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## Comparative efficacy of proximal femoral nail vs dynamic condylar screw in treating unstable intertrochanteric fractures

Ahmed Mohamed Yousif Mohamed, Monzir Salih, Mohanad Abdulgadir, Ayman E Abbas, Duha Lutfi Turjuman

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### Abstract

#### BACKGROUND

Among the most frequent hip fractures are trochanteric fractures, which usually occur from low-energy trauma like minor falls, especially in older people with osteoporotic bones.

#### AIM

To evaluate the treatment efficacy of dynamic condylar screws (DCS) and proximal femoral nails (PFN) for unstable intertrochanteric fractures.

#### METHODS

To find pertinent randomized controlled trials and retrospective observational studies comparing PFN with DCS for the management of unstable femoral intertrochanteric fractures, a thorough search was carried out. For research studies published between January 1996 and April 2024, PubMed, EMBASE, Scopus, Web of Science, Cochrane Library, and Google Scholar were all searched. The complete texts of the papers were retrieved, vetted, and independently examined by two investigators. Disputes were settled by consensus, and any disagreements that persisted were arbitrated by a third author.

#### RESULTS

This study included six articles, comprising a total of 173 patients. Compared to the DCS, the PFN had a shorter operation time [mean difference (MD): -41.7 min,

95% confidence interval (95%CI): -63.04 to -20.35,  $P = 0.0001$ ], higher success rates with closed reduction techniques [risk ratio (RR): 34.05, 95%CI: 11.12-104.31,  $P < 0.00001$ ], and required less intraoperative blood transfusion (MD: -1.4 units, 95%CI: -1.80 to -1.00,  $P < 0.00001$ ). Additionally, the PFN showed shorter fracture union time (MD: -6.92 wk, 95%CI: -10.27 to -3.57,  $P < 0.0001$ ) and a lower incidence of reoperation (RR: 0.37, 95%CI: 0.17-0.82,  $P = 0.01$ ). However, there was no discernible variation regarding hospital stay, implant-related complications, and infections.

## CONCLUSION

Compared to DCS, PFN offers shorter operative times, reduces the blood transfusions requirements, achieves higher closed reduction success, enables faster fracture healing, and lowers reoperation incidence.

**Key Words:** Intertrochanteric fracture; Unstable; Dynamic condylar screw; Proximal femoral nail; Meta-analysis; Comparative study

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**Core Tip:** The management of unstable intertrochanteric fractures frequently utilizes both proximal femoral nails and dynamic condylar screws. This meta-analysis critically examined the effectiveness thereof, aiming to identify the superior treatment option. These findings are pivotal to refine surgical strategies, ultimately aiming to improve patient outcomes in managing these challenging orthopedic injuries.

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## INTRODUCTION

One of the most frequent hip fractures, especially in older people with osteoporotic bones, is the trochanteric fracture, which usually results from low-energy trauma such as simple falls[1]. Fractures in the proximal femur area that run from the extracapsular basilar neck to the lesser trochanter and proximal to the medullary canal are referred to as trochanteric fractures[2]. This type of fracture is prevalent among elderly individuals[3], a trend which is likely influenced by increased life expectancy and osteoporosis. Projections from studies conducted by Cooper *et al*[4] and Gullberg *et al*[5] in the 1990s predicted that by 2050, there would be between 4.50 and 6.26 million hip fractures worldwide, with the Asian subcontinent accounting for 50% of these cases.

Unstable fracture patterns involve fracture lines extending into the subtrochanteric area, lateral wall blowout, comminuted posteromedial wall, reverse oblique, and variants of reverse oblique fractures[3]. These fractures fall within AO/Orthopedic Trauma Association (OTA) categories 31-A2 and A3.

Trochanteric fractures, regardless of their geometric configuration, typically undergo operative intervention unless there are present contraindications, such as severe comorbidities posing risks during the intraoperative or perioperative period. However, managing unstable trochanteric fracture patterns presents a significant challenge, often resulting in high postoperative complication rates, including mortality.

Modern treatment options include intramedullary fixation techniques like cephalomedullary nails and intramedullary hip screws, as well as extramedullary techniques like dynamic hip screw (DHS), compression hip screw, dynamic condylar screw (DCS), and proximal femoral locking compression plates. Empirical evidence has been gathered for both strategies[6].

According to several studies, extramedullary devices are less effective than intramedullary devices in treating unstable trochanteric femur fractures. The use of extramedullary fixation techniques should be performed with caution because of the increased risk of complications and lower functional results.

For stable trochanteric fractures, the most recent study by the American Academy of Orthopedic Surgeons[7] suggests DHS. For AO/OTA 31-A3 fractures, the DCS system featuring a 95° lag screw has been the commonly preferred treatment option[8-10]. However, reports of implant-related complications have been documented[10]. In 1996, the AO/ASIF presented the proximal femoral nail (PFN) as a solution to these DCS system problems[11]. In addition, the AO/ASIF group developed the PFN anti-rotation device in 2004 to improve angular and rotational stability.

This study aimed to perform a comprehensive evaluation of available treatment options for unstable intertrochanteric fractures, specifically comparing the efficacy of PFN *vs* DCS in managing such fractures. A comprehensive evaluation of clinical outcomes, such as surgical time, type of reduction, need for blood transfusions, length of hospitalization, rates of postoperative infection, complications related to implants, and rates of reoperation, were the aims of this study. We hypothesized that PFN would show better results than DCS in the treatment of unstable intertrochanteric fractures.



## MATERIALS AND METHODS

### Protocol and registration

The protocol was registered using regular reporting methods[12] and assigned PROSPERO number CRD42024537426.

### Search approach

This study conducted a meta-analysis using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. The Google database, PubMed, EMBASE, Scopus, Cochrane Library, and Web of Science were all searched without regard to location or type of publication. The following Medical Subject Heading (MeSH) keywords and their combinations were used in the search: (((("Femoral Fractures"[MeSH]) OR ("Hip Fractures"[MeSH]) OR (((((((((((intertrochanteric fractures) OR (intertrochanteric fracture)) OR (trochanteric fractures)) OR (trochanteric fracture)) OR (peritrochanteric fractures)) OR (peritrochanteric fracture)) OR (Femoral intertrochanteric fracture)) OR (intertrochanteric femoral fractures)) OR (IFFs)) OR (IFF))) AND ((dynamic condylar screw) OR (DCS)) OR ("Bone Screws"[MeSH])) AND (proximal femoral nail) OR (PFN).

This search was modified to contain publications spanning from 1 January 1996 to 5 April 2024. There were no other filters used in this search. The year 1996 was chosen because the PFN evolved during this time[11].

This study looked for relevant studies involving adult humans in the reference lists of related reviews and original articles. Every language was considered. Since the data for this meta-analysis was gathered from published articles, ethical approval was not required for this study (Supplementary material).

### Assessing eligibility

Using the Population, Intervention, Comparator and Outcomes paradigm, two authors independently screened each title and abstract. The populations were people with unstable intertrochanteric fractures; the intervention was fixation with a PFN; the comparison was fixation with a DCS; the outcomes included operation time, reduction type, blood transfusion, length of hospital stay, fracture consolidation, implant-related complications, reoperation, and infection rates.

All studies, both prospective randomized controlled trials (RCTs) and retrospective, which compared the efficacy of PFN and DCS in managing intertrochanteric fractures among patients aged 18 years and above, with fractures categorized as unstable (AO/OTA 31-A2 and A3), were considered eligible for inclusion. Studies discussing alternative treatment modalities were excluded. Furthermore, studies lacking quantitative data were also excluded. Technical notes, abstracts, editorials, comments, letters, and commentaries were not accepted, nor were articles containing bio-mechanical evaluations. Research on pathological or periprosthetic fractures, as well as studies on open fractures and previously treated proximal femoral fractures, were omitted.

### Study selection

Data selection for this study was carried out independently by two authors. Initially, titles of articles were manually screened, and those relevant to the research topic were considered for further evaluation. The full text of the article was then retrieved if the abstract matched the study objectives. A third reviewer was consulted to settle any disagreements. Articles for which the full text was not available were not included in the analysis. To find relevant articles, a manual screening of bibliographies was also carried out. All the articles that emerged from these procedures were evaluated, and their eligibility for inclusion was the subject of discussion among the researchers. All disagreements and discrepancies were settled by careful consideration and agreement among the reviewers (Figure 1).

### Data extraction

Two authors (AMYM and DLT), independently extracted data from the eligible studies using pre-prepared data extraction sheets. Cross-checking was then carried out, and disagreements were settled by agreement among the reviewers. Author, year of publication, number of patients, mean age, length of follow-up, type of fracture, conclusion, and patient characteristics (age and sex) were among the information that was retrieved. Clinical outcomes, including operative time, reduction type, blood transfusion needs, postoperative infection rates, implant-related complications, and reoperation rates, were also extracted.

### Risk of bias

This study used the revised Cochrane risk-of-bias tool for randomized trials (ROB-2)[13] to assess the quality of RCTs[14-16] and the Newcastle-Ottawa Scale[17] to assess the quality of observational studies[18-20]. The overall assessment of ROB-2 showed that Ghilzai *et al*[15] and Sadowski *et al*[16] were of some concern, while Jamil *et al*[14] was of high concern. All studies had some concerns in the randomization process domain. However, they were of low concern in all other domains, except for Jamil *et al*[14], which showed a high risk in the domain of missing outcome data (Figure 2).

The evaluation of quality for the observational studies, as presented in Figure 3, indicated that they were of high quality. Specifically, two studies achieved a score of 8[18,19], while Elis *et al*[20] received a score of 7. Across all studies, there was a loss of a quality point in the Comparability domain, with Elis *et al*[20] experiencing an additional deduction in the adequacy of follow-up domain.

### Pooling of outcomes

The stated outcome measures' mean, SD, and range were noted. In cases where SD was not provided, it was calculated using the range[21].

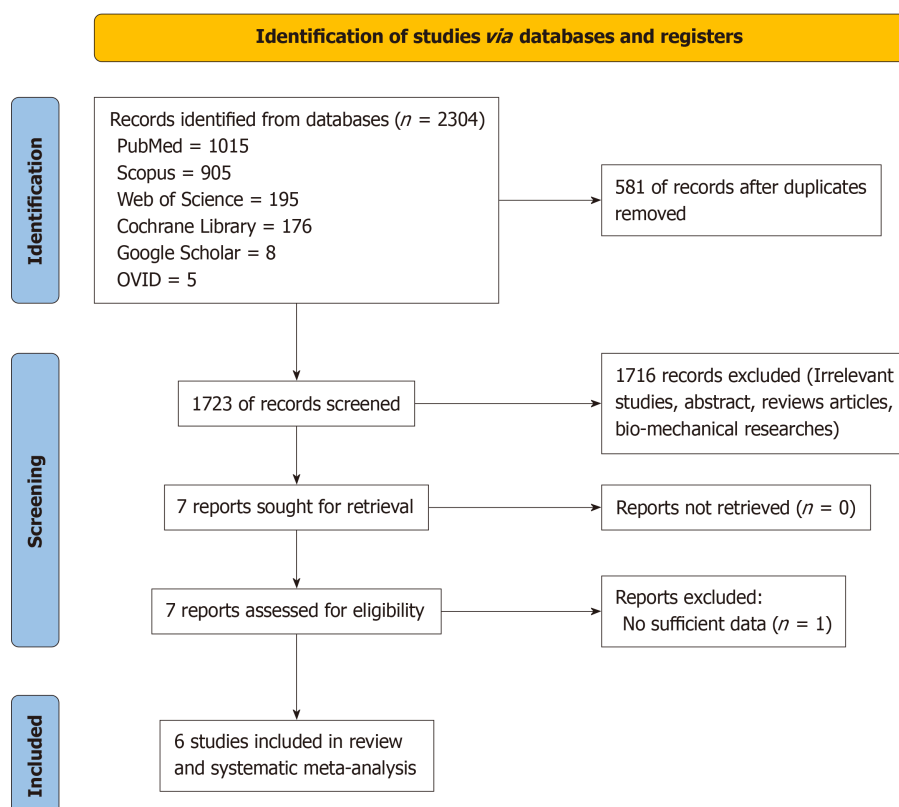


Figure 1 Flowchart of study search and inclusion criteria.

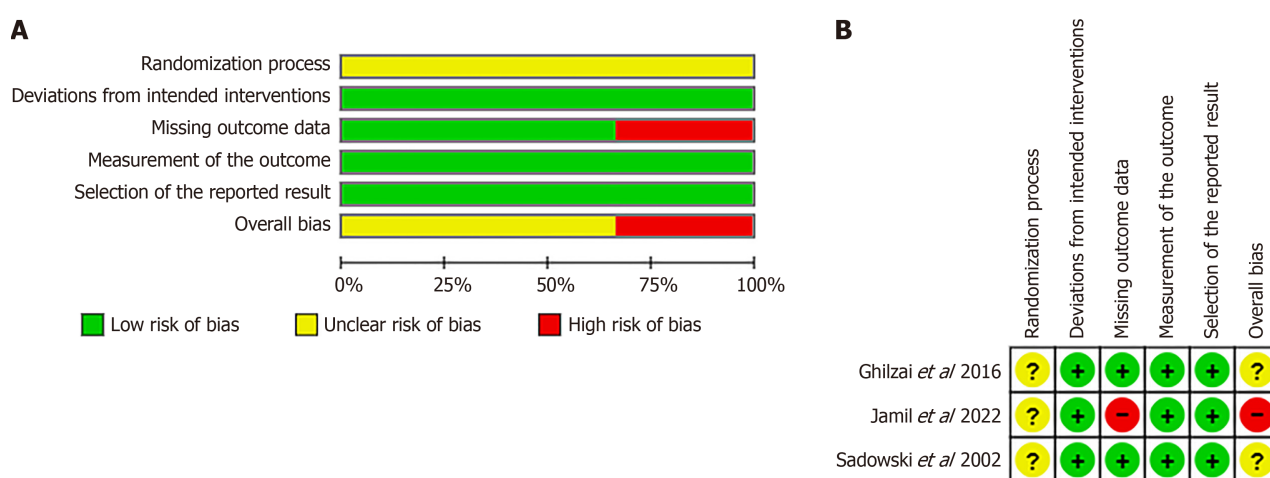


Figure 2 Risk. A: Risk of bias graphical representation; B: Risk of bias of included trials.

### Data synthesis and analysis

The Comprehensive Meta-Analysis program was used to conduct the meta-analysis. A random-effects model was used for pooling as half of the studies used a retrospective cohort design. The effect sizes were represented as MD or risk ratio (RR), with their corresponding 95% confidence intervals (95%CI) based on the measurement scale (continuous[22] and binary[23]) outcomes, respectively.  $P < 0.05$ ,  $I^2 > 50\%$  was defined as high heterogeneity; and  $P \geq 0.05$ ,  $I^2 < 50\%$  was defined as moderate heterogeneity.  $P = 0.05$  was used as the statistical significance criterion.

## RESULTS

### Study selection

A thorough computerized search used many databases and yielded a total of 2304 items. Prominent sources including PubMed ( $n = 1015$ ), Scopus ( $n = 905$ ), Web of Science ( $n = 195$ ), Cochrane Library ( $n = 176$ ), Google Scholar ( $n = 8$ ), and



Study ID	Selection	Comparability	Outcome	Total score
Şensöz <i>et al</i> 2023	★★★★	★★	★★★	8 (Good quality)
Şahin <i>et al</i> 2013	★★★★	★★	★★★	8 (Good quality)
Elis <i>et al</i> 2012	★★★★	★★	★★★	7 (Good quality)

**Figure 3** Quality assessment of observational studies as assessed by the Newcastle–Ottawa Scale.

OVID ( $n = 5$ ) were included in this search. Following the initial screening phase, which involved the removal of articles based on titles and the elimination of duplicates, 1723 articles remained for further evaluation. Subsequently, after scrutinizing the abstracts, 1716 articles were excluded, with one additional article being discarded due to insufficient data, focusing solely on one outcome measure. Following this rigorous screening process, a total of six studies[15–20] met the inclusion criteria for conducting a meta-analysis. The details of the selection method are summarized in a flow chart (Figure 1).

### Study characteristics

A total of six studies, which compared the use of PFN with DHS with patients with unstable trochanteric fractures, were included in this review. Among the studies identified, there were three randomized controlled trials[15–17] involving a total of 173 patients. Within this subgroup, 97 patients were assigned to the PFN group and 76 to the DCS group. Additionally, the analysis incorporated findings from three retrospective cohort studies[18–20]. Among these patients, 56 were treated with PFN and 49 with DCS.

All studies were conducted between 2002 and 2023. All included studies were conducted in various countries, except for Şensöz *et al*[18] and Sahin *et al*[19], both of which were conducted in Türkiye. Although all studies utilized plate fixation as a comparison, the PFN methods varied. Specifically, one study utilized the expandable PFN, while another utilized a PFN with anti-rotation features. The sample sizes ranged from 33 to 79 per study. Most of the patients were older females. Table 1 contains the characteristics of the listed studies.

### Intraoperative clinical outcomes

Fracture union time, a pivotal endpoint in assessing surgical outcomes, was meticulously evaluated by only two studies: Sadowski *et al*[16] and Sahin *et al*[19]. The results showed that the PFN group had significantly reduced fracture union time more than the DCS group and the results showed heterogeneity (MD: -6.92, 95%CI: -10.27 to -3.57,  $P < 0.0001$ ;  $I^2 = 0\%$ ,  $P = 0.96$ ) (Figure 4A). Moreover, the impact of surgical intervention on blood transfusion requirements, a critical consideration in orthopedic procedures, was rigorously examined across four studies[16,17,19,20]. The pooled analysis favored the PFN group over the DCS group, revealing a significant difference in favor of PFN, albeit with low heterogeneity (MD: -1.40, 95%CI: -1.80 to -1.00,  $P < 0.00001$ ;  $I^2 = 24\%$ ,  $P = 0.27$ ) (Figure 4B). Furthermore, hospital stay duration, a crucial indicator of postoperative recovery, was meticulously documented in three studies[15,17,20]. There was no significant distinction between the groups, according to the analysis (MD: -1.42, 95%CI: -4.06-1.23,  $P = 0.29$ ), with high heterogeneity noted ( $I^2 = 66\%$ ,  $P = 0.05$ ) (Figure 4C).

All studies, except for Şensöz *et al*[18], provided comprehensive data on operation duration. The PFN group exhibited a significant reduction in operation time compared to the DCS group with the results indicating high heterogeneity (MD: -41.7, 95%CI: -63.04 to -20.35,  $P = 0.0001$ ;  $I^2 = 86\%$ ,  $P < 0.00001$ ) (Figure 4D).

Interestingly, the type of reduction, a crucial aspect of surgical technique, was meticulously documented in all studies, except Sahin *et al*[19]. Specifically, open reduction was notably less prevalent in the PFN group than in the DCS group (RR: 0.16, 95%CI: 0.07 to 0.35,  $P < 0.00001$ ), showcasing a trend toward a less invasive approach, with high heterogeneity noted among the studies ( $I^2 = 68\%$ ,  $P = 0.008$ ) (Figure 5A). Conversely, closed reduction, indicating a less invasive surgical technique, was substantially more frequent in the PFN group than in the DCS group (RR: 34.05, 95%CI: 11.12 to 104.31,  $P < 0.00001$ ), highlighting a potential advantage of the PFN approach, with minimal/no heterogeneity observed ( $I^2 = 0\%$ ,  $P = 0.980$ ) (Figure 5B).

### Postoperative complications

Notable variations in postoperative complications were observed between the PFN and DCS groups. PFN demonstrated notably lower rates of nonunion fractures compared to DCS, as evidenced by findings from five studies[15–19] (RR: 0.25, 95%CI: 0.08-0.80,  $P = 0.02$ ). Notably, these results showed no heterogeneity across studies ( $I^2 = 0\%$ ,  $P = 0.52$ ) (Figure 6A). However, while implant-related complications trended lower in the PFN group across all studies[15–20] (RR: 0.54, 95%CI: 0.22-1.34,  $P = 0.19$ ), statistical significance was not attained, with moderate heterogeneity noted across studies ( $I^2 = 45\%$ ,  $P = 0.120$ ) (Figure 6B).

Moreover, PFN demonstrated a significant reduction in reoperation rates compared to DCS, with findings consistent across four studies[17–20] (RR: 0.37, 95%CI: 0.17-0.82,  $P = 0.01$ ;  $I^2 = 0\%$ ,  $P = 0.80$ ) (Figure 6C). Furthermore, infection rates were lower in the PFN group across three studies[18–20] (RR: 0.27, 95%CI: 0.07-1.10,  $P = 0.07$ ), although statistical sig-

Table 1 The general characteristics of the included studies

Ref.	Study type	Center	Study period	Follow-up in mo	Number of patients		Average age in yr		Sex as male/female		Fracture type and n	Conclusion
					PFN	DCS	PFN	DCS	PFN	DCS		
Şensöz <i>et al</i> [18], 2023	Retrospective cohort	Dr. Lutfi Kirdar Kartal City Hospital, Istanbul, Turkey	Between 2013 and 2018	At least 2 yr	36	25	65.52	59.36	15/21	13/12	A2.3 61	DCS was superior to PFN in early fracture union time. However, it showed a higher nonunion rate. PFN showed shorter hospital stay time than DCS and is recommended to be applied in that fracture type
Jamil <i>et al</i> [14], 2022	RCT	Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, India	Between November 2019 to December 2021	NA	15	11	54.20	59.82	4/11	6/5	A2.2 16/A2.3 10	PFN showed better results than DCS regarding operative time, union rate, duration for fracture union, and rate of complications
Ghilzai <i>et al</i> [15], 2016	RCT	Liaquat National Hospital, Karachi, Pakistan	February 2012 to August 2013	NA	21	19	80.00	77.00	NA	NA	A2.2 21/A2.3 19	PFN is superior to DCS in the treatment of proximal femur fractures type 31A3
Sahin <i>et al</i> [19], 2014	Retrospective cohort	Izmir Tepecik Education and Research Hospital, Izmir, Türkiye	Between January 2007 and December 2010	At least 1 yr	42	37	51.75	57.50	17/25	18/19	A2.2 44/A2.3 35	PFN is superior to DCS in the treatment of unstable peritrochanteric fractures, owing to its effect in reducing operative blood loss, and biological fixation achievement
Elis <i>et al</i> [20], 2012	Retrospective cohort	Tel Aviv Sourasky Medical Center, Tel Aviv, Israel	Between January 2006 and July 2009	At least 1 yr	19	14	51.75	57.50	3/16	3/11	A2.2 19/A2.3 14	EPFN was as effective as DCS devices for the treatment of reverse oblique hip fractures
Sadowski <i>et al</i> [16], 2002	RCT	University Hospital of Geneva, Geneva, Switzerland	Between March 1998 and June 1999	At least 1 yr	20	19	88.00	77.00	7/13	4/14	A2.2 20/A2.3 19	The results support the use of PFN rather than DCS for the treatment of reverse oblique and transverse intertrochanteric fractures

DCS: Dynamic condylar screws; EPFN: Expandable proximal femoral nail; NA: Not available; PFN: Proximal femoral nail; RCT: Randomized controlled trial.

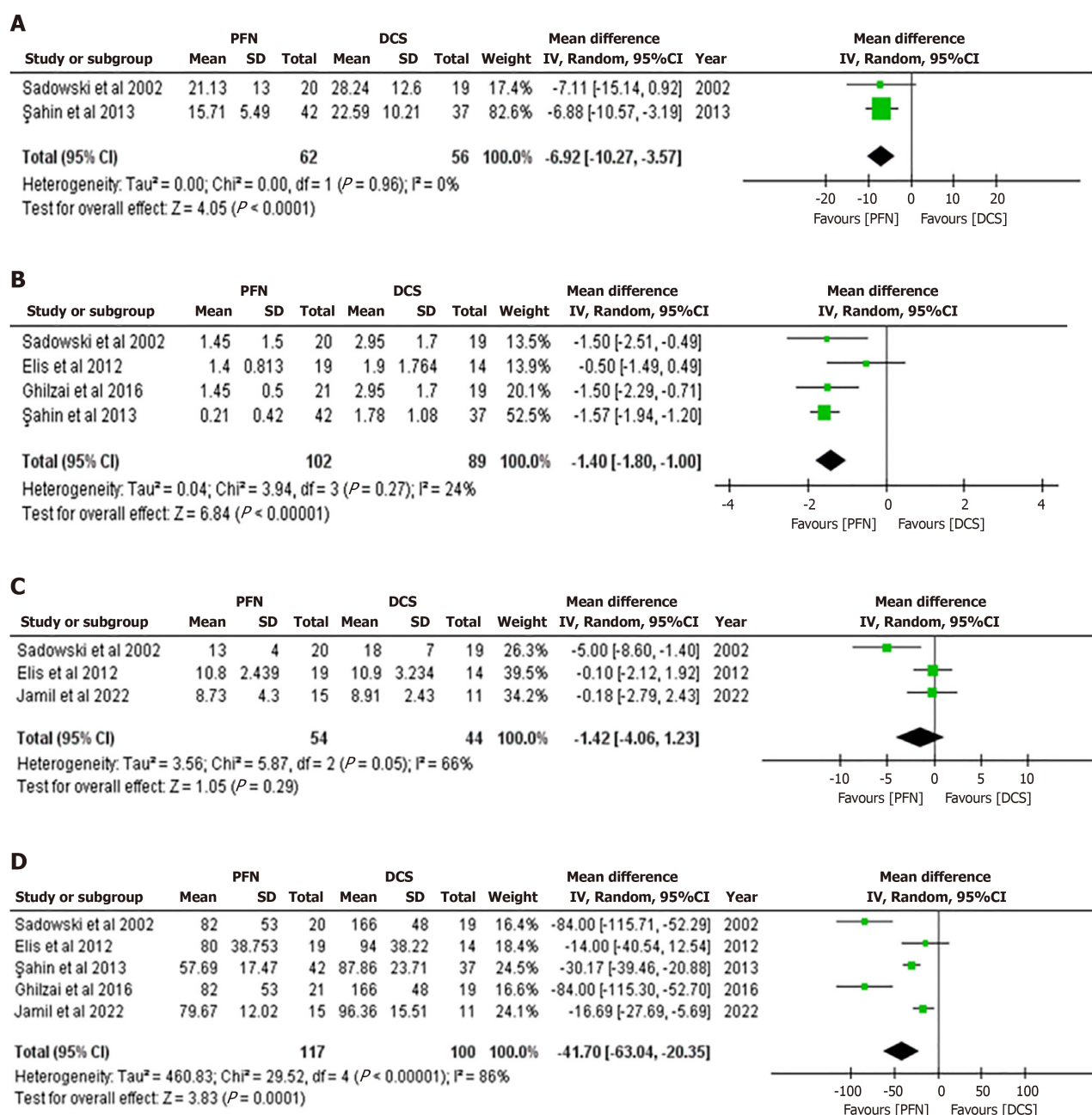
nificance was not achieved. Notably, no heterogeneity was observed in this context ( $I^2 = 0\%$ ,  $P = 0.98$ ) (Figure 6D).

## DISCUSSION

An increased risk of osteoporotic intertrochanteric fractures is seen in elderly people. Hip joint functional exercises in conjunction with prompt surgery for these fractures may reduce complications, including pressure ulcers, deep vein thrombosis, and stiffness in the joints[24]. Because the PFN has a smaller distal shaft diameter and less concentrated stress at the tip, it is useful in preventing femoral shaft fractures. Surgeons can reduce surgical trauma, blood loss, infection, and wound complications by using intramedullary fixation to minimize soft tissue dissection[25,26].

Technical benefits of the DCS include stability in the sagittal plane[19]. However, significant disadvantages of the DCS include the possibility of devascularization of fracture fragments as a result of thorough dissection, which may result in infection, nonunion, or delayed union[27,28].

The findings suggest that the PFN offers several intraoperative advantages compared to the DCS. Specifically, PFN was linked to a notably shorter operation time and a greater success rate in closed reduction techniques, indicating a less invasive procedure. This is crucial because less invasive methods are generally associated with quicker recovery periods and shorter hospital stays. To protect the fracture hematoma, which is essential to the healing process, closed reduction entails aligning the ends of a fracture by manipulating its fragments without surgically exposing the surrounding tissues [29]. This study found that the rate of successful closed reductions was significantly higher in the PFN group than in the DCS group.



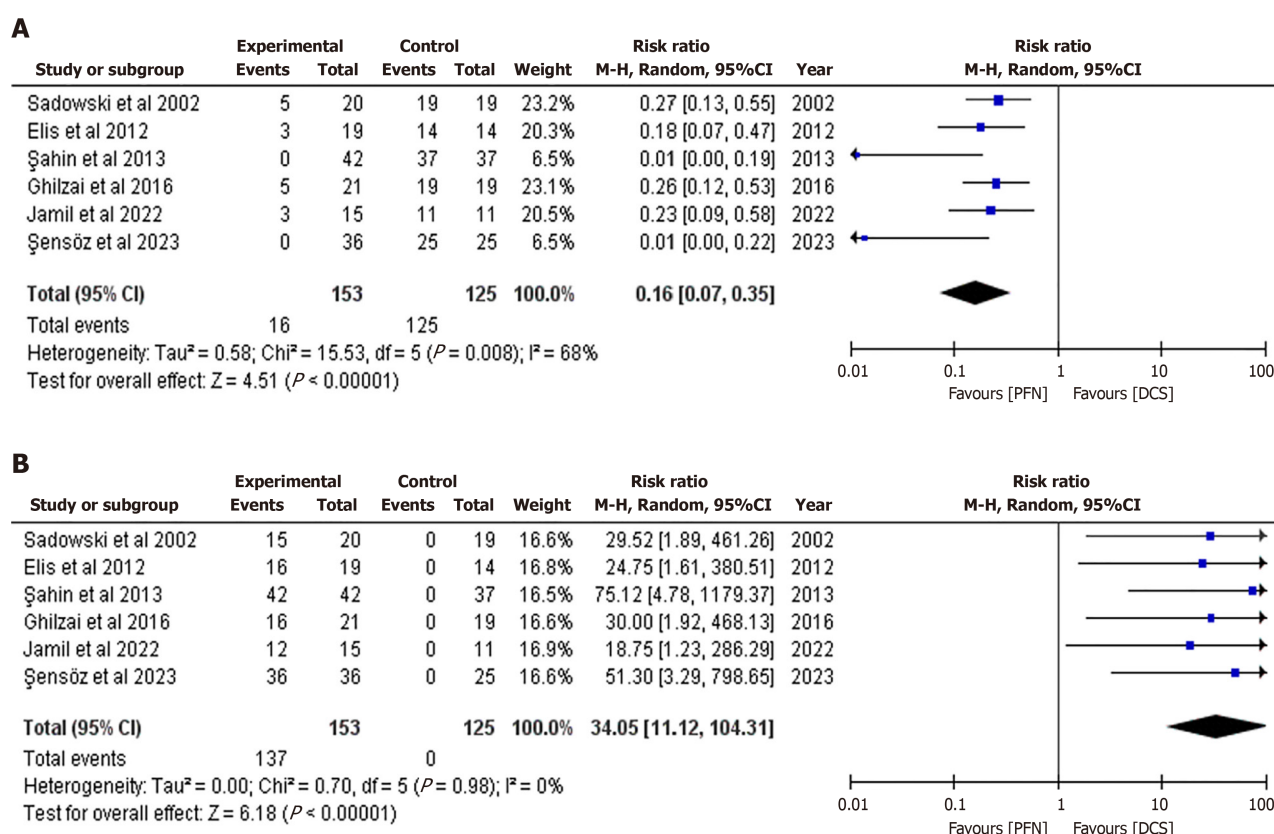
**Figure 4 Effectiveness metrics comparing proximal femoral nails vs dynamic condylar screws by forest plot.** A: Impact on earlier fracture union time in wk; B: Effect on the amount of blood transfused in units; C: Influence on hospital stay duration in d; D: Impact on the length of the operation in min. 95%CI: 95% Confidence interval; DCS: Dynamic condylar screws; PFN: Proximal femoral nails.

On the other hand, the length of hospital stay did not significantly differ between the two groups in this study. Additionally, PFN demonstrated a lower requirement for blood transfusions, which is a substantial advantage given the risks associated with blood transfusion in elderly patients.

The shorter operating duration highlights PFN's effectiveness in treating these fractures surgically, which may be because of the smaller incision and reduced muscle damage. While DCS necessitates a wider incision, PFN implants are generally placed using a minimally invasive procedure without accessing the fracture site[30].

PFN also appears to outperform DCS regarding certain postoperative outcomes. The data has revealed that PFN has a lower incidence of nonunion fractures and implant-related complications, though the latter did not reach statistical significance. In a clinical multi-center study, Simmermacher *et al*[31] documented technical PFN failures following inadequate reduction. PFN is noteworthy for its large reduction in the rate of re-operations when compared to DCS. Re-operations are a crucial indicator of long-term success and patient satisfaction. Complications that are frequently linked to weakened fixation stability include nonunion and implant failure.

However, it is essential to note that infection rates, while lower in the PFN group, did not show a statistically significant difference. This indicates that while PFN may offer some advantages, the risk of postoperative infection remains a consideration that must be managed through stringent perioperative protocols and postoperative care.



**Figure 5 Reduction type comparison between proximal femoral nails and dynamic condylar screws by forest plot. A: Open reduction; B: Closed reduction. 95%CI: 95% Confidence interval; DCS: Dynamic condylar screw; PFN: Proximal femoral nail.**

A significant finding from this study is the reduced fracture union time observed with PFN. This outcome is especially important for older patients, as prolonged immobility can cause additional complications such as deep vein thrombosis, pressure ulcers, and lung problems. PFN has been associated with a faster fracture union time, which may indicate a more effective healing process, allowing for earlier mobilization and a reduction in the total demand on healthcare resources.

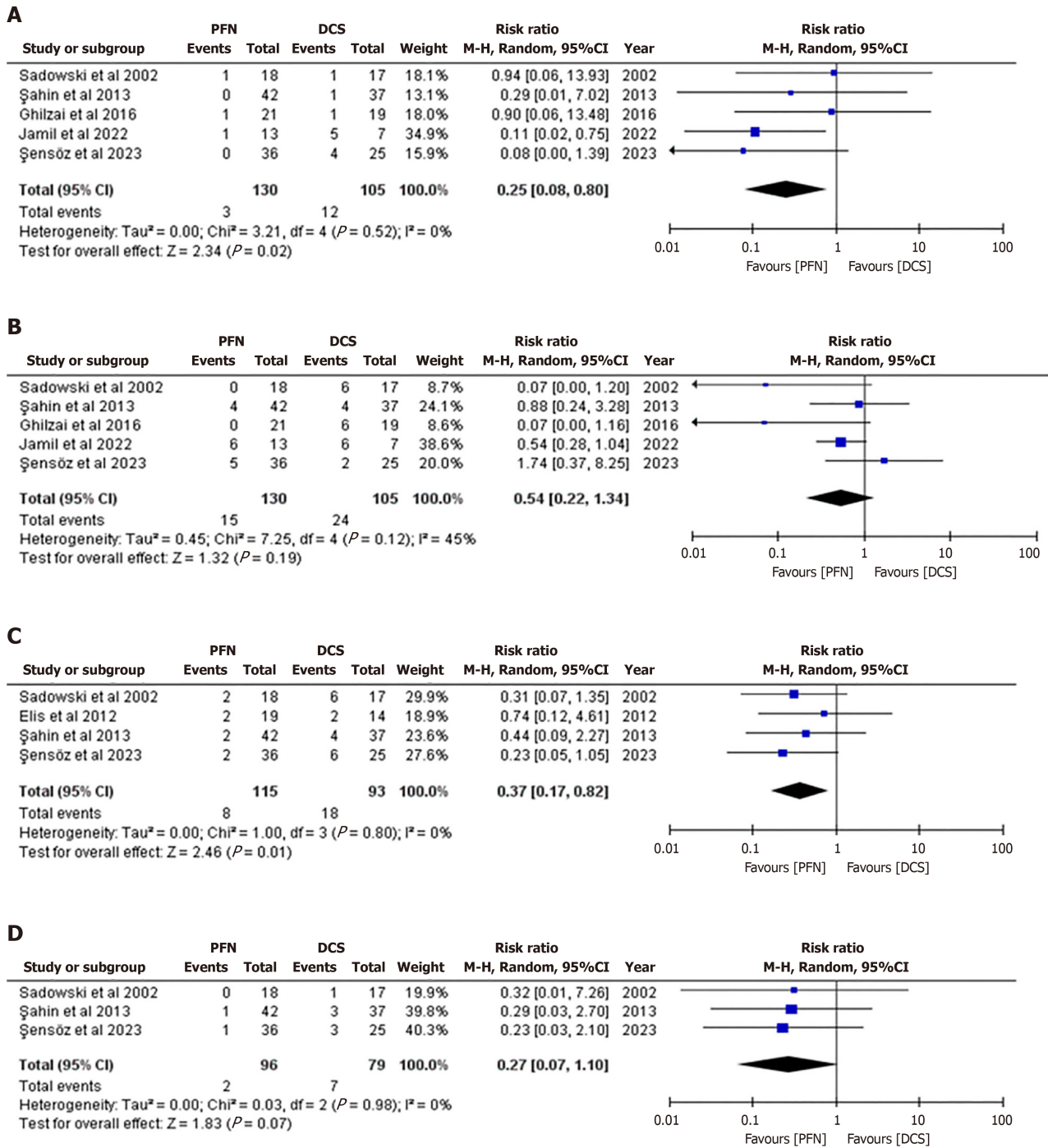
This study had a number of advantages, and was the first meta-analysis to compare PFN with DCS. Moreover, the inclusion of solely comparative studies reduced the possibility of matching and operative bias. Furthermore, the selection procedure demonstrated a high degree of selectivity, which reduced the study's heterogeneity and the possibility of bias.

However, the study also had some limitations. First, there were few comparable studies in the literature that could be included. Furthermore, this study was unable to conduct subgroup analyses to investigate possible sources of heterogeneity, because of the small number of included papers (three RCTs and three retrospective studies). Second, subgroup analysis is a valuable tool in meta-analysis to assess the consistency of findings across different study designs, populations, and interventions. However, with only six studies, subgrouping would have resulted in insufficient statistical power and potentially unreliable estimates. The inclusion of retrospective studies introduces inherent biases that are not present in RCTs. Selection bias, recollection bias, and other confounding factors that might not be sufficiently accounted for can all affect retrospective studies. The validity of this study's pooled results may be compromised by these biases. Third, publication bias was a potential concern in this study's meta-analysis. Studies with positive findings are more likely to be published, while studies with negative or null results may remain unpublished. Although this study conducted a thorough search, the possibility of missing unpublished studies remains, which could skew this study's results. Fourth, the diversity in PFN variations (standard PFN *vs* expandable PFN *vs* anti-rotation PFN) among studies may contribute to variations in outcomes. Finally, the study did not include patient-reported outcomes including hip scores, discomfort, or activities of daily living.

## CONCLUSION

The results of this study show that PFN is a reliable implant that, when used in unstable intertrochanteric fractures, provides acceptable functional and radiological outcomes. Notably, PFN typically improves the healing process for fractures and minimizes the blood transfusions requirements and operating durations, as well as decreases the incidence of reoperation, and achieves higher closed reduction success.





**Figure 6 Safety and adverse events comparison between proximal femoral nails and dynamic condylar screws by forest plot.** A: Nonunion; B: Implant-related complications; C: Revision surgery or reoperation; D: Infection. 95%CI: 95% Confidence interval; DCS: Dynamic condylar screw; PFN: Proximal femoral nail.

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## FOOTNOTES

**Author contributions:** Yousif Mohamed AM, Salih M, Abdulgadir M, Abbas AE, and Turjuman DL designed the research study, extracted and analyzed the data, and prepared the report; All authors have read and approved the final manuscript.



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