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Original Article

Meta-analysis of postoperative complications in distal femoral fractures: retrograde intramedullary nailing versus plating

Aijun Wang[1], Shuangle Zong[1], Lixin Su[1], Weidong Liang[1], Xiaoqiang Cao[1], Qiutao Zheng[1], Lidong Li[1], Xiaoming Zhao[1], Shilian Kan[2]

[1]Department of Orthopedics Institute, The Second Hospital of Tangshan, Tangshan 063000, Hebei Province, People's Republic of China; [2]Department of Orthopedics Institute, Tianjin Medical University, Tianjin 300070, People's Republic of China

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Abstract: Background: With advances in surgical techniques of retrograde intramedullary nailing and plating for distal femoral fractures, conclusions regarding the superior choice remain controversial. This meta-analysis aimed to quantitatively investigate postoperative complications in a comparison of retrograde intramedullary nailing and plating for distal femoral fractures. Methods: The following electronic databases were searched before December 2015: PubMed, Science Direct, Wiley Online Library, and Google Scholar. All prospective and retrospective controlled trials comparing postoperative complications of retrograde intramedullary nailing and plating for distal femoral fractures were identified. The present meta-analysis was undertaken using RevMan 5.3 software. Results: Six studies with a total of 279 patients were eligible for data extraction in our meta-analysis. The pooled analysis showed no significant differences in infection, non-union, malunion, delayed union, metalwork failure, knee stiffness, and knee pain. While subgroup analysis indicated that the dynamic condylar screw plate group had significantly more intraoperative blood loss than the retrograde intramedullary nailing group, the locking-plate fixation group had significantly less intraoperative blood loss than the retrograde intramedullary nailing group. Conclusion: No implant is superior to any other under all circumstances for distal femoral fracture. The available evidence has shown that retrograde intramedullary nailing and plating have similar postoperative complication rates.

Keywords: Distal femur, retrograde intramedullary nailing, plate, meta-analysis

Introduction

Distal femoral fractures (DFF) are relatively uncommon in clinical practice. The estimated frequency is 0.4% of all fractures and 3% of femoral fractures. A classic distribution is found in young patients who sustain high energy trauma and in elderly patients with a domestic accident [1]. Non-operative treatment may be chosen in the rare situation of non-or minimally-displaced fractures in bedridden elderly patients not amenable to operative therapy. Operative repair for DFF is the standard, whether open or closed, intra-articular or extra-articular. The surgical treatment of DFF has continually evolved. The goal of treatment for DFF is to restore limb length and anatomic articular surface alignment and rotation, and to create adequate fixation for early mobilization of the associated joints with minimal complications. A minimally invasive technique using stable fixation implants allows for immediate mobilization, which ensures a high-quality functional recovery. The indications for retrograde intramedullary nailing (RIMN) are classic: extra-articular fractures, and simple intra-articular fractures with little or no displacement that are not appropriately classified as coronal plane fractures, i.e., the Hoffa fracture. There are also multiple alternatives for the definitive treatment of DFF, comprising plate osteosynthesis with either open reduction and internal fixation or closed reduction and minimally invasive plate osteosynthesis (MIPO) [2]. Multiple different plating options are also available, including buttress plate fixation, use of fixed angle devices like the angled blade plate or the dynamic condylar screw (DCS), and the locking plate. In the last

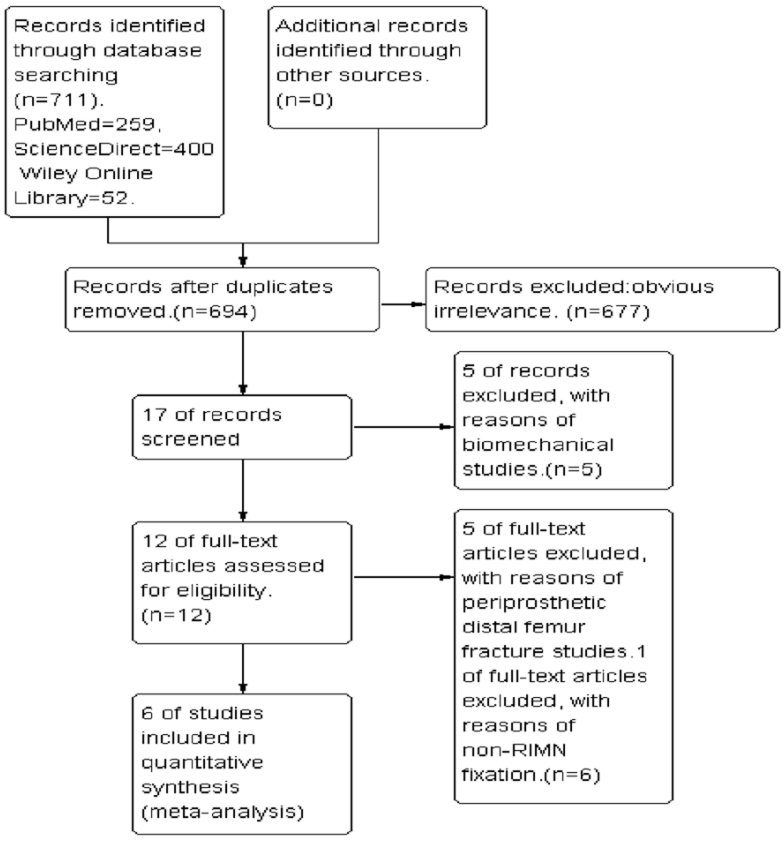

Figure 1. Flow chart of the selection process.

few years, new implants have been developed to enable less traumatic minimally invasive surgery. The trend of indirect reduction led to the development of minimally invasive plate osteosynthesis. The commonly used locking implant in these series is the Less Invasive Stabilization System (LISS) [3]. Submuscular locked plating, LISS plate fixation, and the MIPO technique have recently been used for DFF. The periosteal and medullary perfusion of the MIPO technique was superior when compared to the classic lateral approach to the femur. The locking plate provided an improvement in alignment and stability. The philosophy of MIPO has evolved and gained favor to theoretically preserve bone biology. Owing to the merits of less soft tissue dissection and less periosteal stripping, retrograde intramedullary fixation is also still popularly used for DFF. However, the distal femur has a widening canal, thin cortex, and poor bone stock, all of which make surgical treatment difficult. The diversity of approaches advocated for surgical fixation implied the lack of a gold standard for this challenging fracture type. The established surgical treatments include RIMN and plating. The optimal method for the treatment of DFF remains controversial.

There have been several studies comparing RIMN and plating for DFF. However, both implants have different advantages and disadvantages. Limited by sample size, studies could not demonstrate clear superiority of one modality over the other. Therefore, based on comparative evidence, we conducted a meta-analysis to quantitatively compare postoperative complications of RIMN and plating for DFF. To the best of our knowledge, this is the first meta-analysis on this issue.

Methods

Retrieval strategy

We conducted the meta-analysis according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement, which was established to help authors report a wide array of systematic reviews [4]. The following electronic databases were searched by two independent reviewers before December 2015: PubMed, Science Direct, the Wiley Online Library, and Google Scholar. No language restriction was applied. The search terms included “distal femur” and “compare”. Reference lists of relevant articles were also retrieved for any additional relevant studies.

Selection criteria and quality assessment

The present meta-analysis identified studies with the following inclusion criteria: (1) acute DFF; (2) extra-articular or intra-articular DFF (AO/OTA type 33-A to 33-C); (3) both RIMN and plating were adopted; and (4) the design was comparative, and either prospective or retrospective. Exclusion criteria comprised the following: (1) pathological fractures; (2) fractures associated with neurovascular injuries; (3) periprosthetic DFF following total knee arthroplasty; (4) trials with biomechanical studies, animal studies, or cadaver studies.

Table 1. Characteristics of included studies

Study (author, year)	Christodoulou et al. 2005		Gao et al. 2013		Gh Nabi et al. 2009		Paraschou et al. 2011		Rossas et al. 2011		Thomson et al. 2008	
Design	Quasi-RCT		Retrospective		Quasi-RCT		NA		NA		Retrospective	
Implant	RIMN	DCS	RIMN	Locking plate	RIMN	DCS	RIMN	DCS	RIMN	Plating	RIMN	NA
Sample size	35	37	17	19	37	31	26	27	12	15	11	12
Age (years)	73.2 (60-88)		50.6±16.3	54.7±16.1	47 (21-75)	49 (23-75)	68.3 (37-83)		78.6 (64-91)		50.5	49.9
Male/ Female	25/47		13/4	12/7	23/14	18/13	18/35		10/17		6/5	7/4
Fracture type	A1:12	A1:13	A1:6	A1:8	A1:6	A1:4	Supracondylar femoral fracture		Extrarticular distal femoral fracture		AO 33-C type	
	A2:14	A2:13	A2:8	A2:7	A2:11	A2:9						
	A3:5	A3:6	A3:3	A3:4	A3:16	A3:12						
	C1:3	C1:3			C1:2	C1:3						
	C2:1	C2:2			C2:2	C2:3						
Follow-up (months)	28 (18-42)		26.29±12.7	23.37±5.33	30 (24-36)		36 (30-54)		16.4 (10-26)		80	
Level of evidence	Level I		Level III		Level I		Level III		Level III		Level III	

Quasi-RCT: quasi- randomized controlled trial; RIMN: retrograde intramedullary nailing; DCS: dynamic condylar screw; NA: not available.

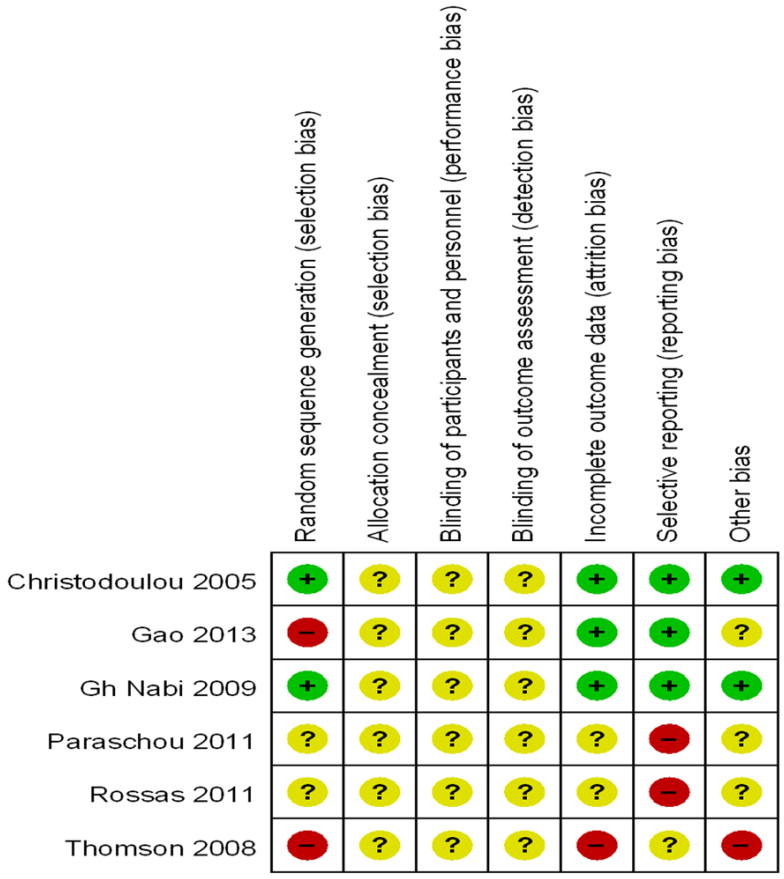

Figure 2. Methodological quality of the included studies. This risk of bias tool incorporates assessment of randomization (sequence generation and allocation concealment), blinding (participants, personnel and outcome assessors), completeness of outcome data, selection of outcomes reported, and other sources of bias. The items were scored with "yes", "no", or "unsure".

According to the Cochrane handbook for systematic reviews of interventions 5.3, the methodological quality of the included studies was assessed by two authors (Zong and Su) independently. Inconsistent opinions were resolved by discussion. When no consensus was achieved, a third author (Kan) was the adjudicator. The "assessing the risk of bias" table was applied to conduct a qualification of bias risk, which included the following key domains: random sequence generation, allocation concealment, blinding of participants and personnel, blind outcome assessment, incomplete outcome data, selective reporting, and other sources of bias.

Data extraction

Two of the authors (Zong and Su) independently extracted all the relevant data from the qualified articles and checked the accuracy. The extracted data were reexamined by another author (Kan).

The following data were extracted: study design, patient characteristics, surgical interventions, implants, and patient-based outcomes. The total sample size was 138 for the RIMN and 141 for plating. All the studies adopted the RIMN. As for the plating, three studies adopted the DCS, one trial chose the locking plate, and the other two studies did not identify the plate type. The primary outcome measurements included postoperative complications: infection, non-union, malunion, delayed union, metalwork failure, knee stiffness, and knee pain. The secondary outcome measurements included intra-operative blood loss and operative time.

Data synthesis and analysis

We performed the meta-analysis with the Review Manager (RevMan version 5.3, Copenhagen, Denmark, The Nordic Cochrane Centre) software program for graphic representation of the pooled data [5]. For dichotomous variables, odds ratio (OR) and 95% confidence interval (CI) were assessed. For continuous data, means and standard deviations were measured for weighted mean differences (WMD) with 95% CI. To assess inconsistency in the study results, statistical heterogeneity between studies was formally tested with the standard chi-square test. I^2 [I^2 = ([Q-df]/Q) × 100%] was used to estimate the size of the heterogeneity. If neither clinical nor statistical heterogeneity was found, we pooled results using a fixed-effect model with the significance level set at P = 0.05. We considered I^2 values of 25%, 50%, and 75% as low, medium, and high heterogene-

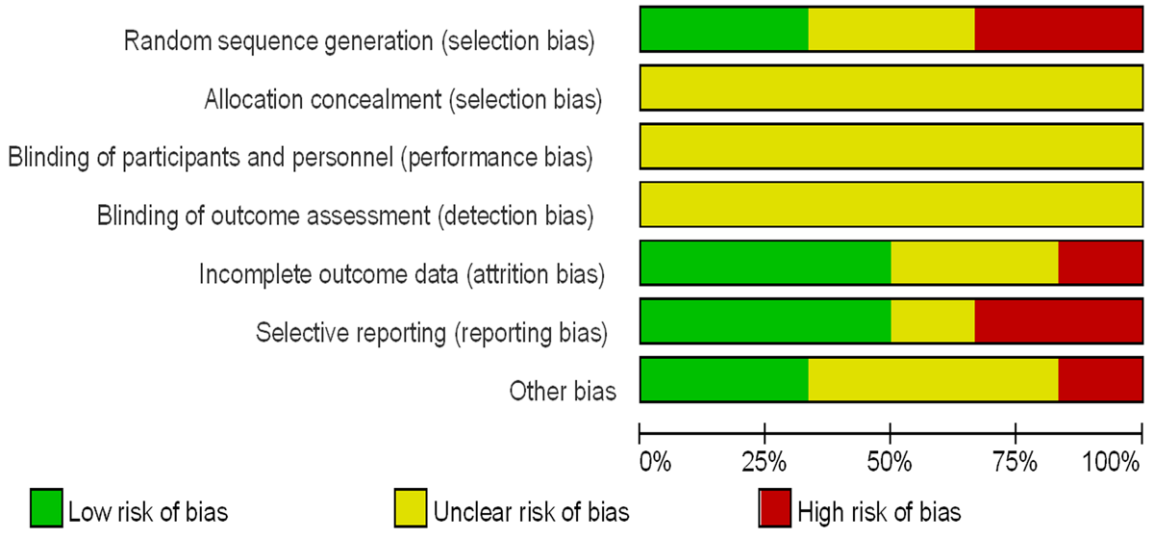

Figure 3. Risk of bias. Each risk-of-bias item presented as percentages across all included studies, which indicated the proportion of different levels of risk of bias for each item.

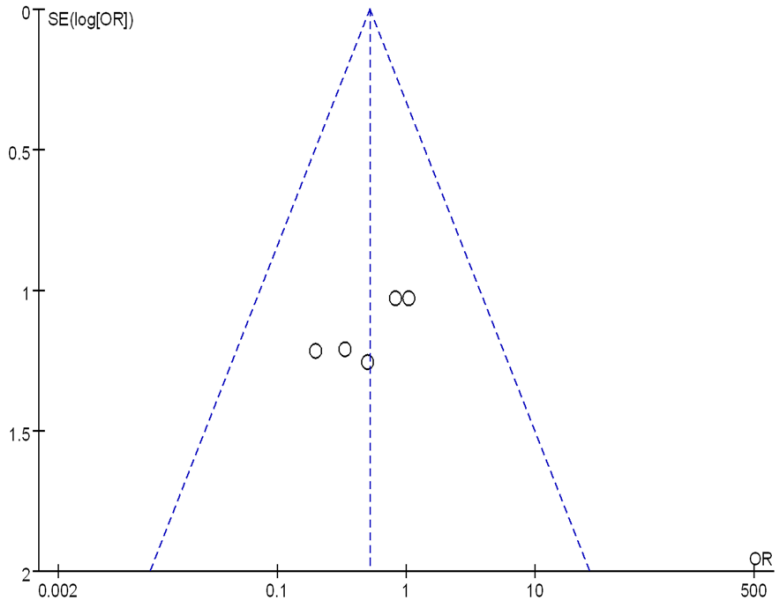

Figure 4. A funnel plot of non-union to assess publication bias.

ity, respectively. When the chi-square test showed $P > 0.05$, or $I^2 < 50\%$, indicating low statistical heterogeneity, a fixed-effect model was used. When the chi-square test showed $P < 0.05$, or $I^2 > 50\%$, indicating high statistical heterogeneity, a random-effect model was used. A probability of $P < 0.05$ was regarded as statistically significant. Subgroup analysis was performed in our meta-analysis, and mainly focused on the types of internal fixations such as the DCS and the locking plate which would affect the mechanical stability and outcome. We assessed publication bias by using a funnel plot of the reported primary outcomes.

Results

Study characteristics

From the selected database, the literature search initially yielded a total of 711 relevant studies. By screening the title and reading the abstract and full article, six studies eventually satisfied our eligibility criteria. The six studies included two quasi-randomized controlled trials (RCTs) [6, 7], two retrospective trials [8, 9] and two oral presentations [10, 11] registering a total of 279 patients eligible for data extraction and meta-analysis. The literature search procedure was shown in **Figure 1**. The Hartin et al. study [12] included periprosthetic DFF following total knee arthroplasty, and was therefore excluded. The Wu et al. study [13] utilized the Grosse-Kempf interlocking nails instead of the RIMN, and was also excluded. The characteristics of

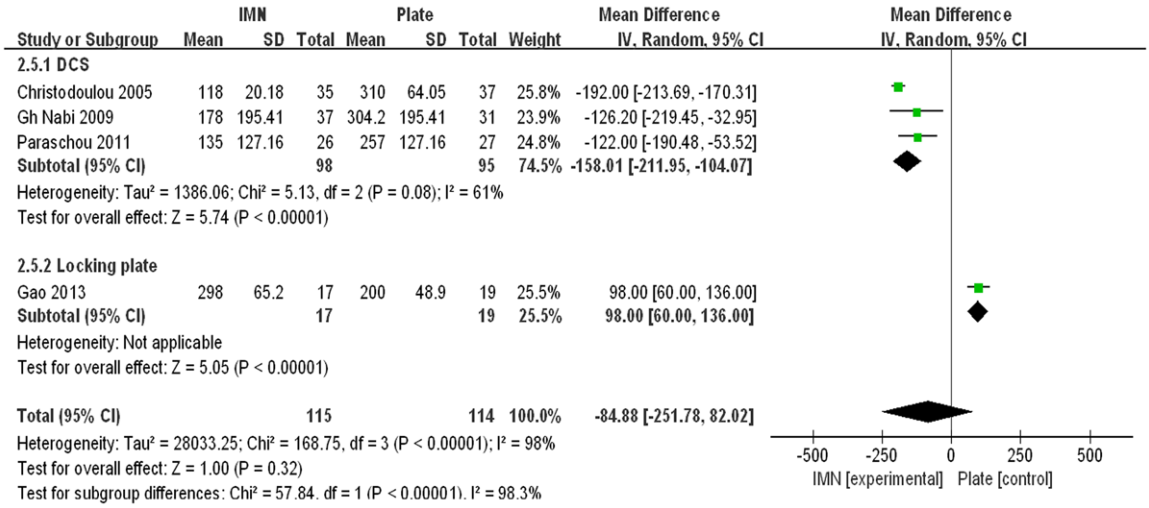

Figure 5. Subgroup analysis of intra-operative blood loss.

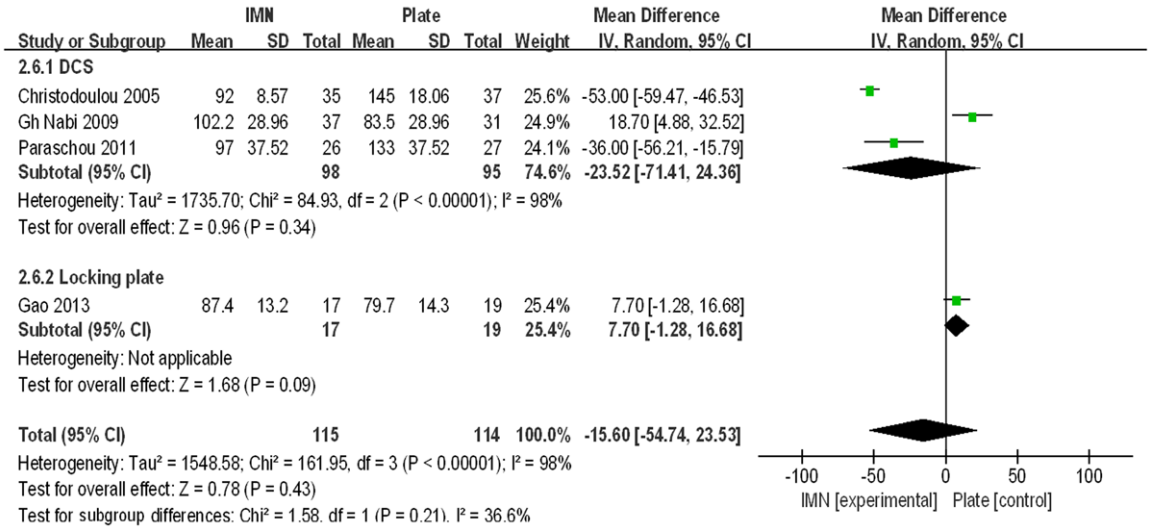

Figure 6. Subgroup analysis of operating time.

included patients are shown in **Table 1**. The included trials had certain methodological limitations (**Figures 2** and **3**).

Meta-analysis results

Intra-operative blood loss

The intra-operative blood loss was documented in four studies [6, 7, 9, 11]. There was no significant difference between the RIMN and plating. (n = 229, MD = -84.88; 95% CI -251.78 to 82.02, P = 0.32; heterogeneity P < 0.00001, I^2 = 98% **Figure 5**). The total heterogeneity was significant (I^2 = 98%). The subgroup analysis showed that the DCS had significant more intra-operative blood loss than the RIMN (MD = -158.01; 95% CI -211.95 to -104.07, P < 0.00001; heterogeneity P = 0.08, I^2 =61% **Figure 5**). The locking plate group showed significantly less intra-operative blood loss than the RIMN group (MD = 98; 95% CI -251.78 to 82.02, P < 0.00001; heterogeneity: not applicable).

Operative time

The operative time was documented in four studies [6, 7, 9, 11]. The forest plot showed no significant difference in the operative time for

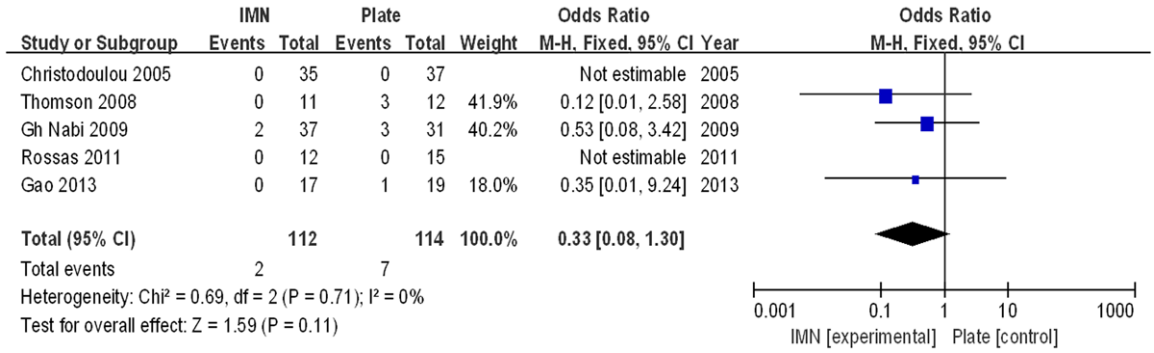

Figure 7. Odds ratio (OR) estimate for rate of infection.

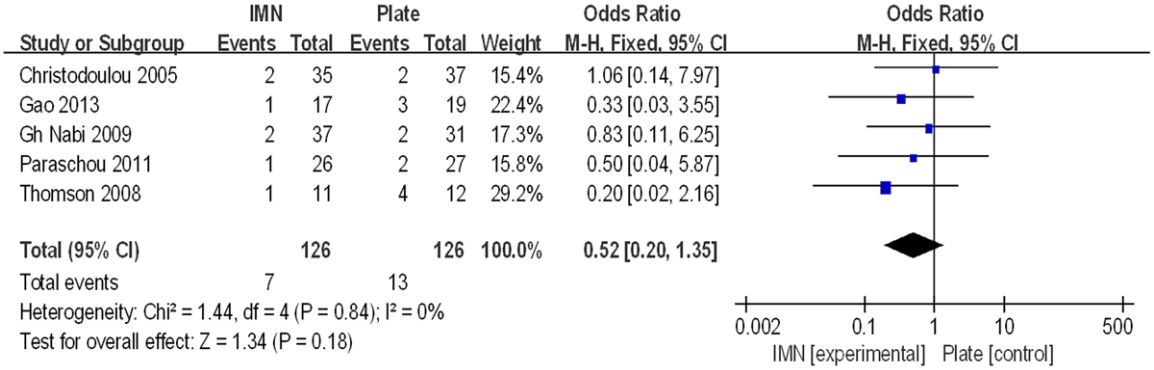

Figure 8. Odds ratio (OR) estimate for rate of non-union.

DFF (n = 229, MD= -15.6; 95% CI -54.74 to 23.53, P = 0.43; heterogeneity P < 0.00001, I^2 = 98%; **Figure 6**). The total heterogeneity was significant (I^2 = 98%). The subgroup analysis showed that the DCS and the locking plate did not differ significantly from the RIMN in operative time.

Infection

The wound infection rate was calculated for five studies [6-10]. The available data demonstrated that the wound infection incidence in the RIMN group was lower than that of the plating group. However, there was no significant difference in the wound infection incidence between the two groups (n = 226, OR = 0.33; 95% CI 0.08 to 1.30, P = 0.11; heterogeneity P = 0.71, I^2 = 0%; **Figure 7**).

Non-union

The non-union incidence was also reported for five studies [6-9, 11]. The data showed that the RIMN group had a lower non-union rate than the plating group. However, no significant difference was found between the two surgical interventions in terms of non-union incidence for the DFF (n = 252, OR = 0.52; 95% CI 0.20 to 1.35, P = 0.18; heterogeneity P = 0.84, I^2 = 0%; **Figure 8**).

Mal-union

Five studies reported the occurrence of mal-union [6-9, 11]. The pooling of outcomes showed that no significant difference was found in mal-union when comparing the two surgical techniques for DFF. (n = 252, OR=0.92; 95% CI 0.35 to 2.46, P =0.87; heterogeneity P = 0.24, I^2 = 27% **Figure 9**).

Delayed union

Three trials reported the incidence of delayed union [6, 7, 9]. The meta-analysis showed no significant difference between the RIMN group and the plating group in terms of delayed union for DFF. (n = 176, OR= 0.52; 95% CI 0.14 to 1.98, P =0.34; heterogeneity P = 0.31, I^2 = 15% **Figure 10**).

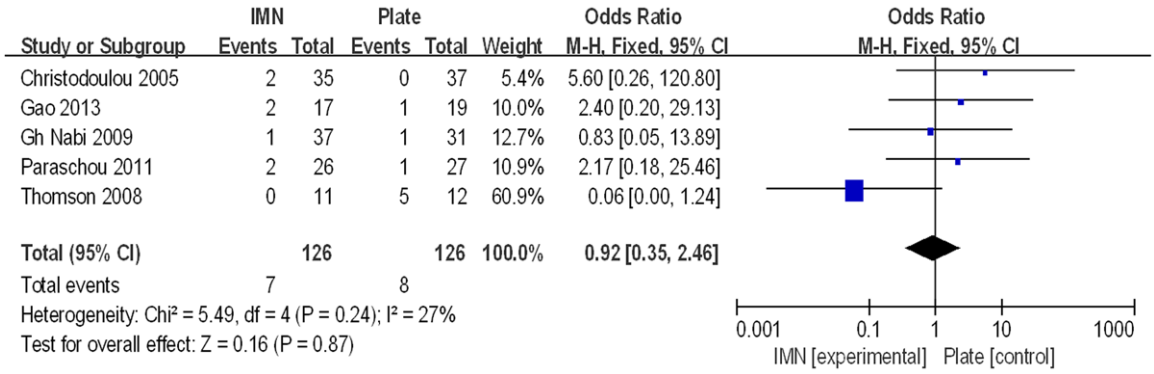

Figure 9. Odds ratio (OR) estimate for rate of mal-union.

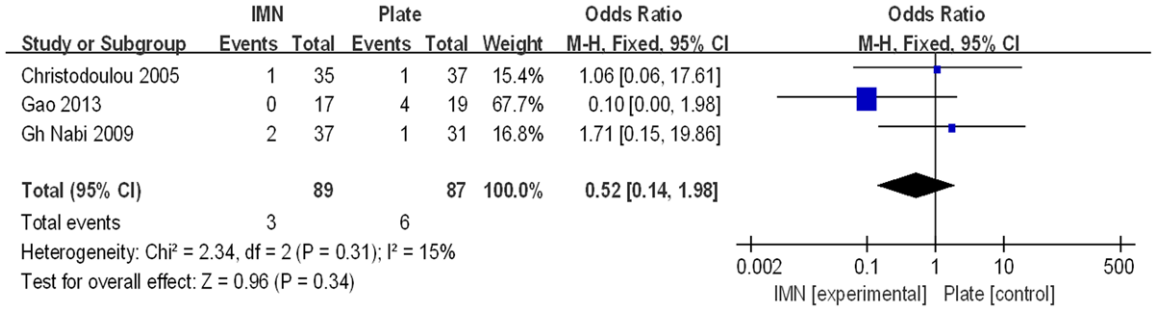

Figure 10. Odds ratio (OR) estimate of delayed union.

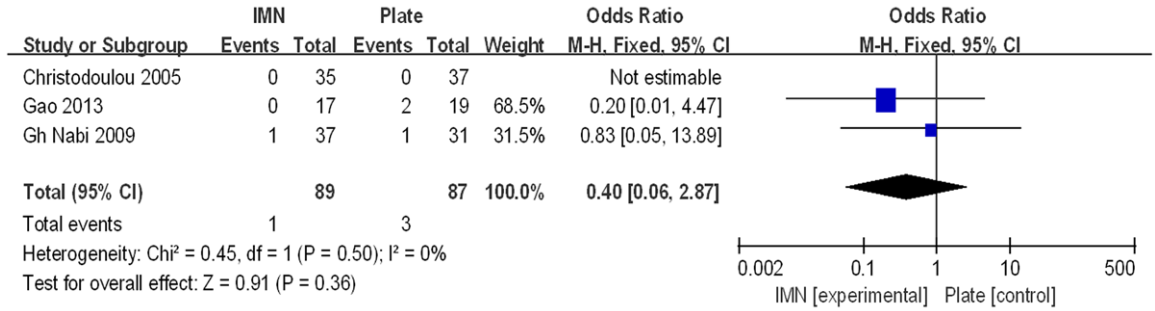

Figure 11. Odds ratio (OR) estimate of metalwork failure.

Metalwork failure

We observed no significant difference in metalwork failure between RIMN fixation and plating fixation in three studies [6, 7, 9]. (n = 176, OR= 0.40; 95% CI 0.06 to 2.87, P = 0.36; heterogeneity P = 0.50, I^2 = 0% **Figure 11**).

Knee stiffness

The knee stiffness rate was calculated for three studies [6, 7, 11]. We observed no significant difference in the knee stiffness between RIMN fixation and plating fixation for DFF (n = 193, OR= 0.75; 95% CI 0.28 to 1.99, P = 0.56; heterogeneity P = 0.79, I^2 = 0%; **Figure 12**).

Knee pain

The knee pain rate was calculated for only two studies [9, 10]. We observed that the knee pain incidence in RIMN was higher than that of the plating group. However, there was no significant difference between the two groups (n = 63, OR

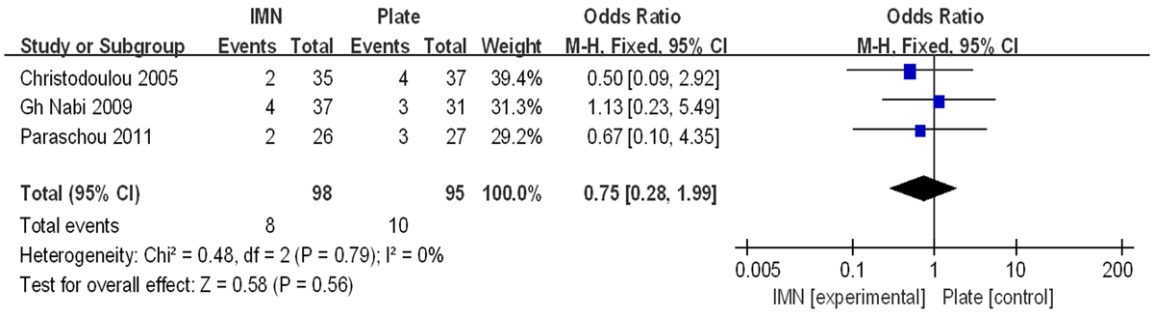

Figure 12. Odds ratio (OR) estimate for rate of knee stiffness.

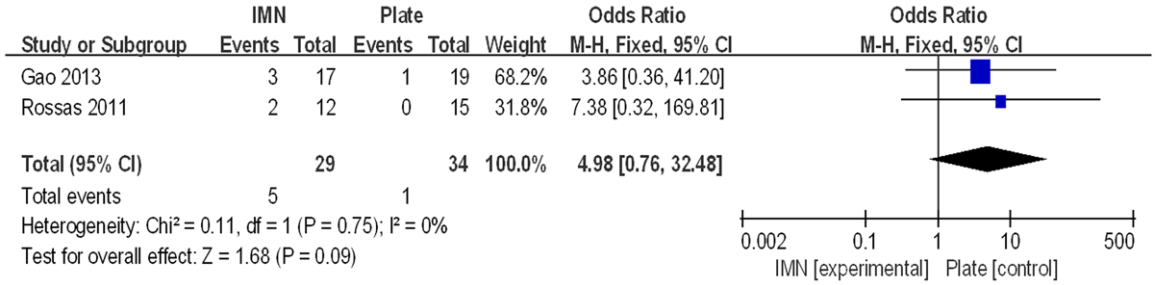

Figure 13. Odds ratio (OR) estimate for rate of knee pain.

= 4.98; 95% CI 0.76 to 32.48, P = 0.09; heterogeneity P = 0.75, I^2 = 0%; **Figure 13**).

Publication bias

We acknowledge that fracture union is the critical endpoint. A funnel plot for non-union rate in the RIMN and plating groups was established to evaluate publication bias (**Figure 4**). The funnel plot of non-union showed limited evidence of small study inclusion and no conspicuous publication bias with a visibly symmetrical diagram.

Discussion

DFF require surgery to achieve optimal outcomes. Various implants have been used in the treatment of DFF. However, there is no consensus on the benefits and harm of different interventions. One previous systematic review [14] only included one prospective cohort and several case series, and therefore the validity was limited. That prospective cohort [15] was not included in our meta-analysis, as it did not meet our inclusion criteria, and involved periprosthetic DFF.

Wound infection remains a basic problem for patients. Our meta-analysis showed that the infection incidence in the RIMN group was lower than that of the plating group. However, there was no statistical difference between the two groups. Theoretically, the RIMN used indirect reduction of the metaphyseal fracture, offering a less invasive approach. The open reduction and internal plate fixation caused extensive wound exposure and soft tissue damage, which could increase the risk of infections. Larger, adequately powered clinical RCTs are needed for verification.

We considered the intra-operative blood loss and operative time as relevant to the infection rate. Therefore, we created a forest plot of the intra-operative blood loss and operative time. In our meta-analysis, the locking plate showed significantly less intra-operative blood loss than the RIMN group. However, the locking plate involved only one study, so the conclusion is not persuasive. The subgroup meta-analysis showed that the DCS has more intra-operative blood loss compared to locking plates and the RIMN group, which was in agreement with current understanding [16]. The meta-analysis

showed no significant difference in the operative time for DFF. The operative time seems to be less dependent on the implant than on a surgeon's technique.

Greater soft tissue dissection could result in non-union in plate fixation. RIMN enables minimally invasive fracture fixation, but the technical pitfalls in RIMN fixation are incomplete reduction due to minimally invasive fracture reposition and relatively little stability, which may also lead to fracture delayed union, malunion, or non-union. There is agreement that closed reduction with RIMN and less invasive plate osteosynthesis are preferred methods of fixation. We know that bone healing needs relatively stable circumstances, which results in some interfragmentary movement to stimulate callus formation; however, the locking plate may be too stiff, suppressing the callus formation necessary for bridging bone healing. Our meta-analysis found no significant difference in terms of delayed union, non-union, and malunion rates between the RIMN group and the plating group. Thus, we could not definitively conclude which implant is better. Recently, the MIPO technique has been widely promoted because of its biological advantages. However, MIPO has the disadvantage of a potentially higher malunion rate and is more technically demanding [17]. Despite the widespread use of the locking plate and MIPO technique to fix DFF, there is insufficient evidence that these devices are superior to previously established methods.

In our meta-analysis, no significant difference was found comparing the RIMN and plating groups in terms of metalwork failure, because of the limited sample size. In the latest biomechanical studies, Christopher et al. [18] and Mehling et al. [19] have shown that both RIMN and plating osteosynthesis have comparable results. The clinical evidence was in agreement with the biomechanical data. Other studies have shown that locking systems are better than traditional internal fixation (DCS plate, retrograde nailing, blade plate) [20].

Several studies reported that the RIMN group had more implant protrusion, knee pain, and knee stiffness [21]. A disadvantage of RIMN is the poor stability of the distal interlocking screws in osteoporotic bone with the risk of nail protrusion into the articular space of the knee, resulting in knee damage and stiffness. There is also evidence that intramedullary nails are less stiff than locking plates [22, 23]. Sufficient implant anchorage is critical. Fixation failures are more common in osteoporotic fractures. In the management of DFF, distal locking has a major impact on the implant anchorage in osteoporotic bone [24, 25]. Studies concluded that the locked distal screw nails exhibited less fracture collapse than unlocked distal screw nails. Longer nails also provided improved initial fracture stability when compared with short retrograde intramedullary nails due to a more stable mechanical interaction between the femoral diaphysis and the nail [26]. Leggon et al. found a trend of more knee pain with RIMN [27]. RIMN also resulted in high rates of malrotation (11%-22%) [28]. Regarding knee stiffness and pain, we found no significant differences between the two groups for DFF. However, the reliability of our results should be treated with caution, as only several studies were included.

For clinical use, knowing the specific qualities of each implant is important for selection of the most suitable one for each specific situation. For each fracture type, the surgeon has to know the advantages and disadvantages of each implant. We must emphasize that high-quality results are more dependent on surgical technique than the choice of implant. The skill and experience of the surgeon is paramount to a successful outcome [3].

The evidence base currently presents a number of methodological weaknesses. Our meta-analysis includes two studies of oral presentations [10, 11]. The quasi-RCT had inadequately concealed randomization. Without a proper double-blind trial, the assessor would have expectation bias and the potential for type II statistical errors in clinical outcomes would probably emerge. Although RCTs are the gold standard for clinical trials, it is difficult to devise an RCT for orthopedic surgeons, because ethical considerations make it difficult to conduct a high-quality clinical trial. The statistical value could be improved by including more RCTs in the future. The variety of fracture types, the different orthopedic technical levels, and a variety of metalwork products caused clinical heterogeneity to a certain extent. Publication bias

may exist, because negative results are less likely to be published.

Conclusion

In the present meta-analysis, no implant was superior to any other under all circumstances for DFF. Current evidence has shown that RIMN and plating have similar postoperative complication rates. RIMN and plate fixation are similar in terms of infection, non-union, delayed union, malunion, and metalwork failure. However, this conclusion must be considered with caution since the evidence presented a number of methodological limitations and used potentially underpowered samples. All the above viewpoints require larger, rigorously powered multicenter RCTs to confirm.

Acknowledgements

We thank all the clinical researchers who were involved in the included studies.

Disclosure of conflict of interest

None.

Authors' contribution

SLZ and AJW designed the study. SLZ, LXS, and WDL collected the data and contributed to the design of the study. SLZ and SLK prepared and revised the manuscript. All authors read and approved the final content of the manuscript.

Address correspondence to: Shuangle Zong, Department of Orthopedics Institute, The Second Hospital of Tangshan, Tangshan 063000, Hebei Province, People's Republic of China. E-mail: zongshuangle@163.com

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