

# A meta-analysis comparing intramedullary with extramedullary fixations for unstable femoral intertrochanteric fractures

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## Abstract

**Purpose:** To find out whether the intramedullary fixations are superior to the extramedullary fixations in treating unstable femoral intertrochanteric fractures (UFIFs).

**Methods:** The meta-analysis of randomized controlled trials (RCTs) was conducted by searching the PubMed, Cochrane Library, and Embase databases to evaluate functional scores, surgical outcomes, and adverse events in adult patients receiving intramedullary fixations in comparison to extramedullary fixations. Risk ratio (RR) or weighted mean difference (WMD)/standard mean difference (SMD) with 95% confidence intervals (CIs) were calculated as effect sizes.

**Results:** A total of 18 RCTs, comprising 2414 patients, were included in this meta-analysis. Primary efficacy outcome: Parker scores [weighted mean difference, 1.10, 95% confidence interval (CI), 0.64–1.55;  $P < .0001$ ] and Harris hip scores [risk ratio, 1.24, 95%CI, 1.09–1.41;  $P = .0008$ ] were higher in the intramedullary fixation group. Moreover, blood loss, operative time, length of incision, hospital stay, and implant failure were superior in the intramedullary fixation group. Other secondary efficacy outcome: No significant differences were found between the 2 groups in terms of fluoroscopy time, mortality, cut-out, nonunion, superficial wound infection, later fracture, and reoperation.

**Conclusions:** This meta-analysis suggested that intramedullary fixation is more effective and safer than extramedullary fixation in treating UFIFs. Furthermore, blood loss, operative time, length of incision, hospital stay, and implant failure were superior in the intramedullary fixation group.

**Abbreviations:** AO/OTA = Arbeitsgemeinschaft für Osteosynthesefragen/ Orthopaedic Trauma Association, CIs = confidence intervals, RCT = randomized controlled trial, RR = risk ratio, SMD = standard mean difference, UFIF = unstable femoral intertrochanteric fracture, WMD = weighted mean difference.

**Keywords:** extramedullary fixation, intramedullary fixation, meta-analysis, randomized controlled trials, unstable femoral intertrochanteric fractures

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## 1. Introduction

A strong correlation exists between the incidence of proximal femoral fractures and high morbidity. Intertrochanteric fractures are described as one of the most common fractures in the elderly; this number is likely to increase dramatically over the next few decades. Definitions of unstable fractures include those with a fractured lesser trochanter, reverse fracture line or intertrochanteric comminution associated with a big posteromedial component, a broken greater trochanter, and lateral cortex breach.<sup>[1]</sup> Unstable femoral intertrochanteric fracture (UFIF) affects around 300,000 people a year, and the number of fractures is expected to increase to 500,000 per year in the United States alone by 2040.<sup>[2]</sup> The injury-related economic costs and physical pain is not only immense but is likely to increase without the implementation of proper preventive measures.

Most doctors agree that conservative treatment of UFIF causes serious complications and sequelae. Therefore, surgical intervention is recommended in patients with this type of fractures, with the use of various implants.<sup>[3,4]</sup> Implants may be either extramedullary or intramedullary in nature.<sup>[5,6]</sup> Surgical treatment of these fractures has developed in the last few decades, in search for an improvement in the mobility and function of this patient population. Initially, the extramedullary sliding screw installed in the 1950s revolutionized treatments of intertrochan-

teric fracture. It soon became the standard of care for treating intertrochanteric fractures. In the 1990s, the use of intramedullary nails began to increase despite the lack of conclusive evidence of superior performance. Several biomechanical studies have shown the advantages of intramedullary nailing in treating proximal femoral fractures.<sup>[7]</sup> The results did not change in treating the femoral intertrochanteric fractures, despite the increase in intramedullary devices.<sup>[8]</sup>

A previous meta-analysis compared the difference between intramedullary and extramedullary fixations in treating unstable femoral intertrochanteric fractures (UFIFs).<sup>[9]</sup> However, the sample size was small, and the alternative of internal fixation for treating UFIFs was still controversial.<sup>[9]</sup> To derive a more precise estimation of the difference between intramedullary and extramedullary fixations in treating UFIFs, the present update meta-analysis was conducted.

## 2. Material and methods

All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

### 2.1. Literature search

The PubMed, Cochrane Library, and Embase databases were searched without language limitations for all related papers using the following key terms:

1. extramedullary OR plate OR screw,
2. intramedullary OR nail, and
3. intertrochanteric OR trochanteric OR pertrochanteric OR (proximal part of the femur).

The last search was updated on September 1, 2017. The reference lists of all retrieved studies and published reviews were manually searched, and all identified relevant articles were included to find additional references.

### 2.2. Study selection

The meta-analysis included the studies that met all of the following inclusion criteria:

1. the study was designed as a randomized controlled trial (RCT);
2. the participants were patients ( $\geq 55$  years old) with UFIFs;
3. study population: patients with unstable intertrochanteric fracture of the femur (Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association [AO/OTA] classification: 2 and 3 or Evans classification: unstable);
4. the trial group was treated with intramedullary fixations, and the control group with extramedullary fixations; and
5. outcomes included functional assessment, surgical outcomes, and adverse events.

The primary outcomes were functional outcome assessed by Parker score and Harris hip score, and adverse events, assessed by the rate of implant failure. Parker score is a pure mobility score, with a maximum of nine points and a minimum of zero.<sup>[10]</sup> However, the minimal clinically important difference (MCID) of the Parker score had never been explored, thus only statistical differences can be proved. Harris hip Score was developed for the assessment of the results of hip surgery, and is intended to evaluate various hip disabilities and methods of treatment in an

adult population.<sup>[11]</sup> The score ranges from 0 to 100, where, the higher the score, the better the patient outcome. The Minimal clinically important difference ranged 15.9 to 18 points.<sup>[12]</sup> Harris hip score below 70 points was considered a poor result; 70 to 80, fair; 80 to 90, good; and 90 to 100, excellent.<sup>[13]</sup> Implant failure was defined as any condition that necessitated revision surgery, including:

1. subsequent fracture around the implant,
2. helical blade, sliding hip screw, or lag screw cut-out,
3. progressive fracture displacement,
4. fracture non-union,
5. implant or screw breakage, or
6. lateral protrusion of the helical blade, sliding hip screw, or lag screw.

The surgical outcomes were secondary outcomes, including blood loss, fluoroscopy time, hospital stay, intraoperative fracture, length of incision, and operative time.

The exclusion criteria were as follows:

1. review articles, conference abstracts, letter, or case reports;
2. if multiple papers were published on the same population, the most recent and complete study was included; and
3. studies without available data for statistics. The studies meeting at least one of 3 criteria were excluded.

### 2.3. Data extraction and quality assessment

The following data from each study were extracted independently by 2 authors: first author's name, year of publication, study location, interventions, assessment criteria of UFIF, age and sex of the study population, follow-up time, sample size, and outcomes. Any disagreements were resolved by a third reviewer. The evaluation of research quality was managed using the Cochrane Collaboration's tool for assessing the risk of bias.<sup>[14]</sup>

### 2.4. Statistical analysis

The meta-analysis was conducted using Review Manager Software (version 5.2, Nordic Cochrane Center). Risk ratio (RR) or weighted mean difference (WMD)/standard mean difference (SMD) with 95% confidence intervals (CIs) were calculated as effect sizes. RR was the effect measurement for dichotomous outcomes, whereas WMD/SMD was applied for the continuous variables. Differences in surgical outcomes, functional assessment, and adverse events between intramedullary and extramedullary fixations were assessed. Lower scores, indicate a higher level of dysfunction due to hip problems. The potential heterogeneity across studies was examined using Cochran's Q-statistic and  $I^2$  statistics.<sup>[15]</sup> If the  $P$  value for heterogeneity was  $<.05$  or  $I^2$  was  $>50\%$ , it indicated that the heterogeneity was statistically significant. Thus, the random-effects model was used to perform the analysis. Otherwise, the summary effect was computed using the fixed-effects model. Relative influence of each study on the pooled estimate was assessed by omitting one study at a time for sensitivity analysis. Further, subgroup analysis and meta-regression were conducted for implant failure. The Begg and Egger tests were conducted to evaluate the presence of a publication bias using Stata 11.0 (Stata Corp., TX).  $P \leq .05$  (2-tailed) was considered statistically significant.

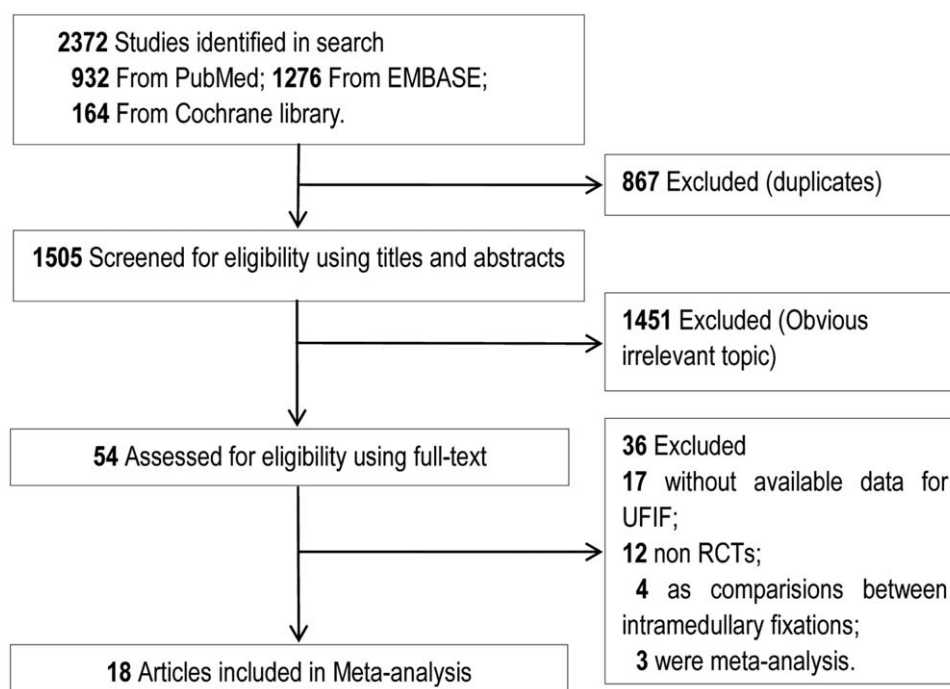


Figure 1. Flow diagram of study selection.

### 3. Results

#### 3.1. Literature search and study selection

A total of 2372 papers were identified from PubMed, Cochrane Library, and Embase, as described earlier. After deleting the duplications, 1505 papers remained. Then, 1451 articles were discarded because of irrelevance with the present issue. Of the remaining 54 papers, 17 articles were excluded due to the lack of data on UFIF; 12 papers were non-RCTs. Besides, 4 papers compared between intramedullary fixations, and 3 studies were meta-analyses. Finally, a total of 18 studies<sup>[13,16–32]</sup> met the inclusion and exclusion criteria for this meta-analysis. The flow diagram of study selection is shown in Figure 1.

#### 3.2. Study characteristics

The key characteristics of all included studies are summarized in Table 1. All of the studies involved patients with intertrochanteric fractures and were followed up for at least 6 months. Eighteen RCT studies, from 1998 to 2015, that compared intramedullary nails with extramedullary plates for treating intertrochanteric fractures, prospectively and randomly, were identified. Complete agreement (100%) was observed between the 2 independent reviewers for the entire data extraction. The 18 RCTs were also assessed qualitatively using tools recommended by the Cochrane Collaboration for the risk of bias. A graph and summary of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases identified in each RCT are shown in Figures 2 and 3. The randomization technique was not mentioned in 3 trials,<sup>[22,26,32]</sup> and the information of allocation concealment was not provided for 7 studies.<sup>[22–26,29,32]</sup> The term “blinding of outcome assessment” was assessed as “high risk” for 15 studies owing to no difference in the postoperative radiological data between the 2 groups.

#### 3.3. Meta-analyses

Table 2 and Figure S1, <http://links.lww.com/MD/D207> summarizes outcomes of the present meta-analysis. Eight studies provided data on intraoperative blood loss and were eligible in the form of mean and standard deviation (SD). A total of 821 patients with fractures were included, 387 with intramedullary fixation and 434 with extramedullary fixation.

### 4. Primary outcomes

#### 4.1. Parker score

Four studies provided data on the Parker score and were eligible in the form of mean and SD. A total of 282 patients with fractures were included: 141 patients with intramedullary fixation and 141 with extramedullary fixation. The meta-analysis indicated a higher *Parker score* in the intramedullary fixation group (WMD, 1.10, 95%CI, 0.64–1.55;  $P < .0001$ ,  $I^2 = 0$ ).

#### 4.2. Harris hip score

Three articles provided data on the Harris hip score. The patients in the intramedullary fixation group achieve higher Harris hip score (RR, 1.24, 95%CI, 1.09–1.41;  $P = .0008$ ;  $I^2 = 0$ ).

#### 4.3. Implant failure

Twelve articles involved 1668 fractures, which provided data on implant failure. The outcome showed that the risk of implant failure was lower in the intramedullary fixation group (RR, 0.43, 95%CI, 0.23–0.81;  $P = .009$ ,  $I^2 = 0$ ; Fig. 4). However, no significant differences were found between the intramedullary and extramedullary groups for the other adverse events when all

**Table 1**  
Characteristics of each included study.

Study year	Country	Intervention	Assessment criteria of UFIF	Sample size	Age (years)	M/F	Follow-up time (months)	Outcomes
				I	I	I		
Aktsells, 2014	Greece	GN vs SHS	AO/OTA	40	82.9±5.8	8/28	7/28	b, d, e, f, g, h, j, k, n, o
Barton, 2010	UK	GN vs SHS	AO/OTA	110	83.1 (42–99)	19/81	25/85	e, g, j, k, m, o
Baumgaertner, 1998	USA	IMHS vs SHS	Tronzo–Evans	36	79±9.8	NR	NR	a, b, d, e
Baumgaertner, 2007	Sweden	PFN vs MSP	Evans–Jensen	87	83 (48–96)	23/64	20/65	f, k, o
Haq, 2014	India	PFN vs reverse-DFLCP	AO/OTA	20	55.55±17.09	10/10	18/2	a, b, d, g, h, i, l
Hardy, 1998	Belgium	IMHS vs SHS	Evans–Jensen	37	81.7±11.8	NR	NR	h, j
Harrington, 2002	USA	IMHS vs SHS	Evans–Jensen	50	83.8±8.5	10/40	11/41	b, d, e, f, g, j, k, l, n
Huang, 2015	China	PFNA vs DHS, PFLCP	Tronzo–Evans	30	75.07±7.87	15/15	33/27	a, b, c, d, e, g, i
Leung, 1992	China	GN vs SHS	Evans–Jensen	63	80.9±8.4	NR	NR	a, b, c, d, e, l
Lin, 2015	China	SBAR-IMN vs DHS	NR	41	71.37±6.93	24/17	23/18	a, b, g
Miedel, 2005	Sweden	GN vs MSP	Evans–Jensen	93	NR	NR	NR	f, g
Papasimos, 2005	Greece	GN, PFN vs DHS	AO/OTA	80	81.1 (NR)	33/47	14/26	b, d, f, g, k, l, m, o
Parker, 2012	UK	PFN vs SHS	AO/OTA	211	82.4 (26–104)	NR	NR	g, k, l, n, o
Reindi, 2015	Canada	InterTAN, TFN, and GN vs DHS	AO/OTA	112	82±8.6	57/55	31/61	g, j, k, m, o
Wu, 2015	China	SBAR-IMN vs PFLCP	Tronzo–Evans	50	76.2±3.7	21/29	24/26	a, b, i
Xu, 2010	China	PFNA vs DHS	AO/OTA	51	78.5±7.97	15/36	16/39	a, b, c, d, e, f, g, h, j, k, l, m, n, o
Zehir, 2015	Turkey	PFNA vs DHS	AO/OTA	96	77.22±6.82	37/59	39/63	a, b, e, j, k, m, n, o
Zou, 2009	China	PFNA vs DHS	AO/OTA	16	65.0±13.5	NR	NR	g, k, l, m, o

AO/OTA = Osteosynthesefragen/Orthopaedic Trauma Association classification, DFLCP = distal femoral locking compression plates, E = extramedullary fixation group, F = female, GN = gamma nail, j = intramedullary fixation group, IMHS = intramedullary hip screw, M = male, MSP = Medoff sliding plate, NR = not reported, PFLCP = proximal femoral locking compression plate, SBAR-IMN = spiral blade anti-rotation intramedullary nail, SHS = sliding hip screw, TFN = trochanteric fixation nail, UFF = unstable femoral intertrochanteric fracture, UK = United Kingdom. Outcomes: a, blood loss; b, operative time; c, length of incision; d, fluoroscopy time; e, hospital stay; f, intra-operative fracture; g, implant failure; h, Harris hip score; i, mortality; j, mortality; k, cut-out; l, nonunion; m, superficial wound infection; n, later fracture; o, reoperation.

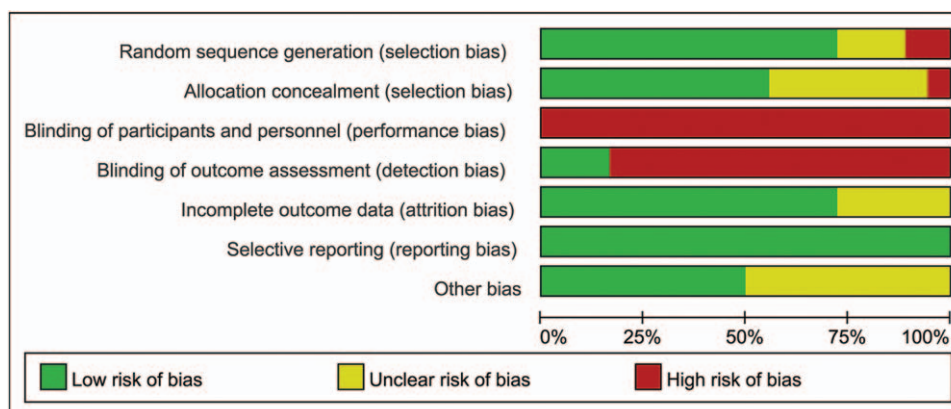


Figure 2. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

of the patients were pooled into the meta-analysis: mortality (RR, 1.11, 95%CI, 0.85–1.45;  $P = .45$ ), cut-out (RR, 1.10, 95%CI, 0.58–2.08;  $P = .77$ ), nonunion (RR, 0.47, 95%CI, 0.14–1.59;  $P = .23$ ), superficial wound infection (RR, 0.61, 95%CI, 0.24–1.52;  $P = .29$ ), later fracture (RR, 1.75, 95%CI, 0.55–5.57;  $P = .35$ ), and reoperation (RR, 0.81, 95%CI, 0.43–1.50;  $P = .50$ ). The fixed-effects model was used because no significant clinical heterogeneity was observed between the studies.

## 5. Secondary outcomes

### 5.1. Blood loss

The heterogeneity test indicated that statistical heterogeneity was present ( $P < .0001$ ,  $I^2 = 98\%$ ). Data were pooled using a random-effects model, which indicated less blood loss in the intramedullary fixation group (WMD,  $-130.97$ , 95%CI,  $-200.90$  to  $-61.03$ ;  $P = .0002$ ).

### 5.2. Operative time

Eleven articles involved 1123 fractures, which provided data on operative time. Statistical heterogeneity was present ( $P < .0001$ ,  $I^2 = 95\%$ ), and the outcome showed that operative time was shorter in the intramedullary fixation group (WMD,  $-8.91$ , 95%CI,  $-15.73$  to  $-2.09$ ;  $P = .010$ ). *Length of incision*: Three articles provided data on the length of incision. The length of incision was longer in the extramedullary than in the intramedullary fixation group (WMD,  $-7.45$ , 95%CI,  $-9.22$  to  $-5.69$ ;  $P < .0001$ ,  $I^2 = 93.2$ ).

### 5.3. Fluoroscopy time

Eight articles provided data of fluoroscopy time. The heterogeneity test indicated a statistical heterogeneity ( $P < .0001$ ,  $I^2 = 97\%$ ), and the outcome showed no significant differences in fluoroscopy time between the 2 groups (SMD, 0.29, 95%CI,  $-0.68$  to 1.26;  $P = .56$ ).

### 5.4. Hospital stay

Eight articles provided data on hospital stay. The pooled analysis indicated that the hospital stay was shorter in the intramedullary

than in the extramedullary fixation group (WMD,  $-0.86$ , 95%CI,  $-1.23$  to 0.49;  $P < .0001$ ,  $I^2 = 38\%$ ).

### 5.5. Intraoperative fracture

Eight articles provided data on intraoperative fracture. The risk of intraoperative fracture was higher in the intramedullary than in the extramedullary fixation group (RR, 4.37, 95%CI, 1.13–16.86;  $P = .03$ ;  $I^2 = 0$ ).

### 5.6. Subgroup analysis and meta-regression

To investigate the effects of various study characteristics on the pooled RR, subgroup analysis and meta-regression were conducted by subgroups for implant failure. In subgroup analyses, the overall effect was non-significant for studies that were conducted in the country ( $P = .57$ ), criteria ( $P = .60$ ), and intervention ( $P = .58$ ) (Table 3). No statistical significance was identified regarding the differences in overall effects for the various subgroups by univariate and multivariate meta-regression. The detailed data are shown in Table 4.

### 5.7. Sensitivity analysis

Sensitivity analyses were performed to assess the influence of individual dataset on the pooled estimate by sequential removing each eligible study. Any single study was omitted, while the overall statistical significance does not change, indicating that our results are statistically robust (Fig. 5).

### 5.8. Publication bias

The outcome of implant failure was chosen to conduct the test of a publication bias. Finally, the Egger regression test showed no evidence of asymmetrical distribution in the funnel plot for implant failure (Begg test,  $P = .350$ ; Egger test,  $P = .177$ ) (Fig. 6).

## 6. Discussion

The incidence of intertrochanteric fractures has shown an upward trend with the rapid growth of the elderly population.<sup>[32]</sup> The current evidence is contradictory and does not always support the treatment modalities widely used in prac-



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aktselis, I 2014	+	+	-	-	+	+	+
Barton, TM 2010	+	+	-	-	+	+	+
Baumgaertner, MR 1998	+	+	-	-	+	+	?
Ekstrom, W 2007	+	+	-	-	?	+	?
Haq, RU 2014	+	+	-	-	+	+	?
Hardy, DC 1998	-	-	-	-	+	+	?
Harrington, P 2002	+	+	-	-	?	+	+
Huang, SG 2015	?	?	-	+	+	+	+
Leung, KS 1992	-	?	-	-	?	+	?
Lin, Y 2015	+	?	-	-	+	+	+
Miedel, R 2005	+	?	-	+	+	+	?
Papasimos, S 2005	?	?	-	-	?	+	+
Parker, MJ 2012	+	+	-	-	+	+	?
Reindl, R 2015	+	+	-	+	+	+	?
Wu, H 2015	+	?	-	-	+	+	+
Xu, YZ 2010	+	+	-	-	+	+	+
Zehir, S 2015	+	+	-	-	+	+	+
Zou, J 2009	?	?	-	-	?	+	?

**Figure 3.** Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

tice.<sup>[27,28,33,34]</sup> Therefore, an updated meta-analysis was performed comparing intramedullary and extramedullary fixations in patients with UFIFs. No statistically significant differences were found between the 2 groups in terms of fluoroscopy time, mortality, cut-out, nonunion, superficial wound infection, later fracture, and reoperation. In contrast, Parker and Harris hip scores were significantly higher in the intramedullary fixation

group. Moreover, blood loss, operative time, length of incision, hospital stay, and implant failure were superior in the intramedullary fixation group. The results of the present meta-analysis suggested that intramedullary fixation was more beneficial than extramedullary fixation in treating UFIFs. However, the risk of intraoperative fracture was higher in the intramedullary than in the extramedullary fixation group. The introduction of the newer long intramedullary nails has reduced the rate of both intraoperative fracture and subsequent femoral fracture in comparison with the rates that were seen in association with the shorter nails.<sup>[35]</sup>

Recent literature has shown that the practice of treating intertrochanteric fractures has changed with the dramatic increase in the number of intramedullary devices used. This growth has not been supported by scientific evidence, but has been driven by other factors, including industry marketing, surgeon preferences and reimbursement.<sup>[36]</sup> In recent years, intramedullary fixation of intertrochanteric fractures in US medical insurance patients has become more frequent, but patient-related factors cannot be used to explain this trend.<sup>[37]</sup> In a study of candidates taking the Part II American Board of Orthopedic Surgery examination, the intramedullary fixation rate of intertrochanteric fractures of the femur increased from 3% to 67% from 1999 to 2006.<sup>[38]</sup> Compared to sliding hip screws, this increase did not improve significantly in terms of functional results or patient satisfaction. However, increased use of intramedullary fixation is associated with a higher incidence of surgical related complications. In addition, the choice of implants has a significant cost effect, and the current price of sliding hip screws is about £1000 (\$1500) lower than that of long gamma nails.

Successful treatment of a fracture by use of implants is a race between rate of fracture healing and metal fatigue of implant used. Implant failure is thus one of the most feared but often encountered complications in the practice of an orthopedic surgeon.<sup>[39]</sup> Biomaterial breakdown may be due to various causes such as: Mechanical, that is, due to creep, wear, stress cracking and fracture; Physicochemical, that is, due to adsorption of biomolecules such as proteins absorption of water or lipids and dissolution; Biochemical reactions, that is, hydrolysis of amide and ester bonds, oxidation and reduction, mineral deposition and excessive fibrous deposition; electrochemical, that is, corrosion. The most commonly reported complication in the internal fixation is the cut-out defined as “the collapse of the neck-shaft angle into varus, leading to extrusion of the screw from the femoral head”.<sup>[39]</sup> This complication is a multifactorial event affected by a number of variables including patient' age, bone quality, fracture pattern, quality of reduction, lag screw positioning in the femoral head, implant design and the choice of CCD-nail angle.

Unlike previous meta-analyses conducted on the topic,<sup>[9]</sup> the present meta-analysis was able to sufficiently pool data across a wide range of outcomes and shed greater insights into clinically important outcomes. Also, the results differed from previous meta-analyses due to the additional studies included and larger amounts of pooling. A previous meta-analysis conducted by Li et al<sup>[9]</sup> was limited because only 11 RCTs were included that compared the interventions in question. The present study included seven additional eligible studies.<sup>[13,19,22,24,25,29,31]</sup> Moreover, the results of this meta-analysis were not completely the same as those of the study by Li on the primary outcomes assessed. Inconsistent with previous meta-analyses, Li et al found

**Table 2**  
Pooled results of the outcomes of the meta-analysis.

Outcomes	N	n (I)	n (E)	Effect measure	Effect size	P <sub>H</sub>	I <sup>2</sup> (%)	P <sub>A</sub>
Surgical outcomes								
Blood loss (ml)	8	387	434	WMD	-130.97 (-200.90, -61.03)	<.0001	98	.0002
Operative time (min)	11	557	566	WMD	-8.91 (-15.73, -2.09)	<.0001	95	.010
Length of incision (cm)	3	174	178	WMD	-7.45 (-9.22, -5.69)	<.0001	93.2	<.0001
Fluoroscopy time	8	370	373	SMD	0.29 (-0.68, 1.26)	<.0001	97	.56
Hospital stay (days)	8	489	535	WMD	-0.86 (-1.23, -0.49)	.13	38	<.0001
Intraoperative fracture	6	401	368	RR	4.37 (1.13, 16.86)	.99	0	.03
Functional assessment								
Parker score	4	141	141	WMD	1.10 (0.64, 1.55)	.55	0	<.0001
Harris hip score*	3	97	124	RR	1.24 (1.09, 1.41)	.72	0	.0008
Adverse events								
Implant failure	12	844	824	RR	0.43 (0.23, 0.81)	.91	0	.009
Mortality	7	486	485	RR	1.11 (0.85, 1.45)	.39	5	.45
Cut-out	10	843	794	RR	1.10 (0.58, 2.08)	.56	0	.77
Nonunion	7	491	458	RR	0.47 (0.14, 1.59)	.75	0	.23
Superficial wound infection	6	455	410	RR	0.61 (0.24, 1.52)	.84	0	.29
Later fracture	5	448	456	RR	1.75 (0.55, 5.57)	.86	0	.35
Reoperation	9	793	742	RR	0.81 (0.43, 1.50)	.45	0	.50

n(I)/n(E) = sample size of participant of intramedullary/extramedullary fixation group, N = number of included studies, P<sub>A</sub> = P value of association, P<sub>H</sub> = P value of heterogeneity, RR = risk ratio, SMD = standard mean difference, WMD = weighted mean difference.

\* Comparing the difference in excellent or good Harris hip scores between the 2 treatments.

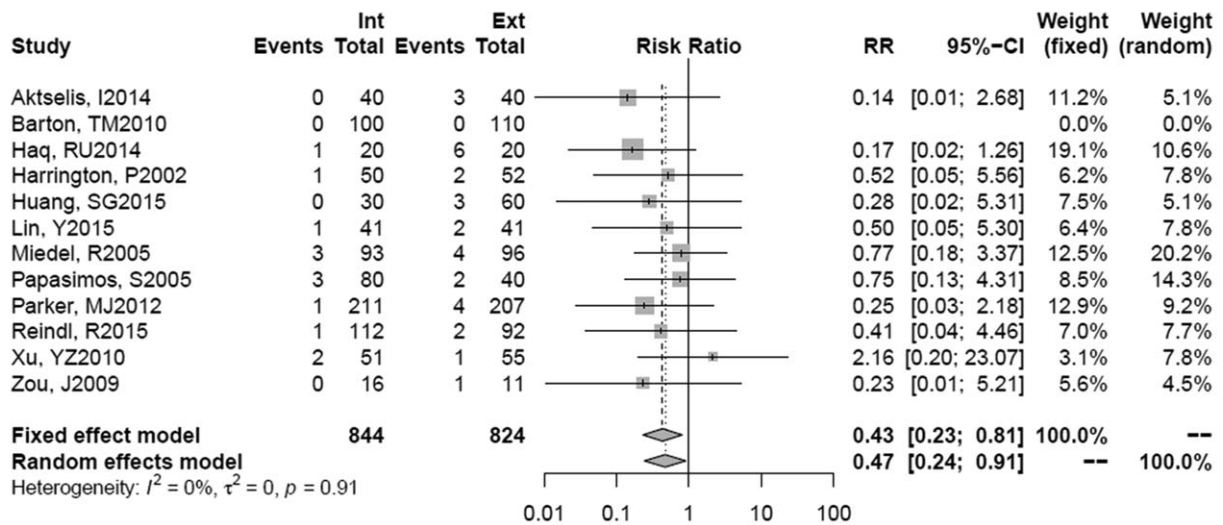


Figure 4. Forest plot of studies showing RR of implant failure.

**Table 3**  
Stratified analyses of implant failure.

Group	No. of studies	Effect		Heterogeneity test		P* for interaction
		RR (95% CI)	P value	P value	I <sup>2</sup> , %	
All studies	12	0.43 (0.23-0.81)	.01	.91	0.0	
Country						.57
China	4	0.59 (0.18-1.96)	.39	.62	0.0	
non-China	8	0.39 (0.19-0.81)	.01	.84	0.0	
Criteria						.60
AO/OTA	7	0.37 (0.17-0.82)	.02	.68	0.0	
non-AO/OTA	5	0.56 (0.20-1.56)	.27	.94	0.0	
Intervention						.58
PFNA	3	0.62 (0.15-2.54)	.50	.42	0.0	
non-PFNA	9	0.40 (0.20-0.80)	.01	.90	0.0	

P\* for interaction was utilized to assess the stratified differences.

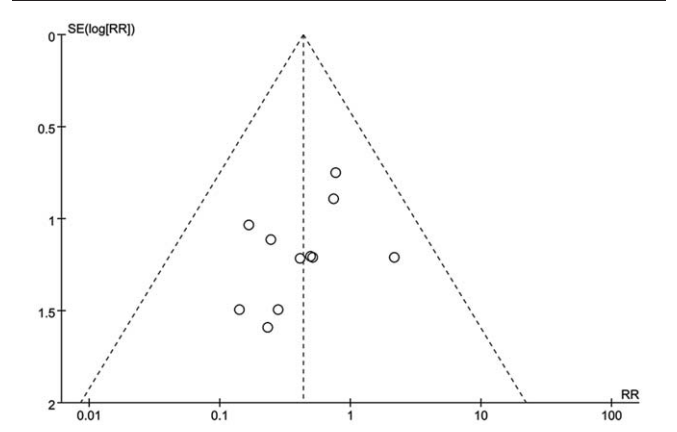
AO/OTA = Arbeitsgemeinschaft für Osteosynthesefragen/ Orthopaedic Trauma Association, CI = confidence interval, PFNA = proximal femoral nail antirotation, RR = relative risk.

**Table 4**  
**Univariate and multivariate meta-regression for implant failure.**

Factor	Univariate regression			Multivariate regression		
	Estimate	Se	P value	Estimate	Se	P value
Country	0.35	0.78	.65	-0.12	1.35	.93
Criteria	-0.36	0.69	.6	-0.42	0.73	.56
Intervention	0.42	0.89	.63	0.59	1.54	.72

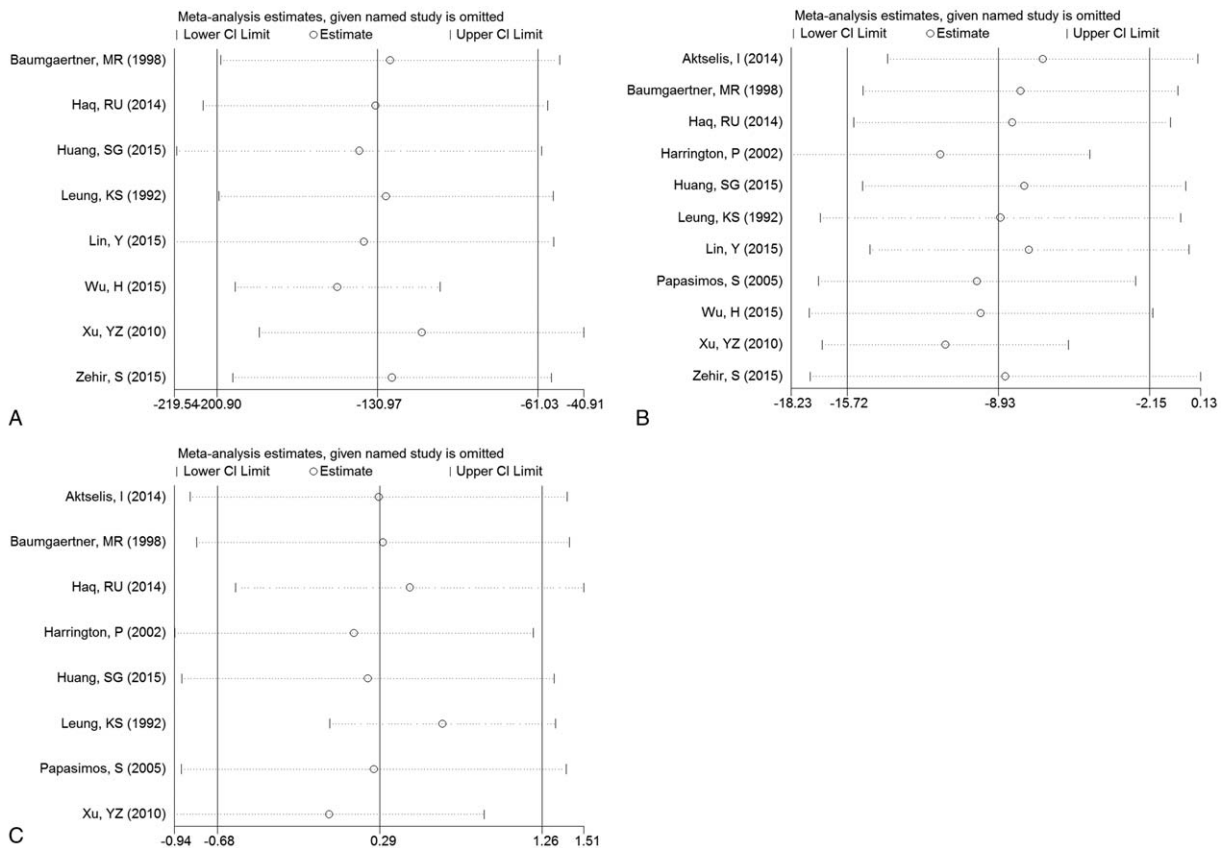
no significant difference in terms of operative time, hospital stay, and implant failure in patients with intramedullary fixation compared with those with extramedullary fixation. However, the present results indicated that operative time, hospital stay, and implant failure were superior in the intramedullary fixation group. The differences in these results are likely attributed, again, to a larger sample size of the present study compared with the previous studies,<sup>[13,22,25]</sup> supporting the use of intramedullary implants in the present meta-analysis. Such as operative time, Li et al found that non-significant discrepancies were observed between 2 groups (SMD -0.13, 95%CI -0.93 to -0.67,  $P = .74$ ), however, Li et al only analyzed 6 studies, whereas we identified 5 additional eligible studies and found that operative time was significantly shorter in the intramedullary fixation group (WMD, -8.93, 95%CI, -15.72 to -2.15;  $P = .010$ ).

Heterogeneity was high in all but one of the meta-analyses, which might be associated with a low number of included studies.<sup>[40]</sup> The high heterogeneity and a relatively low number of



**Figure 6.** Begg funnel plot for a publication bias. Each point represents a separate study for the indicated association.

studies also precluded meaningful assessment of a publication bias<sup>[41]</sup> However, the present meta-analysis did include 2414 patients, which increased the confidence in the results. A significant clinical heterogeneity was observed in blood loss ( $P < .0001$ ,  $I^2 = 98\%$ ), operative time ( $P < .0001$ ,  $I^2 = 95\%$ ) and fluoroscopy time ( $P < .0001$ ,  $I^2 = 97\%$ ). The heterogeneity in this meta-analysis might be partially due to the difference in the internal fixation implant device used in each trial. Moreover, the definitions of unstable fractures, surgical technique, experience of



**Figure 5.** Sensitivity analysis for UFIF patients receiving intramedullary fixations in comparison to extramedullary fixations. A) Blood loss; B) Operative time; C) Fluoroscopy time.



the surgeons, and postoperative rehabilitation could lead to heterogeneity because these variables were difficult to assess. Furthermore, subgroup analysis and regression shown this result was robust, sensitivity analyses were also conducted by sequentially removing each eligible study. With this exclusion, the pooled estimate did not change significantly, strengthening our confidence in our results (Fig. 4).

The present meta-analysis had several strengths. First, it included prospective randomized controlled trials (RCTs) with large sample sizes, which significantly increased the statistical power to detect potential associations. Second, the RCTs included in this meta-analysis were moderate and of high quality. Third, no publication bias was detected, indicating that the whole pooled results might be unbiased.

On the contrary, the limitations of this meta-analysis should also be highlighted. First, the internal fixation implant device used in each trial was not completely equivalent. The definitions of unstable fractures, surgical technique, experience of the surgeons, and postoperative rehabilitation probably varied as well. Second, heterogeneity was significant in this meta-analysis. Due to the significant heterogeneity, a random-effects model was used to calculate the pooled data, which could provide stable results. Third, there are other factors that may affect outcome that are not reported: for example, post-operative physiotherapy, early weight-bearing protocols, etc. Fourth, the definition of implant failure was reoperation due non-union, reoperation due to later fracture, reoperation due to implant failure or reoperation of any cause. Then, the MCID of the Parker score had never been explored, thus only statistical differences can be proved in the meta-analysis. Although the MCID of Harris hip score had been identified (15.9–18 points), all the trials reported Harris hip score as hierarchical data rather than continuous data, then the meta-analysis could not get the mean difference between these 2 groups. Finally, the difference in the quality of life or patient satisfaction was still not evaluated because they were not always reported or were reported in various forms.

## 7. Conclusions

There was no difference in important outcomes such as mortality and total risk of reoperations, but differences in functional outcome according to Parker score and Harris hip score between intramedullary fixation and extramedullary fixation in treating UFIFs. Furthermore, intramedullary fixation could significantly improve blood loss, operative time, length of incision, hospital stay, and implant failure than extramedullary fixation. However, Increased cost with intramedullary nails compared with extramedullary fixation. Future large-scale trials should be conducted focused on patients with specific classify of UFIFs to compare the efficacy and safety of intramedullary nails with extramedullary fixation.

## Author contributions

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**Project administration:** Dawei Sun.

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**Writing – review & editing:** Dawei Sun, Xiaochun Liu, Peng Zhao, Hongan Zhang, Hui Zhou, Chenghe Qin.

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