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Radiographic outcomes of the treatment of complex femoral shaft fractures (AO/OTA 32-C) with intramedullary nailing: a retrospective analysis of different techniques

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Abstract

Objectives: To assess the results of open versus closed reduction in intramedullary nailing (IMN) for complex femoral fractures (Arbeitsgemeinschaft für Osteosynthesefragen Foundation/Orthopaedic Trauma Association [AO/OTA]: 32-C) and to determine the factors involved in bone healing.

Methods: This retrospective study involved 47 consecutive patients with complex femoral diaphyseal fractures who underwent reduction and fixation.

Results: All open-reduction and 12 closed-reduction patients (52.17%) had an anatomical-to-small gap. The closed-small group had the highest bone union rate (100%), followed by the open-reduction (79.17%) and closed-large groups (72.73%); intergroup differences were significant. The closed-small group had the shortest mean union time (7.31 months), followed by the open-reduction group (7.58 months). The closed-large group had a significantly longer union time (9.75 months) than those in the closed-small and open-reduction groups. Femoral radiographic

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union scores in the closed-small and open-reduction groups were similar at three timepoints; scores were higher than those in the closed-large group, with a significant difference 6 and 9 months post-operatively.

Conclusion: IMN with closed reduction for complex femoral shaft fractures had better outcomes and fewer complications versus open reduction. For unsatisfactory closed reduction outcomes (i.e., residual gap >10 mm), minimally invasive techniques or open reduction with minimal stripping should be considered.

Keywords

Comminuted femoral shaft fracture, complex femoral shaft fracture, intramedullary nailing, closed reduction, open reduction, radiographic imaging, retrospective study

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Introduction

Intramedullary nailing (IMN) is considered the gold standard for the treatment of femoral diaphyseal fractures. Specifically, closed reduction and internal fixation with an interlocking nail is the standard treatment for most shaft fractures of the proximal or distal femur.[1,2] However, the management of complex femoral diaphyseal fractures remains challenging and often results in delayed bone union or non-union. The recommended surgical techniques for these fractures are currently controversial.[3,4] While some studies have recommended closed reduction with internal fixation, which avoids the destruction of soft tissue attachments and blood supply,[5] others have suggested that the displacement and size of residual fragments influence the prognosis.[6]

The objective of the present study was to evaluate the radiographic outcomes of IMN for complex femoral diaphyseal fractures and to analyze the influence of different surgical strategies on the prognosis. To the best of our knowledge, this is the first study focusing on complex femoral diaphyseal fractures that compared the efficacy of open vs closed reduction to treat this subgroup (Arbeitsgemeinschaft für Osteosynthesefragen Foundation/ Orthopaedic Trauma Association [AO/ OTA] type: 32C).

Patients and methods

Patients

A retrospective cohort of patients with complex femoral diaphyseal fractures (AO/OTA type: 32-C), who were treated using antegrade intramedullary nails by the same team of surgeons from January 2009 to December 2019, was included.[7] The exclusion criteria were open fracture, periprosthetic fracture, pathological fracture, staged operation following initial external skeletal fixation or skeletal traction, brain injury, and fat embolism in patients with femoral diaphyseal fractures. This study was conducted in accordance with the principles embodied in the Declaration of Helsinki, and the reporting of this study conforms to the STROBE guidelines.[8] The study design was approved by the institutional review board (IRB) of the authors' affiliated hospital (Far Eastern

Memorial Hospital [FEMH], approval No. 110059-E, for the study period: 14 April 2021 to 30 June 2022). The need to obtain informed consent was waived by the IRB owing to the retrospective nature of the study.

Data on age, sex, mechanism of injury, comorbidities, smoking, and alcohol use were obtained from the patients' medical records. The medical data for the included patients was anonymized for this research. Femoral diaphyseal fracture was defined as a fracture of the femur between 5 cm distal to the lesser trochanter and 8 cm proximal to the adductor tubercle.[9] The fracture patterns were classified in accordance with the AO/OTA classification.[10]

Surgery

All fractures were managed by senior attending surgeons or fellowship-trained orthopedic traumatologists in the orthopedic department of a single trauma center. The enrolled patients were subdivided into open- and closed-reduction groups, based on their medical records and the surgical techniques.

In the open-reduction group, the patient was placed in the supine position or in the lateral decubitus position on the fracture table, depending on the surgeon's preference. The incision over the fracture site was made close to the fragments to enable direct reduction and fixation with wiring of fragments as necessary; a reaming bone graft was also performed. The canal was prepared by reaming the diameter to 1.0 mm more than the anticipated nail diameter, which was determined using radiography.

In the closed-reduction group, patients underwent reamed antegrade locked IMN, performed using a standard closed technique. Briefly, patients were placed in the supine position on a fracture table. All reduction attempts were performed using closed methods, namely manipulation and the use of crutches, preoperatively, and cooled mallets, reduction levers, and distraction devices,[11] or manipulation using fingers or percutaneously placed half-pins, with a small incision, intraoperatively.[12] The reamed antegrade IMN principle used here was similar to that used in the open-reduction group.

Range of motion exercises were initiated immediately after surgery. The patients were not allowed to bear weight for 4 weeks post-operatively. Touch-down weight-bearing with a walker was initiated after callus formation, and the ambulation level was progressively increased, thereafter.

Radiographic assessment and outcomes

Pre-operative radiographs were obtained at admission, and post-operative radiographs were obtained immediately after surgery. Anteroposterior and lateral radiographs were acquired at every follow-up visit in the outpatient department (every month for at least 24 months or until bone union was achieved). The quality of reduction was assessed by reviewing the post-operative radiographs and measuring the average gap between the fragments. The numerical value for the gap between the fragments was calculated using a modification of Lin et al.'s method.[6] The reduction in gap size was classified as either an anatomical-to-small gap (2–10 mm) or a large gap (>10 mm).[6]

The main outcome was the radiographic bone union score 6, 9, and 12 months post-operatively and when bone union was achieved (classified as the last visit). One author interpreted all radiographs twice in a blinded fashion, and this evaluation was repeated by a senior staff radiologist to ensure reliability. The radiographic union score of the femur (RUSF) was assessed using each follow-up radiograph. RUSF was based on the assessment of healing at each cortex; i.e., medial and lateral cortices on the anteroposterior plain film as well as anterior and posterior cortices on the lateral film. The RUSF scoring system was modified from the "radiographic union score of the tibia" system described by Whelan et al.,[13] which provides quantitative criteria for radiographic union.[6] This scoring system indicates better biomechanical strength in high-scoring cases than that in low-scoring cases.[14]

The outcomes of treatment, namely bone union rate, RUSF, union time, complication rate, and revision rate, were assessed. Radiographic union was defined as the restoration of continuity by a bridging callus at the fracture gap, with consolidation. Non-union was defined as disturbed consolidation of a fracture that required re-operation, or prolonged bone healing of >12 months.[15,16] A revision operation was performed if there were no visible progressive signs of healing for 3 consecutive months, non-union, failure of internal fixation, infection, or surgical complications. The re-operation techniques comprised secondary autogenous/allogeneic bone grafting, dynamization, or changing the interlocking nail.

Data analysis

Statistical correlation was analyzed using the Mann–Whitney U test and one-way analysis of variance. The level of statistical significance was set at $p < 0.05$. Statistical analyses were performed using SPSS version 22 (IBM Corp., Armonk, NY, USA).

Results

Between January 2009 and December 2019, 319 patients with a femoral shaft fracture were included, and 59 complex femoral shaft fractures (AO/OTA/32-C) were identified. After 8 patients were excluded, 51 patients with complex femoral shaft fractures were considered eligible. Four patients were excluded owing to a short follow-up duration and loss to follow-up (Figure 1). Therefore, 47 patients (36 men and 11 women) were enrolled consecutively. There were 24 (21 men, 3 women) and 23 (15 men, 8 women) patients in the open- and closed-reduction groups, respectively.

Demographic characteristics

The mean age of the patients was 30.33 and 32.95 years in the open- and closed-reduction groups, respectively. There was no significant difference in the demographic characteristics between the two groups (Table 1).

Reduction outcomes

In the open-reduction group, all patients had anatomical-to-small gaps. In the closed-reduction group, 12 (52.17%) patients had small gaps, and 11 (47.83%) patients had large gaps. The difference in reduction quality between the two groups was significant ($p = 0.001$; Table 2). To elucidate the effect of reduction on prognosis, the closed-reduction group was divided into two subgroups based on the residual gap after closed reduction as a closed-small group (gap <10 mm, $n = 12$) and a closed-large group (gap >10 mm, $n = 11$; Table 2).

Bone healing outcomes

The overall union rate at 12 months, postoperatively, was 82.97%, with 39 and 8 patients showing bone union and non-union, respectively. The closed-small group had the highest bone union rate (100%), followed by the open-reduction group (79.17%) and closed-large group (72.73%). The statistical difference between the three groups was significant ($p = 0.018$). Furthermore, the closed-small group had the shortest mean time to bone union (average, 7.31 months). The open-reduction

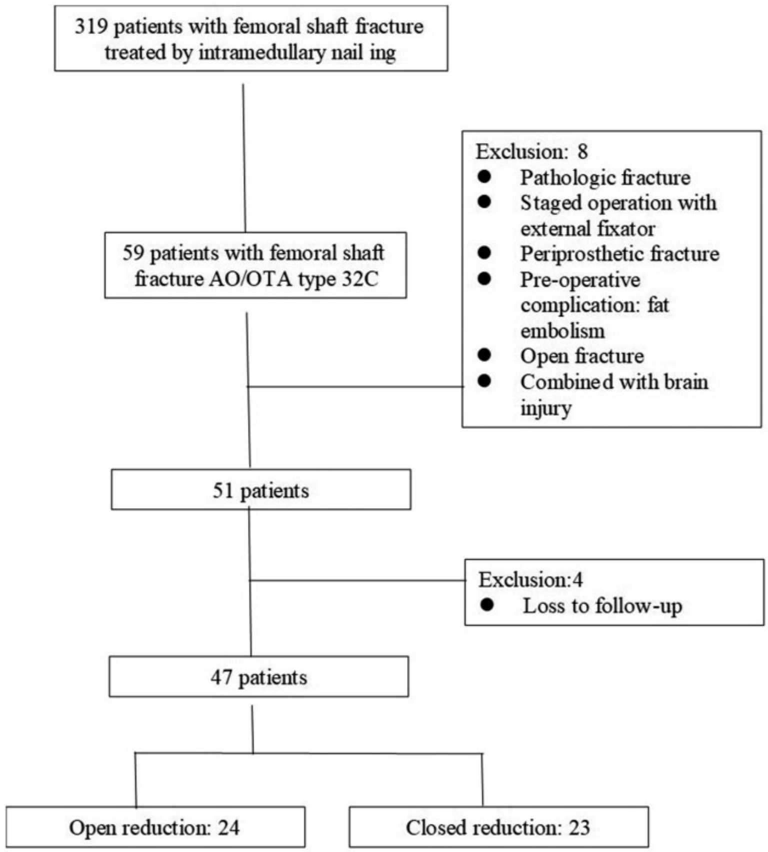

Figure 1. Flow diagram showing patient enrolment.

Table 1. Demographic data of the open- and closed-reduction groups.

Characteristic	Open (*n* = 24)	Closed (*n* = 23)	*p*-value
Age, years, mean (SD)	30.33 (12.61)	32.95 (16.17)	0.856
Sex (*n*, %)			0.071
Male	21 (87.50)	15 (65.21)	
Female	3 (12.50)	8 (34.79)	
BMI (SD)	23.8 (17.70)	20.6 (19.10)	0.594
Smoking (*n*, %)	6 (25)	2 (8.69)	0.137
Side (*n*, %)			0.654
Right	12 (50)	10 (43.47)	
Left	12 (50)	13 (56.52)	
Subtype			0.430
C1 (spiral)	12	13	
C2 (segmental)	2	4	
C3 (irregular)	10	6	
Multiple trauma (*n*, %)	8 (33.33)	9 (39.13)	0.679

SD, standard deviation; BMI, body mass index.

Table 2. Comparison of the outcomes between the open- and closed-reduction groups.

Outcome measure	Open ($n = 24$)	Closed ($n = 23$)		p-value
Anatomical-to-small gap, n (%)	24 (100%)	12 (52.17%)		*0.001
	Open ($n = 24$)	Closed-small ($n = 12$)	Closed-large ($n = 11$)	
Union in 12 months, n (%)	19 (79.17%)	12 (100%)	8 (72.73%)	*0.018
Mean union time, months (SD)	7.58 (2.28)	7.31 (2.27)	*#9.75 (2.12)	*0.049 #0.005
RUSF				
Score at 6 months	9.25 (2.23)	8.92 (2.19)	*7.55 (2.16)	*0.022
Score at 9 months	10.87 (2.02)	10.83 (0.83)	*9.73 (1.85)	*0.047
Score at 12 months	11.33 (1.81)	11.75 (0.45)	11.09 (1.04)	0.224
Complication, n or n (%)	5 (20.83%)	1 (8.33%)	4 (36.36%)	*0.015
Non-union	5 (20.83%)	0	3 (27.27%)	
Infection (n)	0	0	0	
Malrotation	0	0	1 (9.09%)	
Limb discrepancy	0	1	0	
Re-operation, n (%)	5 (20.83%)	1 (8.33%)	4 (36.36%)	*0.015

Data are expressed as mean (standard deviation) or as stated.
RUSF, radiographic union score of the femur.
*$p < 0.05$.
#closed-small vs. closed-large, $p < 0.05$.

group achieved bone union after 7.58 months, and the closed-large group had a longer time to bone healing (9.75 months). Differences between the closed-small and closed-large groups ($p = 0.005$) and between the open-reduction and closed-large groups ($p = 0.049$) were significant (Table 2).

RUSF

The mean RUSF at 6 months post-operatively was 8.92, 9.25, and 7.55 in the closed-small, open-reduction, and closed-large groups, respectively. There was a significant difference between the open-reduction and closed-large groups ($p = 0.022$; Table 2). The significant difference persisted until 9 months post-operatively (RUSF in the open-reduction vs. closed-small vs. closed-large groups: 10.83 vs. 10.87 vs. 9.73, respectively; $p = 0.047$; Table 2). The mean RUSF was not significantly different at 12 months post-operatively; however, the closed-small group sustained the highest score (closed-small vs. open-reduction vs. closed-large groups: 11.75 vs. 11.33 vs. 11.09, respectively; $p = 0.224$; Table 2). Throughout the period of bone healing, the open-reduction and closed-small groups sustained similar RUSF; however, the scores for both of these groups were better than those of the closed-large group (Figure 2).

Complications

Overall, the closed-small group had the lowest complication rate (8.33%), followed by the open-reduction group (20.83%) and the closed-small group (36.36%). There was a significant difference between the groups ($p = 0.015$). No patients developed post-operative infections (Table 2).

In the open-reduction group, two patients (Nos. 3 and 4) underwent early dynamization at 6 and 7 months post-operatively, respectively. One of these

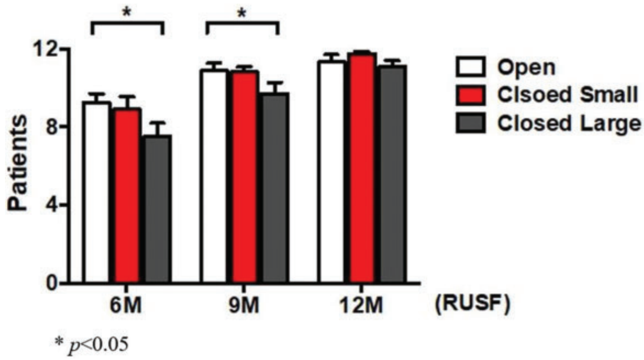

Figure 2. The radiographic union score of the femur (RUSF) at three post-operative stages. The white bar represents the open-reduction group, the red bar represents the closed-small group, and the gray bar represents the closed-large group. The RUSF in the open-reduction group and closed-small group was higher than that in the closed-large group (*$p < 0.05$).

patients (No. 3) achieved union 12 months post-operatively. Patient No. 4 developed non-union and underwent a revision surgery (nail change and secondary bone grafting) 12 months post-operatively. Two patients (Nos. 1 and 2) had a failed implant with a broken nail 12 and 7 months post-operatively, respectively; both underwent revision surgery. One patient (No. 5) developed non-union and underwent revision surgery (nail change and bone grafting) 1 year post-operatively. All of these patients eventually achieved bone union (Table 3).

In the closed-reduction group, there were five patients with complications. One patient (No. 7) underwent prompt revision surgery, which was indicated for femoral malrotation on the third day after the first operation. One patient (No. 6) had lower limb discrepancy and was managed by dynamization 4 months post-operatively. Two patients (Nos. 9 and 10) developed non-union and were managed by secondary bone grafting 6 months post-operatively and dynamization 9 months post-operatively, respectively. One patient (No. 8) developed non-union and had a reversed fragment. This patient underwent revision reduction and fixation with wiring and secondary bone grafting 5 months post-operatively (Figure 3). All patients achieved bone union at the last follow-up evaluation (Table 3).

Discussion

The rate of non-union after IMN of femoral shaft fractures ranges from 1% to 20%.[17] Compared with simple fractures, in complex fractures, delayed union or non-union after IMN is more frequent, with a rate of up to 30%.[18] In our study, the overall rate of bone union was 82.97% 12 months post-operatively, which was comparable to the rate reported in a previous study.[19] Overall, the closed-small group had an optimal outcome in terms of bone union rate, complication rate, bone union time, and RUSF. The open-reduction group had similar outcomes regarding union time, but with a lower bone union rate and higher complication rates than those in the closed-small group. RUSF, indicating union strength, was similar between the groups during bone healing. The closed-large group showed inferior outcomes to those of the other two groups for all results.

The most significant finding in the current study was that a residual gap of

Table 3. Demographic characteristics of the patients who underwent re-operation.

Case no.	Sex/age (years)	Etiology	Gap	Timing of complications post-operatively	Secondary intervention	Time to union (months)
Open-reduction group						
1	Male/28	Non-union/broken nail	Small	12th month	Nail change and bone grafting	20
2	Female/25	Non-union/broken nail	Small	7th month	Nail change and bone grafting	14
3	Male/20	Non-union	Small	7th month	Dynamization	12
4	Male/25	Non-union	Small	6/10th month	Dynamization/nail change and bone grafting	20
5	Male/52	Non-union	Small	12th month	Nail change and bone grafting	15
Closed-reduction group						
6	Male/21	Limb discrepancy	Small	4th month	Dynamization	12
7	Male/17	Femoral malrotation	Large	3rd day	De-rotation, adjustment of distal screws	12
8	Female/23	Non-union and reversed fragment	Large	5th month	Revision reduction and fixation with wiring, secondary bone grafting	12
9	Male/50	Non-union	Large	6th month	Secondary bone grafting	20
10	Male/21	Non-union	Large	9th month	Dynamization	15

Figure 3. A 23-year-old woman (case No. 8) sustained a left complex femoral shaft spiral fracture (AO/ATO type 32-C1). Anteroposterior (left panel) and lateral (right panel) plain radiographic views (a). Closed-reduction following intramedullary nail fixation was performed. A reversed butterfly fragment and residual large gap were observed after the first operation (anteroposterior view, left panel; lateral view, right panel) (b). A secondary surgery was performed in the 5th post-operative month comprising revision reduction and fixation with wiring, and secondary bone grafting (anteroposterior view, left panel; lateral view, right panel) (c) and This patient achieved union in the 12th post-operative month (d) (anteroposterior view, left panel; lateral view, right panel).
AO/ATO, Arbeitsgemeinschaft für Osteosynthesefragen Foundation/Orthopaedic Trauma Association.

>10 mm had negative effects on bone healing after reduction of complex femoral shaft fractures treated with nailing. The effect of the presence of a third fragment and a residual gap has been investigated in several studies.[6,19,20] A residual gap persists after closed reduction, indicating a worse bone healing environment caused by huge fragment diastasis, potential soft tissue interposition, and poor axial load-bearing ability.[2,3] Additionally, the excessive fragmentary motion between the large gap has a negative effect on callus formation.[21,22] Lin et al. concluded that

a fragmentary displacement of >10 mm in a femoral shaft fracture after nailing affected bone healing.[6] In our retrospective study, the closed-large group had the poorest bone union rate, longest bone union time, and the lowest union strength. Additionally, the complication rate was significantly higher in this group.

Several risk factors for non-union have been reported, such as the severity of the fracture, and fragment size and displacement.[20] In addition, non-union develops significantly more frequently in femoral shaft fractures with longer fragments (≥8 cm) or when the proximal displacement is ≥20 mm and the distal displacement is ≥10 mm, compared with when these conditions are not present. Moreover, the degree of displacement has a greater influence on the development of non-union than that of third fragment size.[19] Among these risk factors, only displacement can be modified by intra-operative reduction.[20] Therefore, we suggested that properly executed reduction may result in improved post-operative outcomes compared with poorly executed reduction because well-reduced fragments and small residual gaps are associated with enhanced union quality and quantity.

In analyzing the cases with complications, all cases in the open-reduction group developed non-union, and most required major revision surgery. The closed-reduction group revealed the possibility of biomechanical abnormalities, and an increased risk of non-union was observed in cases with residual large gaps compared with cases with residual small gaps. However, all of the complications were treatable with relatively minor surgery. Closed reduction has the advantage of preserving the soft tissue integrity and blood supply, leading to better outcomes and lower complication rates compared with open reduction.[2,23–25] However, open reduction disturbs bone union and predisposes patients to complications, although several studies comparing both techniques have yielded conflicting results regarding outcomes.[6,19,20,26] Based on our results, we speculate that open reduction and IMN of femoral shaft fractures did not significantly disturb bone union or increase the risk of infections. However, open reduction and IMN caused additional tissue trauma that predisposed patients to major complications.

Primary bone grafting can be performed through an incisional wound and can help enhance bone healing. Although this issue is controversial, primary bone grafting for complex long-bone diaphyseal fractures is recommended.[27–29] Among the orthobiologic agents for bone enhancement, evidence supporting the use of bone grafts is strong, whereas evidence supporting the use of demineralized bone matrix and synthetic ceramics is moderate.[30,31] In our open-reduction group, primary bone grafting with reamed intramedullary autografts was performed in all patients, which should have helped bone healing.

The difference in outcomes between closed and open nailing in femoral diaphyseal fractures is controversial.[32–34] Therefore, individualization of treatment is a better approach. Ghouri et al. suggested that in cases of difficult closed reduction (i.e., closed reduction could not be achieved in 15 minutes) open reduction is preferred.[35] From our results, we believe that achieving quality reduction and minimizing the residual gap should be prioritized to facilitate bone healing. In cases where the residual gap is >10 mm after closed reduction, minimally invasive techniques or open reduction with minimal stripping are recommended.

The limitations in this study of the relatively small sample size and short follow-up duration may have impacted outcomes and led to different conclusions. Additionally, only radiographic outcomes were evaluated. Further studies of the clinical outcomes and radiographic findings in similar cases are mandatory to confirm our findings.

In conclusion, IMN with closed reduction for complex femoral shaft fractures remains the preferred technique, and this approach is associated with better outcomes and fewer complications compared with open reduction. Because the quality of reduction is important for bone union, if the outcomes of closed reduction are not satisfactory (i.e., residual gap >10 mm), surgeons should consider a minimally invasive technique or open reduction with minimal stripping. IMN with closed reduction restores anatomical reduction, enables primary bone grafting, and results in an optimal union rate and strength.

Author contributions

YHC and TYL participated in the study design, data collection, statistical analyses, and drafting of the manuscript. HJL participated in the data analysis. SML participated in the study design. CHC and SPR provided advice and assisted in the drafting of the manuscript. All authors read and approved the final manuscript.

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Data availability statement

The datasets are not publicly available as they will be used for further research. However, the datasets are available from the corresponding author on reasonable request.

Declaration of conflicting interests

The authors declare that they have no competing interests.

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References

1. Klemm KW and Börner M. Interlocking nailing of complex fractures of the femur and tibia. *Clin Orthop Relat Res* 1986; 212: 89–100.
2. Wiss DA, Fleming CH, Matta JM, et al. Comminuted and rotationally unstable fractures of the femur treated with an interlocking nail. *Clin Orthop Relat Res* 1986; 212: 35–47.
3. Winquist RA and Hansen ST Jr. Comminuted fractures of the femoral shaft treated by intramedullary nailing. *Orthop Clin North Am* 1980; 11: 633–648.
4. Salminen ST, Pihlajamäki HK, Avikainen VJ, et al. Population based epidemiologic and morphologic study of femoral shaft fractures. *Clin Orthop Relat Res* 2000; 372: 241–249.
5. Winquist RA, Hansen ST Jr and Clawson DK. Closed intramedullary nailing of femoral fractures. A report of five hundred and twenty cases. *J Bone Joint Surg Am*1984; 66: 529–539.
6. Lin SJ, Chen CL, Peng KT, et al. Effect of fragmentary displacement and morphology in the treatment of comminuted femoral shaft fractures with an intramedullary nail. *Injury* 2014; 45: 752–756.
7. Trompeter A and Newman K. Femoral shaft fractures in adults. *Orthop Trauma* 2013; 27: 322–331.
8. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007; 147: 573–577.
9. Böstman O, Varjonen L, Vainionpää S, et al. Incidence of local complications after intramedullary nailing and after plate fixation of femoral shaft fractures. *J Trauma* 1989; 29: 639–645.
10. Fracture and dislocation compendium. Orthopaedic Trauma Association Committee

for Coding and Classification. *J Orthop Trauma* 1996; 10 Suppl 1: v–ix 1–154.
11. McFerran MA and Johnson KD. Intramedullary nailing of acute femoral shaft fractures without a fracture table: technique of using a femoral distractor. *J Orthop Trauma* 1992; 6: 271–278.
12. Georgiadis GM and Burgar AM. Percutaneous skeletal joysticks for closed reduction of femoral shaft fractures during intramedullary nailing. *J Orthop Trauma* 2001; 15: 570–571.
13. Whelan DB, Bhandari M, Stephen D, et al. Development of the radiographic union score for tibial fractures for the assessment of tibial fracture healing after intramedullary fixation. *J Trauma* 2010; 68: 629–632.
14. Panjabi MM, Walter SD, Karuda M, et al. Correlations of radiographic analysis of healing fractures with strength: a statistical analysis of experimental osteotomies. *J Orthop Res* 1985; 3: 212–218.
15. Bellabarba C, Ricci WM and Bolhofner BR. Results of indirect reduction and plating of femoral shaft nonunions after intramedullary nailing. *J Orthop Trauma* 2001; 15: 254–263.
16. Marsh D. Concepts of fracture union, delayed union, and nonunion. *Clin Orthop Relat Res* 1998; S22–S30.
17. Gelalis ID, Politis AN, Arnaoutoglou CM, et al. Diagnostic and treatment modalities in nonunions of the femoral shaft: a review. *Injury* 2012; 43: 980–988.
18. Metsemakers WJ, Roels N, Belmans A, et al. Risk factors for nonunion after intramedullary nailing of femoral shaft fractures: remaining controversies. *Injury* 2015; 46: 1601–1607.
19. Lee JR, Kim HJ and Lee KB. Effects of third fragment size and displacement on non-union of femoral shaft fractures after locking for intramedullary nailing. *Orthop Traumatol Surg Res* 2016; 102: 175–181.
20. Hamahashi K, Uchiyama Y, Kobayashi Y, et al. Clinical outcomes of intramedullary nailing of femoral shaft fractures with third fragments: a retrospective analysis of risk factors for delayed union. *Trauma Surg Acute Care Open* 2019; 4: e000203.
21. Claes L, Eckert-Hübner K and Augat P. The effect of mechanical stability on local vascularization and tissue differentiation in callus healing. *J Orthop Res* 2002; 20: 1099–1105.
22. Lienau J, Schell H, Duda GN, et al. Initial vascularization and tissue differentiation are influenced by fixation stability. *J Orthop Res* 2005; 23: 639–645.
23. Winquist RA. Locked femoral nailing. *J Am Acad Orthop Surg* 1993; 1: 95–105.
24. Singh D, Garg R, Bassi, et al. Open grade III fractures of femoral shaft: outcome after early reamed intramedullary nailing. *Orthop Traumatol Surg Res* 2011; 97: 506–511.
25. Kempf I, Grosse A and Beck G. Closed locked intramedullary nailing. Its application to comminuted fractures of the femur. *J Bone Joint Surg Am* 1985; 67: 709–720.
26. Burç H, Atay T, Demirci D, et al. The intramedullary nailing of adult femoral shaft fracture by the way of open reduction is a disadvantage or not? *Indian J Surg* 2015; 77: 583–588.
27. Gogus A, Ozturk C, Tezer M, et al. “Sandwich technique” in the surgical treatment of primary complex fractures of the femur and humerus. *Int Orthop* 2007; 31: 87–92.
28. Marongiu G and Capone A. Atypical periprosthetic acetabular fracture in long-term alendronate therapy. *Clin Cases Miner Bone Metab* 2016; 13: 209–213.
29. Kashayi-Chowdojirao S, Vallurupalli A, Chilakamarri VK, et al. Role of autologous non-vascularised intramedullary fibular strut graft in humeral shaft nonunions following failed plating. *J Clin Orthop Trauma* 2017; 8: S21–S30.
30. Marongiu G, Dolci A, Verona M, et al. The biology and treatment of acute long-bones diaphyseal fractures: overview of the current options for bone healing enhancement. *Bone Rep* 2020; 12: 100249.
31. Marongiu G, Contini A, Cozzi Lepri A, et al. The treatment of acute diaphyseal long-bones fractures with orthobiologics and pharmacological interventions for bone healing enhancement: a systematic review of clinical evidence. *Bioengineering (Basel)* 2020; 7: 22.

32. Wu CC and Lee ZL. Treatment of femoral shaft aseptic nonunion associated with broken distal locked screws and shortening. *J Trauma* 2005; 58: 837–840.
33. Taitsman LA, Lynch JR, Agel J, et al. Risk factors for femoral nonunion after femoral shaft fracture. *J Trauma* 2009; 67: 1389–1392.
34. Liao JC, Hsieh PH, Chuang TY, et al. Mini-open intramedullary nailing of acute femoral shaft fracture: reduction through a small incision without a fracture table. *Chang Gung Med J* 2003; 26: 660–668.
35. Ghouri SI, Alhammoud A and Alkhayarin MM. Does open reduction in intramedullary nailing of femur shaft fractures adversely affect the outcome? A retrospective study. *Adv Orthop* 2020; 2020: 7583204.