

## Review Article

# Is early intramedullary interlocked nailing an effective treatment option for open grade III femoral shaft fractures: a systematic review of literature and pooled analysis of 176 cases

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**Abstract:** Background: Open Grade 3 femoral fractures are high-velocity injuries, often associated with other co-morbid injuries and are highly prone to infections; these fractures are commonly treated by staged procedures to minimize the complications. Early definitive fixation by intramedullary (IM) interlocking nails (ILN) has advantages like early mobility and better outcomes. Study question: Are early definitive fixations of grade III shaft femur fractures with debridement & IM ILN effective in union and infection rates? Materials and methods: Using relevant keywords, a total of 3357 articles were screened from the PubMed, Scopus and Embase database. 6 studies that evaluated at least 10 cases of grade III open femoral shaft fractures treated with early IM ILN during the index surgery were included in this review. Results: Out of the 6 studies, only 1 was prospective, and the remaining 5 were retrospective in design. Out of 176 Grade III fractures, there were 8 non-unions, 3 malunions and 1 case of delayed union. Pooled analysis showed union rates of 94.8% for these fractures (4 studies). Infection was the most common complication. Pooled analysis showed that the mean rate of infection in these grade III fractures was 6.7%. Other complications included limb length discrepancy and stiff knee. Conclusion: Intramedullary nailing in grade 3 femoral fractures as an early method of definitive fixation is an effective option. In such cases, optimizing controllable variables like surgical expertise and adequate antibiotic prophylaxis can improve outcomes.

**Keywords:** Open femur fractures, intramedullary nailing, infection, union, shaft femur fracture

## Introduction

A high energy open grade III femoral shaft fracture's standard treatment is initial debridement and temporary stabilization with an external fixator. It is followed by delayed definitive fixation, commonly with an intramedullary (IM) interlocked nail (ILN) [1, 2]. On the other hand, early definitive fixation has been consistently advocated for Gustilo Anderson grades 1 and 2 fractures, with advantages of early long bones stabilization and no additional risks of infections and non-unions [3, 4]. External fixators are associated with complications like pin tract infections/gaping, pin loosening/breakage and loss of fracture alignment and length [1, 2, 4-6]. Additionally, at centres with high footfalls

and limited resources, the delayed conversion to nailing can further get delayed, which could accentuate these complications [7]. Therefore, a school of thought professes early IM nailing for grade III open femoral shaft fractures during index surgeries. Early intramedullary nailing can impart advantages like early mobilization, improved pulmonary function and avoiding unnecessary surgical delays. It also helps to reduce hospital stay and follow-ups [6-9].

It is vital to assess the pros and cons of this line of treatment by weighing in these advantages against the possible risks of infections and non-unions [10]. We follow the standard protocol of damage control surgery followed by delayed nailing for these fractures at our cen-

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**Table 1.** Search strategy through database

S. no	Search Engine	Search period: from inception to 10/05/2021	Search results
1	PubMed	((("fracture fixation, intramedullary" [MeSH Terms] OR ("fracture" [All Fields] AND "fixation" [All Fields]) AND "intramedullary" [All Fields])) OR "intramedullary fracture fixation" [All Fields]) OR ("intramedullary" [All Fields] AND "nailing" [All Fields])) OR "intramedullary nailing" [All Fields] AND ("open" [All Fields] AND (((("femoral fractures" [MeSH Terms] OR ("femoral" [All Fields] AND "fractures" [All Fields])) OR "femoral fractures" [All Fields]) OR ("femur" [All Fields] AND "fractures" [All Fields])) OR "femur fractures" [All Fields]))	967
2	Scopus	TITLE-ABS-KEY (intramedullary AND nailing AND open AND femur AND fracture)	1226
3	Embase	(Intramedullary AND ('nailing'/exp OR nailing) AND open AND ('femur'/exp OR femur) AND fracture)	1164
Total			3357

tre. Therefore, the present review was conceptualized to systematically evaluate the literature to determine the outcomes with the alternative protocol of debridement and early IM ILN in open grade III femoral shaft fractures to incorporate the results into practice.

## Materials and methods

### Study design

This systematic review was performed following the PRISMA guidelines [11].

### Search strategy

A primary electronic search of PubMed, Embase and Scopus on 10/05/2021, using a well-defined search strategy (Table 1). A secondary search from the bibliography section of the relevant studies was done for any additional articles for inclusion.

### Inclusion and exclusion criteria

Studies in the English language that evaluated at least 10 cases of grade III open femoral shaft fractures treated with early IM ILN during the index surgery following debridement were included in this review.

Studies reporting <10 cases, case reports, conference abstracts, posters, non-English and review articles, biomechanical studies, technical tips and cadaveric studies were excluded. Studies that included only grade 1 or 2 fractures were also excluded.

### Study selection

All the studies were screened based on their titles and abstracts, independently by two

authors, and relevant articles were identified. Full texts of all those articles were read and the ones fulfilling the inclusion/exclusion criteria were finally included in the present review. Discrepancies related to the selection of articles between the two authors were resolved by discussion and consensus.

### Data extraction

The data extracted from each included article were entered in pre-specified excel sheets. They had the authors' names, year of publication, the number of included patients/fractures, relevant demographic parameters like age and gender, follow up periods, union time/rates, complications like non-unions/mal unions, infection rates etc (Tables 2-4).

### Risk of bias

The risk of bias of the included studies was done using the Methodological Index for non-randomized studies (MINORS) tool [12]. MINORS tool assesses the methodological quality of non-randomized surgical studies. We included 8 subheadings under which the quality of the study was assessed. These subheadings include "clearly stated aims, inclusion of consecutive participants, prospective collection of the data, end point appropriate to study aim, unbiased assessment of study endpoint, follow up period appropriate for the study, less than 5% loss of follow up and prospective sample size calculations".

### Outcome measure

The primary outcome measure of interest was union rate and complications. Union was labelled as clinical ability to bear weight without pain at the fracture site and radiological union of 3 cortices out of 4. Complications that we-

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**Table 2.** Characteristics of the studies

Characteristics	Williams MM et al. 1999	Mitchell SE et al. 2010	Takashi Noumi et al. 2004	O'brien et al. 1991	Brumback et al. 1989	Singh et al. 2011
Type of the study	P	R	R	R	R	R
Level of evidence	II	IV	IV	IV	IV	IV
Mean age	36 (17-72)	35.5 (14-71)	24.8 (15-62)	28 (13-82)	29.1 (14-67)	(22-58)
Sex						
• Male	30	23	72	46	68	42
• Female	12	06	16	14	18	04
Sample size						
• Patients	42	29	88	60	86	46
• Fractures	42	31	89	63	89	46
Fracture classification						
• Grade I	12	0	22	22	27	0
• Grade II	16	0	43	26	16	0
• Grade III	14	31	24	15	46	46
○ IIIA	06	14	12	-	19	10
○ IIIB	05	15	07	-	27	34
○ IIIC	03	03	05	-	-	2
Fracture type			AO/ASIF			
Winquist			A-50			
○ I	13	01	B-27	24	17	07
○ II	11	30	C-12	39	19	13
○ III	09				34	18
○ IV	09				19	08
ISS	25	-	20.3	-	23	-
Avg Follow Up	20 months	22.5 months	36 months	18 months	NR	NR

AO/ASIF: association of surgeons for internal fixation.

re considered were post-operative infections (Superficial infection and Deep infection), stiff knee, pulmonary complications, limb length discrepancy and nail breakage.

### Statistical analysis

Pooled analysis was done for union and infection rates using Open MetaAnalyst, with statistical heterogeneity determined using the  $I^2$  test [13]. A visual summary was provided by constructing forest plots.

### Results

#### Search and screening

We had 3357 hits in the databases using the specific keywords, and the full text was retrieved from 34 studies after excluding duplicates and irrelevant titles and abstracts. After reading the full texts, 28 studies were excluded, and six studies were included in the review (**Figure 1**).

#### Characteristics of the studies

A total of 6 studies were identified in the final review (**Table 2**). Only 1 study by Williams et al. was prospective, while the other 5 studies were retrospective in nature [8]. Among the 6 studies, 350 open fractures were recorded, of which 176 fractures were open grade III, which was the area of interest in our study. The various studies also classified the fractures as per the Winquist classification, which is depicted in **Table 2** [14]. The follow-up period was shown in 4 studies ranging from 18 to 36 months.

#### Risk of bias

The risk of bias assessed by the MINORS tool was moderate, owing to the retrospective nature of 5 studies out of 6 (**Figures 2 and 3**). The score was 11 out of 16 in one study, 9 out of 16 in three studies and 8 out of 16 in two studies.

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**Table 3.** Union rates

Characteristics	Williams MM et al. 1999	Mitchell SE et al. 2010	Takashi Noumi et al. 2004	O'brien et al. 1991	Brumback et al. 1989	Singh et al. 2011
Fixation methodology						
○ Early IMN	64% (27)	100% (19)	39% (36)	100%	63% (56)	100%
○ Delayed IMN	36% (15)		61% (51)		37% (33)	
Union time	15.2 weeks	51 weeks	-	-	20.8 weeks	27 weeks
Non union		-	12	3	0	4
● Gr-1			2			
● Gr-2	1	-	6			
● Gr-3			4			4
Malunion		1		2	0	
Delayed union	1		-			
● Gr-3		-		-		

Gr: Grade; IMN: intramedullary nail.

**Table 4.** Complications

Characteristics	Williams MM et al. 1999	Mitchell SE et al. 2010	Takashi Noumi et al. 2004	O'brien et al. 1991	Brumback et al. 1989	Singh et al. 2011
Infection						
● Superficial (S)	-	-	-	5	1	-
● Deep (D)	1	-	5	3	3	2
1. Gr-1			0	1 (S); 1 (D)	-	-
2. Gr-2			1	1 (S); 1 (D)	-	-
3. Gr-3			3	3 (S); 1 (D)	3 (3-b) (D)	2
Stiff knee	-	6	-	3	-	2
● Gr-1						
● Gr-2						
● Gr-3						2
Pulmonary complication	2	-	-	14	-	-
● Gr-1						
● Gr-2						
● Gr-3a	1					
● Gr-3b	1					
LLD	-	6	-	2	2	2
● Gr-1						
● Gr-2						
● Gr-3						2
Locked nail	36		-	30		
○ Static locking	26					
○ Dynamic locking	10	-			-	-
Unlocked nails	6					
Nail breakage	-	-	-	-	1	-

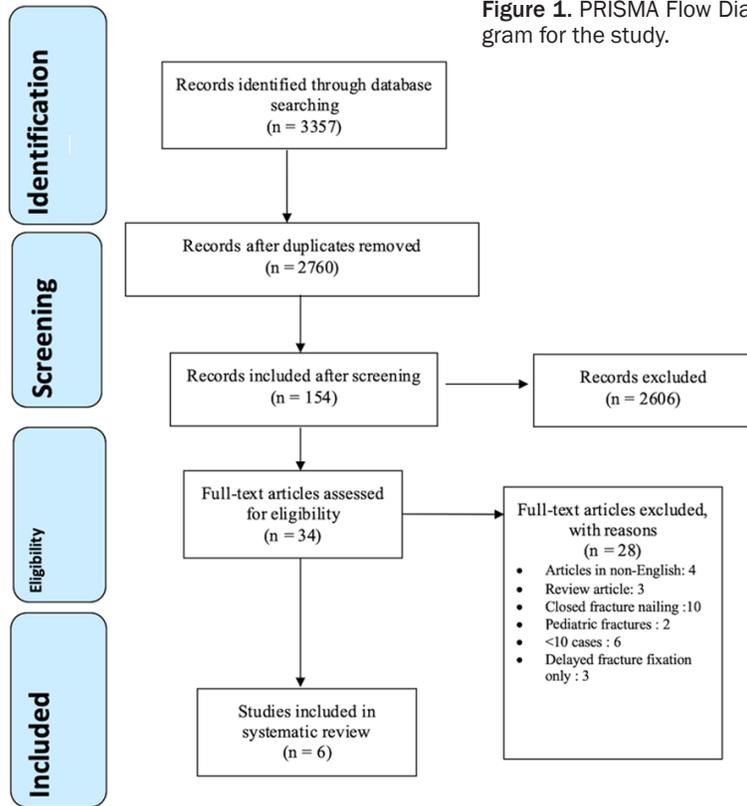
Gr: Grade; D: deep; S: superficial.

### Union rates

Of the 176 Grade III fractures in the study, there were 8 cases of non-unions, 3 cases of mal-

unions and 1 case of delayed union. Pooled analysis showed union rates of 94.8% for these fractures (95% CI: 0.904, 0.991; I<sup>2</sup>: 41.38%) (**Figure 4**). The union time was reported in 4

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studies and ranged from 15.2 to 51 weeks (Table 3).

### Complications

The various complications observed with intramedullary nailing are shown in Table 4. The main complication associated with Grade III fractures was infection. 15 cases of these fractures had superficial or deep infections. Pooled analysis showed that the mean rate of infection in these types of fractures was 6.7% (95% CI: 0.013, 0.120, I<sup>2</sup>=56.65%) (Figure 5). Other complications that were noted commonly included limb length discrepancy and stiff knee (Table 4).

### GRADE summary

Data from the studies was computed to ascertain the quality of evidence as per “GRADE working groups grades of evidence”. The quality of evidence of both the union rates and infection rates are depicted in Table 5.

### Discussion

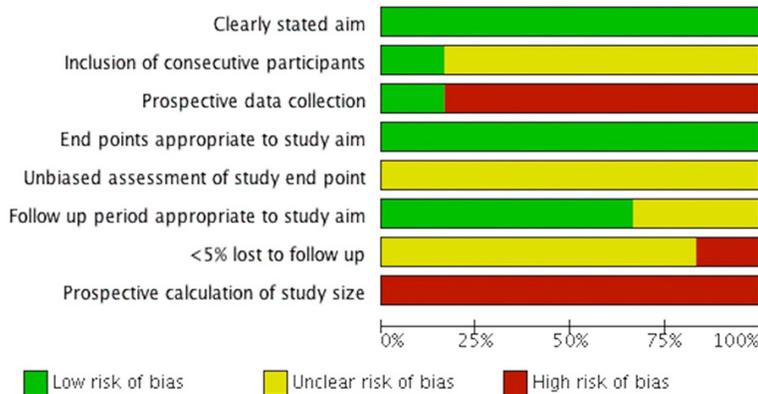
Early nailing of grade 3 open femoral shaft fractures falls in a grey zone between damage control and early total care. Therefore, the decision should be based on the extent of injuries like multisystem involvement, the actual contamination in the open wound and the availability of expertise/implant for adequate management [2, 8, 15-18]. A seriously ill patient with polytrauma, wherein the second hit of surgery would do more harm than good, must be a candidate of damage control [19].

The decision making becomes unclear in a patient who is placed in the borderline and

	Clearly stated aim	Inclusion of consecutive participants	Prospective data collection	End points appropriate to study aim	Unbiased assessment of study end point	Follow up period appropriate to study aim	<5% lost to follow up	Prospective calculation of study size
Bumback 1989	+	?	-	+	?	?	?	-
Mitchell 2010	+	?	-	+	?	+	?	-
O'brien 1991	+	?	-	+	?	+	?	-
Singh 2011	+	+	-	+	?	?	-	-
Takashi 2004	+	?	-	+	?	+	?	-
Williams 1999	+	?	+	+	?	+	?	-

Figure 2. Risk of bias summary.

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**Figure 3.** Risk of bias graph.

low-risk groups [19]. It factors in various parameters like hypothermia, acidosis and coagulation, determining the suitability of injury for primary nailing. Early appropriate care becomes crucial in those patients.

When an open femoral shaft fracture is suitable for early nailing, the next dilemma arises due to the chances of infection. A post-operative infection after an intramedullary nail could be devastating for the patient. It can progress to eventual osteomyelitis, septic arthritis and non-unions. Further treatment becomes difficult, and the quality of patients' lives suffers. Grades 1 and 2 open fractures have shown infection rates from 2-4%, but these injuries have a lower degree of soft tissue injury, contamination and necrosis [8, 15]. However, in grade 3 injuries where the size of the wound is more than 10 cm with more severe soft tissue injury, the risk of infections is higher, especially if debridement is not extensive. Therefore, adequate surgical expertise is paramount if early nailing is planned.

The present review showed an infection rate of 6.7% in grade III fractures, which is relatively higher than grades 1 and 2 for the reasons mentioned above. However, the union rate was almost 95%; the average union time ranged from 15-52 weeks. The results are encouraging because when the pros and cons of a procedure are compared, the weightage of union rates seem higher.

In closed femur fractures managed with IM ILN, non-union rates from 1-5% have been described by Ghouri et al. and Wolinsky et al. [20, 21]

Young et al. described the infections rates to be 3.2% after femoral nailing in closed femur fractures [22]. Therefore in the present review, although nailing a grade 3 femur fractures caused infections at a double rate (6.7%) than that reported in closed fractures (3.2%), the union rates were comparable. Furthermore, it is said that prophylactic antibiotics can reduce infections by 29% [22]. Therefore when controllable variables like surgical expertise and antibiotic prophylaxis are optimized, early nailing in grade 3 femur fractures are fruitful surgeries. The added advantages like early mobilization, better cardiopulmonary reserves and better patient satisfaction are further reasons for prescribing early nails for these patients.

At our tertiary center we practice 'delayed nailing' in cases of open grade III femur fractures. If the wound is linear and more than 10 cm with minimal stripping of periosteum (IIIA), after adequate surgical debridement we nail the femur in the same setting. In grade IIIA with significant comminution and periosteal stripping, IIIB and IIIC we nail the femur once adequate flap/split skin graft cover is settled. Until then they are stabilized using modular external fixator. It is important to consider the level of contamination as some of them present with farmyard injuries. Such injuries despite best of surgical debridement may present with subsequent infection. It is important to consider many factors like "time from injury till presentation to hospital, receipt of appropriate antibiotics, adequate first aid and splinting, addressing other comorbid injuries, time from injury to first surgical debridement and post op care". When these factors are optimum it is imperative to nail the femur in the index surgery after surgical debridement. With the evidence of relative equivalent rates of union and complications, nailing in open grade III fractures can be considered.

The present review has certain limitations, as all but 1 of the studies were retrospective; additionally, the studies published are relatively old, with no newer work on the topic available after 2011. So further research is warranted to conclusively ascertain the study question regard-

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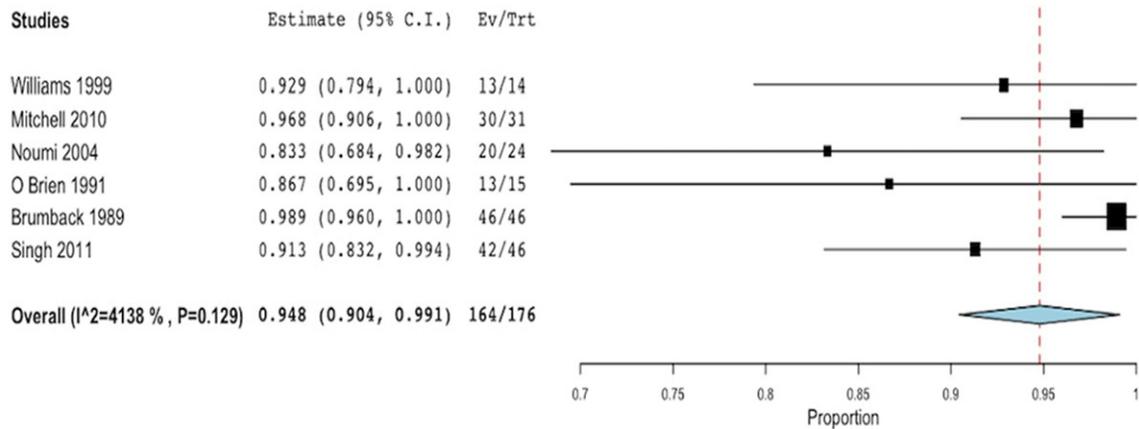


Figure 4. Union rates for Grade III fractures.

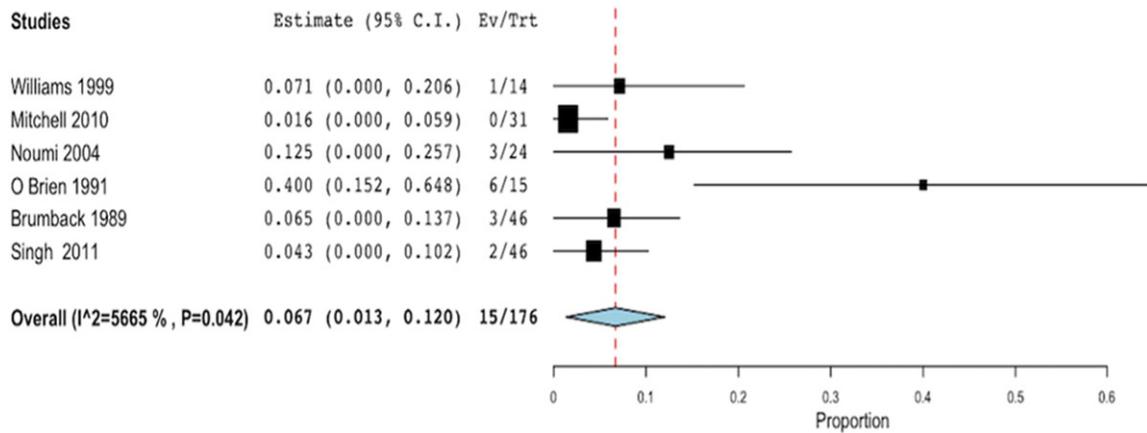


Figure 5. Rates of infections for Grade III fractures.

Table 5. GRADE summary of findings table

Outcomes	No. of participants (studies)	Absolute Effect	Relative Effect (95% CI)	Quality of evidence (GRADE)
Union Rates	176 (6)	0.948	0.904-0.991	Low, due to risk of bias and inconsistency.
Infection	176 (6)	0.067	0.013-0.120	Low, due to risk of bias and inconsistency.

CI: Confidence Interval. GRADE Working Groups Grades of Evidence: High Quality: Further research is unlikely to change our confidence in the effect of the estimate; Moderate Quality: Further research is likely to have an important impact on our confidence in the effect of the estimate and may change the estimate; Low Quality: Further research is likely to have an important impact on our confidence in the effect of the estimate is likely to change the estimate; Very Low Quality: We are very uncertain about the estimate.

ing randomized trials and prospective case series.

### Conclusions

Although infection rates are higher than closed and open grades 1 and 2, grade 3 femoral fractures, when nailed early, have excellent union rates. Early intramedullary nailing can be a viable option if an optimum surgical debridement

is done under cover of adequate antibiotic prophylaxis. In addition, other co-morbid injuries should also be addressed simultaneously to improve the prognosis. Furthermore, prospective research is warranted to supply more information to the existing data.

### Disclosure of conflict of interest

None.

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