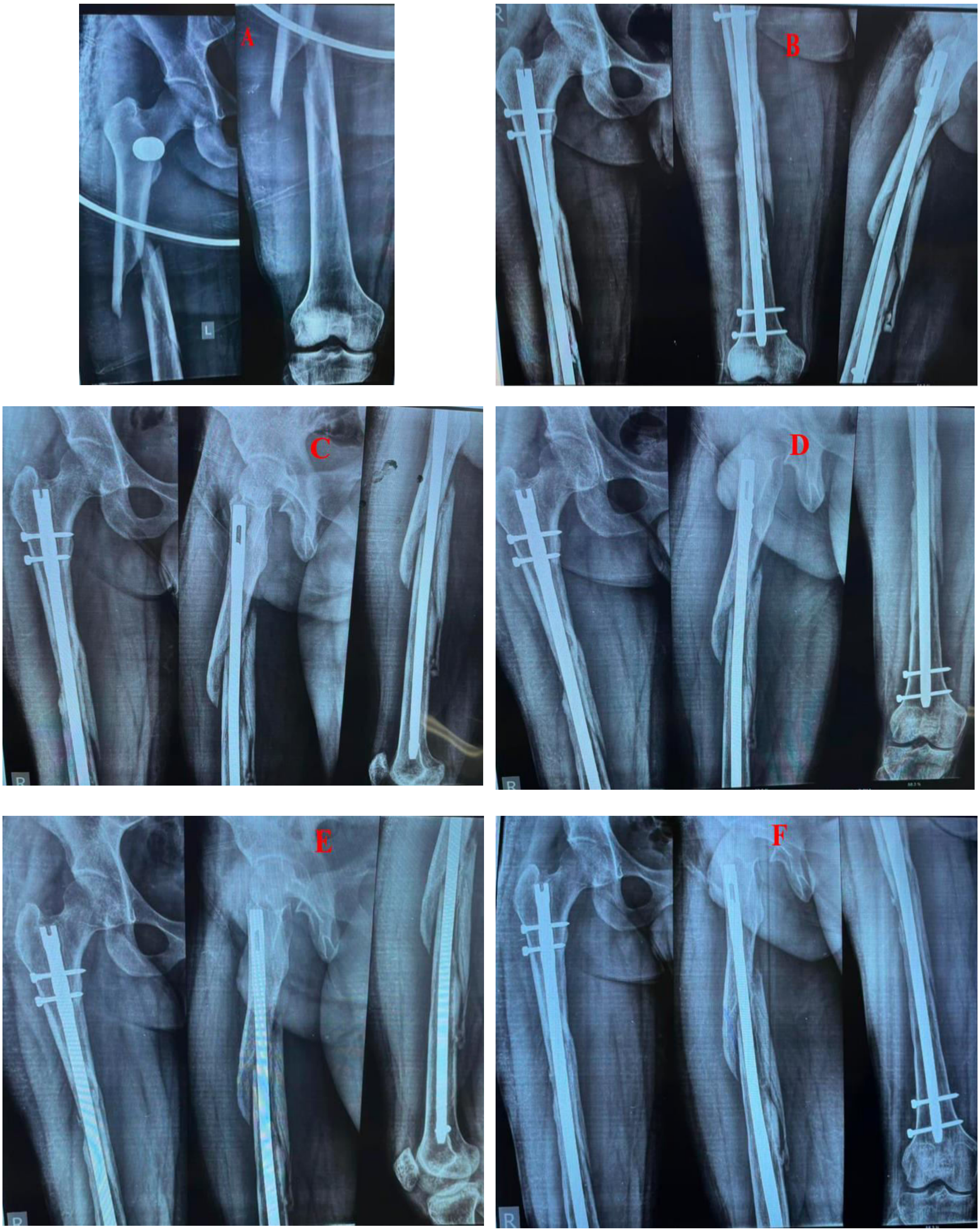

Fig. 3. Radiographic progression of the fracture treatment: (A) Preoperative X-ray, (B) Immediate postoperative X-ray, (C) X-ray at 1 month, (D) X-ray at 3 months, (E) X-ray at 6 months, and (F) X-ray at 9 months.

Discussion

With a reported union rate ranging from 85 to 100 %, IMN is a widely approved treatment for patients with femoral shaft fracture **(Hasan et al., 2024)**, regardless of IMN elevated success rates, reported the associated nonunion of up to 12.5% **(Kruppa et al., 2017, Walter et al., 2021)**.

Currently, nonunion of the femoral shaft following failed plating is not extensively addressed in developed nations. However, it remains a prevalent issue in the third-world countries. Current evidence suggests prioritizing nail fixation over alternative methods such as plating or external fixation for treating fresh midshaft fractures and aseptic non-united fractures. This preference is backed by the notably high union rate associated with nail fixation **(Aliakbar et al., 2017)**.

Nonunion represents a frequent challenge for orthopedic surgeons. Although its relatively low occurrence rate, addressing non-union typically necessitates multiple procedures to achieve union. This multi-step process escalates costs and poses disadvantages to the patient's recovery **(Devendra et al., 2024)**. Oesman et al.**(Oesman et al., 2023)** advised to consider IMN for patients experienced previous plate failure, as it offered structural support to fractures and promoted quicker union, resulting in shorter hospital stays and faster restoration of limb function. IMN helped in preserving anatomical integrity, enhancing functional recovery, and minimizing soft tissue damage.

Although, acute nonunion of the femoral shaft following IMN is uncommon in comparison to nonunion of other bone localizations **(Greco et al., 2021, Perisano et al., 2021)**, recent research indicates that its prevalence can vary between 1.1 % and 14 % **(Pihlajamäki et al., 2002, Lai et al., 2019)**. Our results revealed that the incidence of nonunion of the femoral shaft following IMN was 16 (8%).

According to Ma et al.**(Ma et al., 2023)**, 2.8% of patients had femoral nonunion. Femoral nonunion occurred 10.5% of the time, according to Wu et al. **(Wu et al., 2019)**. A rate of 11.3% was shown by Metsemakers et al. **(Metsemakers et al., 2015)** for femoral nonunion. There was a 4.1% rate of femoral nonunion, according to Taitsman et al. **(Taitsman et al., 2009)**.

The incidence of nonunion and fixation failure may be influenced by a combination of biological (including factors such as the extent of soft tissue damage and bone injury, open fractures, prolonged comminution, fragment interposition, smoking, diabetes, neuropathies, alcoholism, corticosteroids, malnutrition, or prior radiotherapy) and mechanical factors (as inadequate stability resulting from small nail size, instability during rotation, absence of locking, or misalignment in the upper or lower third fractures, particularly when combined with comminution) **(Perisano et al., 2021)**.

To minimize the incidence of nonunion after IMN in femoral shaft fractures, multiple studies have attempted to determine the associated risk factors **(Malik et al., 2004, Taitsman et al., 2009, Kook et al., 2023)**.

The present results revealed that BMI, DM, the use of NSAIDs, and delayed weight bearing due to multiple fractures are correlated with an increased risk of nonunion, (P= 0.037, 0.004, and 0.002, respectively). The type of fracture had a fundamental role in healing outcomes, with significant differences observed between the nonunion and union groups (P <0.001). Nail insertion was antegrade in all patients in both groups.

Our results came in line with Wu et al. **(Wu et al., 2019)** who noticed that both BMI and DM significantly raised the risk of nonunion. However, NSAIDs and type of fracture were insignificantly different between union and nonunion groups. This difference may be attributed to the included fractures type (only 32-A1 to 32-B3). Also, Metsemakers et al.

(Metsemakers et al., 2015) reported that the AO/OTA fracture type was recognized as a contributing risk factor for nonunion, whereas fracture reaming did not show such association. Additionally, Taitsman et al. **(Taitsman et al., 2009)** noted that delayed weight bearing was associated with a higher risk of nonunion. Moreover, Malik et al. **(Malik et al., 2004)** demonstrated that the use of reaming was associated with nonunion.

Obesity can lead to impaired blood flow and chronic inflammation, which negatively affect bone healing. Adipose tissue releases cytokines that can inhibit the formation of new blood vessels and bone growth **(Gao et al., 2018)**. The mechanical stress on bones from excess weight may also disrupt the healing process **(Mavčič and Antolič, 2012)**.

DM, particularly when poorly controlled, leads to microvascular complications that impair blood supply to the fracture site, crucial for delivering nutrients and oxygen for bone healing. Also, it can cause a chronic inflammatory state that interferes with the healing process **(Jiao et al., 2015)**.

NSAIDs inhibit cyclooxygenase enzymes, reducing prostaglandin synthesis. Prostaglandins have a vital role in bone healing by mediating inflammation, bone resorption, and formation processes. Their inhibition can therefore delay or impair healing **(Pountos et al., 2008, Chapman, 1998, Albareda et al., 2021)**.

Early weight-bearing (weight-bearing before 6 weeks) after fracture treatment can stimulate bone healing through mechano-transduction pathways, where mechanical stress is converted into cellular responses that promote bone formation **(Ma et al., 2023)**. Delayed weight bearing (weight-bearing after 6 weeks) might deprive the fracture site of these beneficial mechanical stimuli, prolonging the healing process **(Song, 2022)**. Weight-bearing enhances vascularization adjacent to the fracture site, which is necessary for delivering the necessary nutrients and cells for bone repair **(Chen et al., 2023)**.

The study was limited by several factors, notably its retrospective design and the limited size of the sample. Additionally, it was conducted at a single center, and crucial clinical parameters were not evaluated, potentially hindering the ability to predict nonunion during the initial phases of bone healing. Furthermore, data on surgical diameters (e.g., nail diameter compared to canal diameter), operation durations, and estimated surgical blood loss were not collected, which could be relevant in understanding the correlation with nonunion.

Conclusion

The incidence of nonunion of the femoral shaft following IMN was 16 (8%). The significant risk factors leading to nonunion in femoral shaft fractures treated by IMN include higher BMI, the presence of DM, the use of NSAIDs, certain types of fractures, and delayed initiation of weight bearing.

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