



Management of Distal Femoral Non-union: A Systematic Review

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Abstract

Introduction Managing distal femur fracture nonunion is complex, with unpredictable results. The present investigation systematically updates current evidence, reviews existing modalities, innovations and related outcomes, and discusses future perspectives on the management of nonunion of the distal femur.

Methods This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the 2020 PRISMA statement. In April 2024, PubMed, Web of Science, Google Scholar, and Embase were accessed without time constraints. No additional filters were used in the database search. All the clinical studies investigating treatment options for nonunion of distal femur fractures were accessed.

Results 35 clinical studies (832 patients) were included. Of them, 34.2% (239 of 698 patients) reported an open fracture, and 24.5% (78 of 319 patients) reported infection at the fracture site. The mean length of the follow-up was 28.9 ± 13.2 months. The mean age of the patients was 53.8 ± 14.7 years.

Conclusion 84.5% (703 of 832) of patients reached complete union without major complications, and 3.8% (32 of 832) reached complete union with major complications at a mean of 21.7 ± 20.9 months. 8.7% (72 of 832) patients showed signs of persistent non-union.

Level of evidence Level III, systematic review.

Keywords Distal femoral fractures · Nonunion · Fracture fixation · Fracture healing

Introduction

Distal femoral fractures account for about 3–6% of all femoral fractures [1–3]. Previously published reviews on distal femoral nonunion have provided valuable insights into the epidemiology, risk factors, and treatment of this condition [4–6]. The distal femoral nonunions, although

rare, negatively impact the quality of life (QOL) and pose considerable treatment challenges [7, 8]. Patients with open and comminuted fractures and infections are most prone to develop nonunion [9, 10]. Open reduction and internal fixation (ORIF) combined with cancellous autografting is the most successful treatment option, with a union rate of 97.4% and an average time to heal of 7.8 months [11, 12].

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Several non-modifiable and modifiable risk factors for non-union have been identified, including open fractures, fractures with bone loss, and those associated with osteoporosis, diabetes, obesity, and malnutrition [13, 14]. In addition, certain patient-related factors like smoking, advanced age, and obesity are also considered to affect fracture healing negatively [14, 15]. Importantly, inadequate fracture fixation is primarily responsible for non-union and implant failure [16]. The rigidity score has been advocated to predict the risk of nonunion [17, 18]. This score was significantly associated with the risk of non-union [18]. Still, no significant association was detected between non-union and postoperative weight-bearing status or other previously identified risk factors [17]. Karam et al. [19] reported an overall similar non-union rate of 17.8% in both locked plating of closed periprosthetic and non-periprosthetic distal femoral and comminution, which was the most crucial predictor of non-union.

Although nonunions are a well-known complication of fractures, evidence on this condition is limited. The present investigation systematically updates current evidence, reviews existing modalities, innovations, and related outcomes, and discusses future perspectives on the management of nonunion of the distal femur.

Methods

Eligibility Criteria

All the clinical studies investigating treatment options for nonunion distal femur fractures were accessed. According to the author's language capabilities, English, German, Italian, French, and Spanish articles were eligible. Only studies with levels I to V of evidence, according to the Oxford Centre of Evidence-Based Medicine [20], were considered. Reviews, opinions, letters, and editorials were not considered, as were animals, in vitro, biomechanics, computational, and cadaveric investigations. Missing quantitative data under the outcomes of interests warranted the exclusion of the study.

Search Strategy

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the 2020 PRISMA statement [21]. The following PICO algorithm was established for the database search:

- P (Problem): nonunion distal femur fractures;
- I (Intervention): management;
- C (Comparison): different modalities of fracture healing;

- O (Outcomes): union.

In May 2024, PubMed, Web of Science, Google Scholar, and Embase were accessed without time constraints. The Medical Subject Headings (MeSH) used for the database search are reported in the Appendix. No additional filters were used in the database search.

Selection and Data Collection

Two authors (FM and LS) independently performed the database search. All the resulting titles were screened by hand and, if suitable, the abstract was accessed. The full text of the abstracts which matched the topic was accessed. If the full text was not accessible or available, the article was not considered for inclusion. A cross reference of the bibliography of the full-text articles was also performed for inclusion. Disagreements were debated and mutually solved by the authors. In case of further disagreements, a third senior author (RV) decided.

Data Items

Two authors (FM and LS) independently performed data extraction. The following data were extracted: author and year, name of the journal and study design, level of evidence, length of the follow-up, number of included patients, mean age, percentage of women, type of initial and definitive treatment, time to definitive treatment, number of unions with or without major complications and main findings. Data were extracted in Microsoft Office Excel version 16.72 (Microsoft Corporation, Redmond, USA).

Assessment of the Risk of Bias and Quality of the Recommendations

The risk of bias was evaluated following the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions [22]. Nonrandomised controlled trials (non-RCTs) were assessed using the Risk of Bias in Non-randomised Studies of Interventions (ROBINS-I) tool [23]. Seven domains of potential bias in non-RCTs were assessed. Possible confounding and the nature of patient selection before the start of the comparative intervention are assessed by two domains. A further domain is used to determine bias in the classification during the intervention. The final four domains assess the methodological quality after the intervention comparison has been implemented and relate to deviations from previously intended interventions, missing data, erroneous measurement of outcomes, and bias in the selection of reported outcomes. The figure of the ROBINS-I

was elaborated using the Robvis Software (Risk-of-bias Visualization, Riskofbias.info, Bristol, UK).

Synthesis Methods

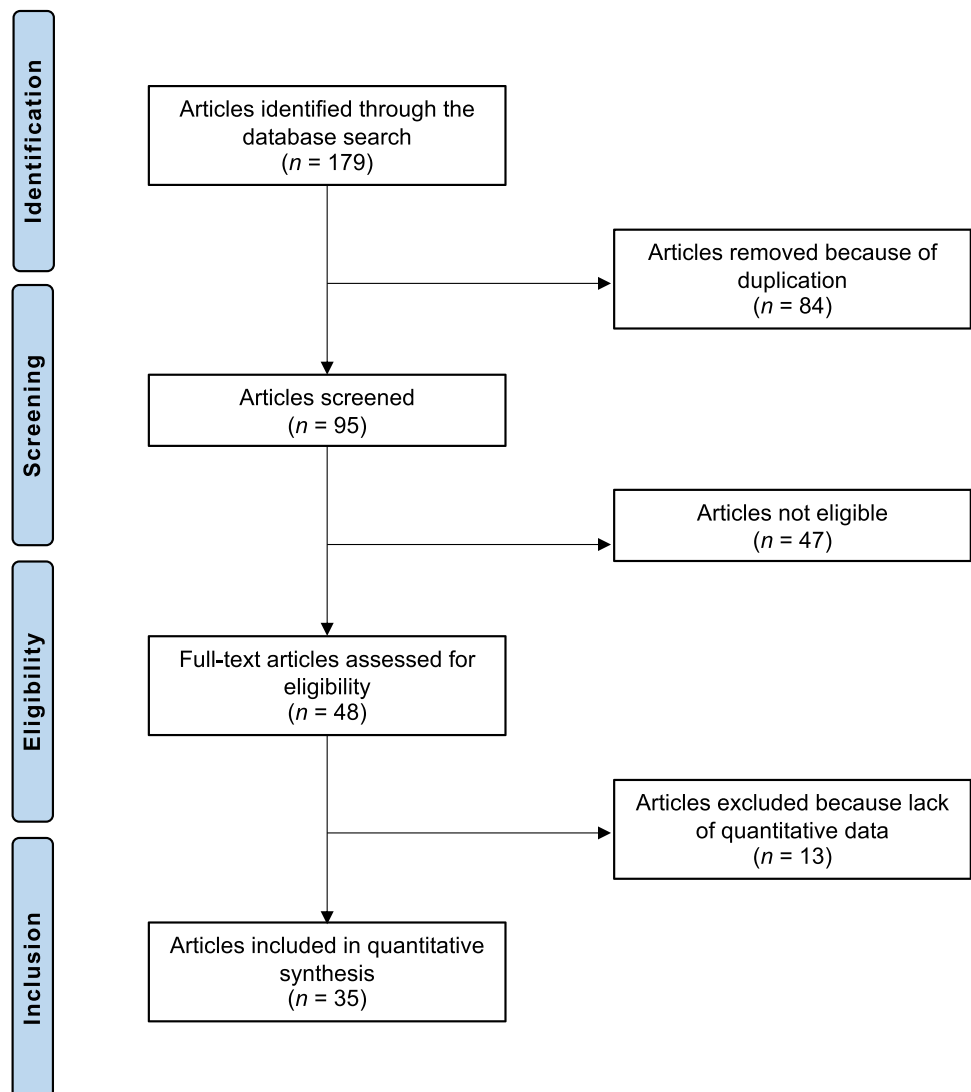
The main author (FM) performed the statistical analyses following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions [22]. The IBM SPSS software (version 25) was used. For dichotomous data, the number of events and observations were reported. For continuous data, the arithmetic mean and standard deviation were used.

Results

Study Selection

The literature search resulted in 179 articles. All search results were extracted and checked for relevance. Of these, 84 studies were discarded because they were duplicates. Following the defined inclusion criteria, the abstracts of 95 articles were reviewed, and 47 studies were excluded because they did not match the eligibility criteria. The reasons that led to exclusion were: study design (N=28), low level of evidence (N=2), not evaluating the un-union of distal femur fracture (N=9), and language limitations (N=8). An additional 13 articles were excluded because they did not offer quantitative data on the outcomes of interest. In conclusion, 35 investigations were included in the present analysis. The results of the literature search are shown in Fig. 1.

Fig. 1 PRISMA flow chart of the literature search



Methodological Quality Assessment

The ROBINS-I was applied to investigate the risk of bias in the included studies. Given the small number of patients studied in the included investigations, the risk of bias based on confounding and the selection of participants was rated in four studies as serious and in four other studies considered critical because they reported data from only one or two patients. The remaining studies were rated as having a low to moderate risk of bias in these domains. The protocol of intervention was well reported in most studies, and no significant deviation from the interventions was identified, leading to an overall low to moderate risk of bias in the classification of interventions and deviation from intended interventions. Data were adequately reported in the most included studies, and the measurement of the outcomes was equivalent among the groups. Given the lack of randomisation of the investigators and patients, the measurement of the outcomes was evaluated with a moderate risk of bias in all of the studies. When described, the reported results corresponded to the planned protocol in most included studies. However, the exact details of a protocol are often missing, leading to a moderate risk of bias in most of the studies. Given the overall poor methodological quality in the included studies, the overall risk of bias was predominantly moderate. The assessments of the methodological quality are given in Fig. 2.

Study Characteristics and Results of Individual Studies

Data from 832 patients were collected. Of them, 34.2% (239 of 698 patients) reported an open fracture, and 24.5% (78 of 319 patients) reported infection at the fracture site. The mean length of the follow-up was 28.9 ± 13.2 months. The mean age of the patients was 53.8 ± 14.7 years. The

generalities, patient characteristics and main results of the included studies are reported in Table 1.

Result Syntheses

At a mean of 21.7 ± 20.9 months, 84.5% (703 of 832) of patients reached complete union without major complications, and 3.8% (32 of 832) reached complete union with major complications. On the other hand, 8.7% (72 of 832) patients showed signs of persistent non-union.

Discussion

The present systematic review revealed that with surgical management of the distal femoral nonunion 84.5% (703 of 832) of patients reached complete union without major complications, and 3.8% (32 of 832) reached complete union with major complications at a mean of 21.7 ± 20.9 months. But, 8.7% (72 of 832) patients showed signs of persistent non-union.

Distal femoral nonunions are challenging to manage, and patient risk factors should be critically evaluated when treating acute distal femoral fractures, since several modifiable risks, such as intake of alcohol and steroids, smoking, and diabetic control, might reduce the risk of nonunion [4, 10, 24]. In addition, optimal fracture alignment and compression are also essential when treating acute fractures [25]. Infections are important risk factors, especially in open fractures or fractures that fail to heal [26, 27]. There is good evidence to guide decision-making and successful union with conventional trauma fixation techniques in the majority of patients. Biological augmentation of fracture healing is not necessary in most cases but needs to be considered in higher-risk cases with a mobile atrophic pattern.

The definition of nonunion is heterogeneous and is related to the time elapsed from the injury to the diagnosis

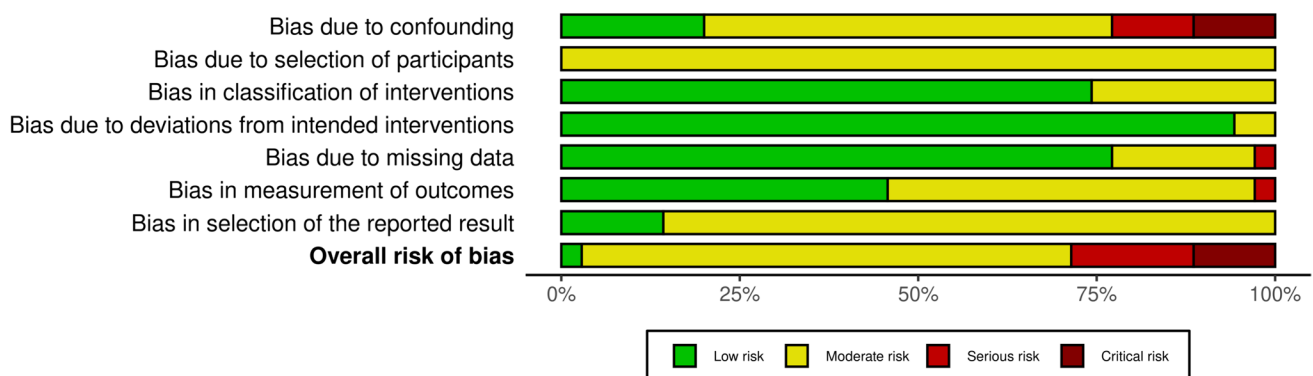


Fig. 2 The ROBINS-I of non-randomised control trials

Table 1 Generalities, patient characteristics, and main results of the included studies

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Ali & Saleh, 2002 [72]	<i>Egyptian Orthopaedic Journal</i>	Retrospective case series	IV	35.3	12	41.7	0	9	9	AO/OTA classification: 33A2 (2) 33A3 (4) 33C2 (6)	DFLP (7) Unilateral external fixator (3) Retrograde IMN (2)	Ilizarov fixator	The Ilizarov EF technique can be used as an effective treatment option with low complications in the management of non-united distal femoral fractures that may be difficult to manage using other means of fixation
Ali & Saleh, 2002 [72]	<i>Injury</i>	Retrospective case series	IV	55.2	15	35.4	40	9	5	Femoral osteotomy (1)	DCS in (7) Blade plate (7) Retrograde femoral nail (1)	EF	The advantages of preservation of soft tissue, immobilisation of the fracture site by crossing the knee joint and the facility for proximal lengthening make EF definite option in the management of distal femoral nonunions

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Alt et al., 2007 [73]	<i>J Orthop Trauma</i>	Case Report	V	24	1	49	0	1	0	Left lateral femoral neck fracture Gustilo Anderson grade I Open distal femoral shaft fracture (same side) Comminuted fracture of the left tibia and fibula	EF Angle blade plate	rhBMP-s	rhBMP-2 has the potential to heal non-unions of the femur when combined with stable fixation of the nonunion sites
Bellabarba et al., 2002 [74]	<i>J Orthop Trauma</i>	Prospective case series	IV	23	20	48	40	7	1	Gustilo and Anderson Type: IIB (1) IIIA (3) II (3) AO/OTA classification: 33-A (11) 33-C (9) 33-2, 33-3 (8) 33-C3 (3)	ORIF (19) Plaster cast (1) Condylar blade-plate (7) DCS (7) Condylar buttress plate (5) DCP(1) Osteoset bone graft substitute (1)	Indirect reduction techniques using the 95-degree condylar blade plate, condylar buttress plate, or locking condylar plate with autologous cancellous bone grafting in 45% of 20) of patients	Contemporary plating techniques are effective in the treatment of distal femoral nonunions. Union occurred reliably with few complications, resulting in a majority of good or excellent clinical results

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Chen et al., 2011 [75]	<i>Chin J Traumatol</i>	Case Report	V	15	1	23	0	0		AO/OTA classification: 33-C2	1. ORIF with cloverleaf plate 2. Exchanging the cloverleaf plate with an LCP and using the autolilac bone graft to fill the nonunion gap	Remove of the plate and screws Insertion of IMN Place laterally and medially to the fracture site, drilled two holes respectively, and fastened with suture Auto-ililac bone grafting with nonunion bone grafts	An autologous graft of double strut fibular cortical bone plate is effective in managing long-bone fractures and defects of the lower extremities. This procedure may also be preferable in reconstructing the femur in cases of multiple failures of fracture fixation

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Cone et al., 2023 [10]	<i>J Orthop Trauma</i>	Retrospective cohort study	III	27	438	48	47.3	168		OTA/AO 33A type fractures (108) OTA/AO 33C type fractures (330)	LLP IMN LLP+IMN Ex-Fix	The surgical approach and technique were at the discretion of the operating surgeon and determined by the fracture characteristics	Segmental bone loss, open fractures, chronic anaemia, and increasing body mass index are significant risk factors in the occurrence of distal femoral nonunion. Lateral-locked plating characteristics did not seem to affect nonunion rates

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Davila et al., 2001 [76]	<i>J Orthop Trauma</i>	Case Report	V	24	2	68	100	1	0	C3 supracondylar distal femur fracture Open right supracondylar femur fracture	IMN Condylar buttress plate Bone grafting ORIF	TKA with kinematic rotating hinge mega prosthesis	TKA using a mega prosthesis is a good solution for elderly patients with a persistent distal femoral nonunion despite multiple attempts at obtaining union. Patients can expect excellent pain relief and a good range of motion. We do not advocate arthroplasty for an acute fracture since the majority of these fractures do well following internal fixation

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Ebraheim et al., 2016 [77]	<i>Orthop Surg</i>	Retrospective series	IV	29	14	65	92.9	1	0	AO/OTA classification: 33-A1 (3) 33-A2 (6) 33-A3 (2) 33-C3 (3)	LCP	ORIF revision (11) Revision without ORIF—only iliac crest stem cell auto-graft, bone graft sub-stitute, or rh-BMP-2 (3) Additional to ORIF revision: rh-BMP-2 (12) Iliac crest bone autograft (5), Iliac crest stem cell auto-graft (2), Crushed cancellous bone allograft (3), CaSO 4 tricalcium phosphate bone graft substitute (2) dem-inalized bone matrix (1) Medial plate (2)	Definitive treatment of distal femur nonunion after initial treatment with a locking plate had a low rate of success in this study, suggesting that this procedure is ineffective as a definitive treatment for distal femur nonunion

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Gardner et al., 2008 [78]	<i>J Trauma</i>	Retrospective series	IV	41.5	31	57.6	71	4	4		Plate (1) Ex-Fix (3) Condylar buttress plate (2) DCS (14) DCP (1) Blade plate (4) IMN (2) Ilizarov (1) Allograft (1) Plate and cast (1)	ORIF Debridement of the non-union Correction of the deformity in the coronal and sagittal planes Bone grafting (100%) Iliac crest bone graft (71%) Demineralized bone matrix (29%) Arthrolysis when necessary Fixed-angle implant and lag screws	Distal femoral nonunions may be treated successfully with correction of deformity, stable fixed-angle internal fixation, lag screw placement, and supplemental bone grafting. Knee joint manipulation and arthrolysis are important components of the treatment plan if knee motion is limited because of fibrosis. This yields predictable functional outcomes after the surgical intervention

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Graves et al., 2005 [79]	<i>J Orthop Trauma</i>	Case Report	V	24	1	55	100	1	0	Gustilo and Anderson Type: Type 3C AO/OTA classification: 33A-1	IMN Debridement anterior iliac crest bone grafting Nail dynamization	The joint procedure with vascular and orthopaedic surgeons: Mobilisation of vessel repair Ligating aneurysmal feeder vessels Bridge plating and iliac crest autograft	The importance of preoperative vascular assessment in the case of nonunions or malunions associated with a previous vascular injury is emphasized

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Hailer and Hoffmann, 2006 [80]	<i>Arch Orthop Trauma Surg</i>	Case Report	V	48	1	82	100	0	0	AO/OTA classification: 33 A	DCS	LISS plate Autologous bone graft laterally Strut cortical autograft medially	LISS adequately addresses the important aspects of a nonunion fixation of the distal femur in elderly patients. A precise surgical plan may mostly include bone grafting and in selected cases limb shortening. Bone healing and preservation of knee function can be achieved even in severe osteoporosis with substantial bone defects

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Holzman et al., 2016 [81]	<i>Clin Orthop Relat Res</i>	Retrospective case series	IV	18	22	58	72.7	8	15	Distal femoral osteotomy (1) Periprosthetic non-union above a TKA (3)	ORIF with a lateral locking plate (2) ORIF with autogenous bone graft (2) ORIF with allograft and an implanted bone stimulator (1) TKA (3)	Single-stage procedure (16): stable lateral plate involved the addition of an MLP and autogenous bone graft Two-stage treatment (7): lateral plate failure involved placement of a new LLP followed by the addition of a medial locking plate with autogenous bone graft at least 2 months after the first procedure	A very high proportion of patients achieve union when using medial locking plates to treat distal femoral nonunions after lateral plating of the original injury. The addition of bone graft staged reconstruction, and revision of the initial lateral plate is indicated when the nonunion is associated with fatigue failure of the initial lateral plate

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Kim et al., 2015 [9]	<i>Eur J Orthop Surg Traumatol</i>	Retrospective case series	IV	48.5	22	44.3	45	10	22	AO/OTA classification: A type (7) B type (5) C type (10)	Screws (1) LCP (9) Blade (3) Plate (1) EF (5) Nail (3)	Debridement of the non-union Autologous bone grafting with or without additional plating Long-term antibiotics if intraoperative cultures were positive	Surgeons should consider indolent infection as a possible cause of nonunion in distal femoral fractures. An intraoperative biopsy tissue culture verifies the presence of indolent infection and antibiotics treatment based on identified organisms leads to successful treatment and better prognosis

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Ma et al., 2017 [82]	<i>Arch Orthop Trauma Surg</i>	Retrospective case series	IV	23.4	12	33	41.7	7	0		CBP (6) Nail (3) LCP (2)	Three-stage treatment protocol: Remove hardware and debride-ment Lengthening of soft tissue Correct alignment Definitive fixation with locked plate Cement spacer Bone defect reconstruction (Masquelet technique or vascularized bone graft)	In conclusion, even though the current study included small sample size and required three stages of intervention, the protocol helped achieve bony union, leg length equality, and normal limb alignment, as well as excellent ambulatory capacity in all cases. Hence, this technique can serve as a valuable alternative for the treatment of recalcitrant distal femoral nonunion with bone loss

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Monroy et al., 2014 [83]	<i>J Knee Surg</i>	Prospective clinical trial	II	29.4	22	58	59.1	6	4		Screws and Plate (19) Nail (3)	Plate and screw fixation in (19) IM nail in (3) Autogenous iliac crest (IC) bone grafts or IC aspirates (19) Cancellous chip allograft (1) Additionally bone morphogenic protein (BMP) (15)	The presence of an open fracture at the initial injury may increase the likelihood of developing a distal femur nonunion, and a nonunion will likely take longer to heal

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Mukhopad- haya et al., 2022 [43]	<i>Strategies Trauma Limb Reconstr</i>	Retrospec- tive clinical trial	III	39.5	31	43.1	29	1	0	AO/OTA classifi- cation: 33-A2 (1) 33-A3 (16) 33-C2 (14)	ORIF with lock- ing plate (21) Only DFLP (17) DFLP with PFN (1) DFLP with medial plate (1) LCP with can- cellous screws (2) DCS (1) DFN (3) EF (4) Skeletal traction (1) Thomas splint in (1)	Debridement and tissues sent for microbial culture and sensitivity (31) Fixation with bone graft inserted (29) DFLP (com- pression by lag screw or AO- Muller's compression device) (31) DFLP applied over the DFN (1) Additional lag screws (17)	Optimal stabil- ity, good compression at the non- union site (either by lag screws or a compression device or both), main- taining the axial align- ment strictly, freshening of bone ends, using an adequate amount of cortico- cancellous bone graft, respecting the biology along with the correct choice of the implant (including the size) are essential to achieve union at the fracture site

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Oh et al., 2011 [84]	<i>Arch Orthop Trauma Surg</i>	Case Report	V	12	1	58	100	0	0	AO/OTA classification: 33-A1	MIPO with seven-hole LCP-DF plate	Taken the lag screw out, motion at the fracture site, adopting the concept of “dynamization” in nailing	The screw removal employed by the authors, in this case, report can be used as a simple operation under local anesthesia before attempting other operations such as a bone graft
Oransky et al., 2023 [85]	<i>Eur J Orthop Surg Traumatol</i>	Retrospective case series	IV	13.5	10	48.3	30	1	0	AO/OTA classification: 33-A3 (5) 33-C1 (3) 33-C2 (1) 33-C3 (1)	Medial endosteal plate + lateral locking plate	Endosteal medial plate Lateral locking plate Autogenous bone grafting (RIA)	A medial endosteal plate is a useful augmentation for lateral plate fixation in nonunion or malunion following distal femur fractures, particularly in cases of medial bone loss, severe comminution, or poor bone quality

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Özdemir et al., 2023 [86]	Sci Rep	Retrospective case series	IV	40	13	34	15.4	0	0	Recalcitrant non-union of the distal two-thirds of the femur	Exchange RIM-nail Nail dynamization Iliac crest bone grafting Allograft Artificial growth factors (bone marrow injection, autologous platelet-rich plasma) Bone stimulator	Pedicle periosteal MFC flap	A pedicle MFC flap for femur distal two-thirds has been effective in the treatment of recalcitrant femur nonunions without significant bone defects There is no dependence on microvascular anastomosis Besides, the operation time is relatively short, and the donor site morbidity is minimal. Surgeons may consider this flap as a useful reconstruction option for patients with previous failed femur nonunion treatments

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Palatnik and Rozbruch, 2011 [87]	<i>Adv Orthop</i>	Retrospective clinical trial	IV	53.3	10	41.5	20	1	1		Knee arthrodesis EF IMN	Ilizarov external fixator or monolateral external fixator	Ilizarov method with the use of the external fixator, as well as its latter modifications, provides surgeons with a comprehensive approach to multiple femur pathologies and by its inherent adaptability to various clinical situations can be expected to continue to play important roles in the future. It is particularly useful in the setting of bone loss, LLD, infection, large and complex deformity, and poor soft-tissue envelope

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Pao and Jiang, 2005 [88]	<i>J Formos Med Assoc</i>	Case Report	V	34	3	74.7	0	0	0		ORIF with an anatomic plate and allogenic bone grafts DCS and side-plate TKA	IMN Bone graft	In conclusion, retrograde intramedullary nailing is a useful treatment option for nonunion of distal femoral fractures, especially after failure of plate-screw fixation. The design of total knee prostheses should consider this point and spare the intercondylar notch of the femoral component from metal coverage

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Rajasekaran et al., 2020 [89]	<i>Int Orthop</i>	Retrospective clinical trial	VI	22.1	24	71.8	29.7	0	0			Distal femur replace- ment using cemented modular endopros- thesis	By permitting immediate full weight- bearing ambulation and with most patients returning to an acceptable functional status, cemented mega prosthesis is a viable and useful single-stage manage- ment option in elderly patients with DFN
Reynolds et al., 2021 [90]	<i>J Orthop Case Rep</i>	Retrospec- tive case series	VI	25.8	4	66.75		0	1		rIMN TKA	Off-label use of tantalum trabecular metal aug- ments Bone-graft- ing from either RIA or autolo- gous iliac crest bone grafting	The use of tan- talum metal cones for the reconstruc- tion of distal femur non- union with segmental bone defects can be a successful technique in a complex group of patients

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Rollo et al., 2019 [91]	Med Glas (Zenica)	Retrospective cohort study	III	12	35	52.5	37.1			AO/OTA classification: 33-A (16) 33-B (19)	Plate and screws (22) Plat and cerclage cable (4) Retrograde nail (6) Various treatments (wires, screws, cerclage, etc.) (3)	ORIF (29) CRIF(6)	Functional "restitutio ad integrum" is possible. The role of bio-metallic solution in the treatment of nonunions and malunions is to recreate a knee anatomy and functionality compatible with a satisfactory quality of life
Saridis et al., 2006 [92]	J Bone Joint Surg Br	Retrospective case series	IV	42.4	13	34.6	23.1	13	13	Gustilo and Anderson Type: Type 3 B Type 3 C	ORIF (5) Unilateral transarticular EF (7) Hybrid external fixation (1)	Iliizarov fixator	The use of the Iliizarov external device for definitive fixation of fractures of the distal femur is the safest and most effective method since it provides adequate fixation and stabilisation at the site of the fracture, thus increasing osseous healing and decreasing infection

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Saxena et al., 2023 [47]	<i>Cureus</i>	Prospective clinical trial	IV	12	10	55	0				IM-nail (1) Extramedullary implants (4)	Implant removal Fixation with nail plate construct Bone grafting	In our experience, this relatively novel technique of combining nail plate constructs offers encouraging outcomes in the management of non-union distal femur fractures, especially in elderly and osteopenic patients

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Tis et al., 2005 [93]	Injury	Case Report	V	9	1	68	100	0	0	Oblique fracture of the distal femur	ORIF Bone allograft DCS Removing DCS and plate Proximally and distally locked supracondylar nail Bone allograft	Nail removing Square osteotomy Autogenous bone grafting Angled blade plate and cortical screws	Shortening has potential problems which include vascular insufficiency, knee stiffness, instability, and knee however, it is a safe and well-proven method technique of utilizing a transverse osteotomy. It is thought that it is the reduced shear force and not necessarily the method of fixation which contributed to success

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Vaishya et al. 2011 [53]	<i>Knee Surg Sports Traumatol Arthrosc</i>	Retrospective case series	IV	48	8	74	37.5	0	0			Megaprosthesis	Megaprosthesis can be offered as a one-stage salvage procedure for difficult nonunion in distal femoral fractures associated with bone loss, osteoporosis, and secondary knee arthritis
Vellingiri and Nagakumar, 2021 [94]	<i>Cureus</i>	Case Report	V	6	1	45	0	0	1	LCP	LCP	LCP removal Distal femoral nail fixation Allogenic bone grafting	For infected non-union distal femur, the patient in our study had a successful clinical and functional outcome following allograft with distal femoral nailing. Loadsharing devices are significant with better practical performance

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Wang and Weng, 2003 [95]	<i>J Bone Joint Surg Am</i>	Retrospective case series	IV	34	13	60	84.6	2	2		Blade plate or condylar buttress plate (10) Antegrade locked nail (2) Antegrade locked nail and a compression plate (1)	ORIF Deep-frozen cortical allograft struts Autogenous iliac bone grafts	Open reduction and internal fixation supplemented with allograft struts and autogenous bone graft is an effective treatment for nonunion of the distal part of the femur
Waseem et al., 2010 [96]	<i>PMR</i>	Case Report	V	36	1	77	50	1	0	Open comminuted left distal femur fracture Closed right distal femur fracture	Left: Irrigation and debridement ORIF with an LCP Irrigation and debridement Removal of hardware Refixation with a new, longer LCP and new, nonlocking and locking screws Right: ORIF with LISS plate Removal of the LISS plate and fixation with an LCP Removal LCP, repeat ORIF with a new LCP Right iliac crest autologous bone graft	LIPUS	Rapid recovery could potentially be attributed to a dose-dependent effect given the twice-daily application of LIPUS

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Wu, 2011 [97]	<i>Arch Orthop Trauma Surg</i>	Retrospective case series	IV	30	13	36	15.4	0	0		Plates External fixation Antegrade locked nails	Retrograde locked nailing: Closed removal of all previous implants Insertion of a retrograde dynamic locked nail, Cancellous bone grafting from the lateral tibial condyle with or without plate augmentation	Retrograde dynamic locked nailing is an excellent alternative treatment for the treatment of aseptic nonunions of femoral supracondylar after antegrade locked nailing. However, this technique may only be used when antegrade exchange locked nailing is unsuitable for use. The technique is not complex and its success rate is high

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Wu, 2011 [98]	<i>J Trauma</i>	Retrospective case series	IV	30	20	77	75	0	0		Plates	Retrograde femoral-locked nail in the dynamic mode Bone cement Cancellous bone graft with or without a bone graft substitute	Retrograde femoral-locked nail may comitantly provide sufficient stability and initiate osteogenic potential, thus facilitating bone union. This technique is simple with a low complication rate and thus should be considered as a useful alternative for treating this complex lesion

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Yoshida et al., 2009 [99]	<i>J Reconstr Microsurg</i>	Case Report	V	2	2	48	0	0	0		IMN EF and cancellous bone grafting from the iliac crest LIPUS	Free vascularized bone graft harvested from the supracondylar region of the femur	The described technique is the best indication for an intractable nonunion without significant bone defects of the distal half of the femur when the standard techniques such as cancellous bone graft, dynamization, and LIPUS treatment are not practical

Table 1 (continued)

Author, year	Journal	Design	LoE	Follow-up (months)	Patients (n)	Mean age (years)	Women (%)	Open fracture (n)	Infected (n)	Fracture type	Initial treatment type (n)	Definitive treatment type	Results
Zhang et al., 2023 [100]	<i>J Int Med Res</i>	Retrospective observational study	III	17.9	5	52	20	0			LISS plate (MIPPO) Variable angle plate, autogenous posterior iliac crest bone graft Medial plate Retrograde nail RIA	IM-nailing and an LLP combined with RIA bone grafting	Combining intramedullary nailing and a lateral locking plate with the RIA bone grafting technique enhances biological properties, provides good structural support, and achieves good union and functional results in the management of resistant nonunion of the distal femur

OTA Orthopaedic Trauma Association, *DFLP* distal femur locking plate, *MLP* medial locking plate, *LLP* lateral locking plate, *DSC* dynamic condylar screw, *PFN* proximal femoral nail, *LISS* less invasive stabilisation system, *LIPUS* low-intensity pulsed ultrasound, *MIPPO* minimally invasive plate osteosynthesis, *EF* external fixation, *IMN* intramedullary nail, *P* plate, *rh-BMP-2* recombinant human bone morphogenetic protein-2, *LCP* locking compression plates, *LOWDFO* lateral open wedge distal femur osteotomy, *MFC* medial femoral condyle, *RIA* reamer-irrigator aspirator

[28]. Reported time intervals ranged from 3 to 12 months [28]. A cut-off of 6 months was most commonly used to define nonunion [28]. Few studies reported a cut-off of 12 months and 9 months [28]. More recently, the US Food and Drug Administration (US FDA) proposed a cut-off of 9 months without evidence of progression to healing over the previous 3 months [29, 30]. The diagnosis of nonunion is often achieved through imaging using plain radiography [31]. However, consensus on the appropriate criteria still needs to be improved [32, 33]. The absence of bridging callus on at least three of four cortices on radiographs is a common assessment criterion, as is the movement of the fracture during radiographic stress testing, lack of bony/cortical continuity, or lack of bridging bone trabeculae [34]. Clinical criteria used to diagnose nonunion are also heterogeneous and not commonly used; among them are pain over the fracture site, pain during weight bearing and natural mobility at the fracture site [35, 36].

Several strategies are used for the management of distal femoral nonunion, with each treatment option having merits and demerits [37–40]. Dynamisation is occasionally attempted as a less invasive method to achieve union in femoral diaphyseal fractures with an axial stable fracture configuration [41, 42]. The main surgical technique used is the revision ORIF, which involves osteosynthesis with freshening of bone ends and bone grafting [43, 44]. It offers a high chance of achieving union and allows for restoring the joint alignment [43, 44]. Another minimally invasive technique involves retrograde intramedullary nailing, which is more suitable for fractures where the original surgery used plates and screws [45, 46]. Being less invasive, it reduces soft tissue disruption. It may potentially provide faster healing, but it is not suitable for all nonunion types, and there may be the possibility of malalignment if nail placement is inaccurate. A combined plate and nail fixation construct is also used, using a locking plate and an intramedullary nail for enhanced stability [47, 48]. Ilizarov external fixator is another surgical option used for treating distal femoral nonunion, and it can provide high union and low complication rates in experienced hands [49, 50]. Although autologous bone grafting is usually considered an essential part of any surgical fixation technique to promote bone growth and improve the chances of healing of nonunion, it requires an additional surgical site for graft harvesting, increasing the potential for pain and discomfort [51, 52]. It is also beneficial for complex nonunions or those with significant bone loss [52]. However, being more invasive than single procedures, there may be an increased risk of infection and hardware complications. In resistant and challenging distal femoral nonunion in older people with associated bone loss, osteoporosis, and secondary knee osteoarthritis, mega prosthesis has

been successfully used as a one-stage salvage procedure [53–55].

Saxena et al. [47] reported the outcomes of 10 cases of non-union of distal femur treated by fixation with nail plate construct and bone grafting, achieving union in 10.3 months on an average duration.

The only previously systematic review on this topic was done by Ebraheim et al. [4], who assessed 19 studies and found that the most common initial treatment was ORIF with plating, and the most common definitive treatment was with fixed angle plating combined with cancellous autografting, with a union rate of 97.4% and average union time of 7.8 months.

In a retrospective study of 31 cases of distal femoral non-union, which were treated by anatomical lateral locking plates and autogenous bone grafting, stable union was achieved in all cases, with a significant improvement in the functional scores [43]. The authors concluded that optimal stability, good compression at the non-union site, maintenance of axial alignment, bone end freshening, adequate use of cortico-cancellous bone autograft, respecting the biology, and the correct choice of the implant (including the size) are essential to achieve union at the fracture site [43].

In a retrospective study of 18 cases of atrophic distal femoral non-union that were managed using a combination of J-shaped bone graft and double plating union was achieved in all cases at an average of 22.1 ± 5.5 months (range 14–34 months) postoperatively [56]. The average healing time was 6.72 ± 2.80 months [56].

A recently published bibliometric study (1990–2023) found a growing interest in fracture non-union globally through published studies [57].

Distal femoral fractures are complex injuries, and even with advancements in treatment, non-union remains a potential complication. While there has been progress in understanding and treating this condition, there are still gaps in the current research. Studies have not yet established a clear consensus on the most optimal surgical technique for nonunions, and guidelines for managing nonunion, especially of the distal femur, are missing. More research is needed on long-term patient outcomes after treatment for non-union. This can help assess the effectiveness of different approaches and identify areas for improvement. More research is needed to better understand the influence of patient characteristics, such as age, comorbidities, and bone quality, on the risk of developing non-union and treatment success. Further investigations into these areas can lead to more standardised protocols, improved success rates, and improved outcomes. Strategies to improve the outcome of the surgical management of nonunion treatment are evolving.

Logistic regression predictive models can help develop and identify patients at high risk of non-union before surgery. This would allow for early intervention and potentially

a reduction in non-union rates [14]. Specific growth factors, like bone morphogenetic proteins (BMP), are used locally at the fracture site to stimulate bone formation, enhance healing, and potentially reduce the need for extensive grafting procedures [58]. However, its use is still limited, as it is a relatively new approach with ongoing research and high cost compared to traditional methods [59, 60]. Genetic influence has been proposed, especially polymorphisms in the genes *ANXA3*, *BMP2*, *CALY*, *CYR61*, *FGFR1*, *IL1 β* , *NOG*, *NOS2*, *PDGF gene*, and *TACR1* are susceptible to nonunion [61, 62]. Hence, gene therapy may help stimulate bone growth and improve healing rates in non-unions [63]. Refinement in minimally invasive surgical (MIS) techniques for treating non-unions could lead to faster recovery times and less surgical burden on patients [64, 65]. In this context, there is also interest in robotic-assisted surgery (RAS), which might improve precision and accuracy during revision surgery for non-unions [66, 67]. Developing bioactive implants that promote bone healing and enhance the fusion rate at the fracture site could be crucial [68]. Using biodegradable implants would also eliminate the need for a second surgery to remove hardware. Moreover, advanced imaging techniques like Magnetic Resonance Imaging (MRI) may better assess bone healing progress in patients [24, 69]. However, the presence of metallic implants may generate artefacts. Developing biosensors to monitor the bone healing process in real-time may thus allow for adjustments to treatment plans as needed [70, 71]. Focusing on these areas, researchers are developing more effective strategies for distal femoral nonunion, leading to improved patient outcomes and a faster return to function.

Conclusion

This systematic review of distal femoral nonunion based on 35 studies and 832 cases revealed that with appropriate surgical treatment 84.5% of patients reached complete union without major complications, and 3.8% (32 of 832) reached complete union with major complications at a mean of 21.7 ± 20.9 months. But, 8.7% (72 of 832) patients showed signs of persistent non-union.

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Declarations

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Ethical Approval This study complies with ethical standards.

Informed Consent For this type of study informed consent is not required.

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