Original article

Proximal femoral nails antirotation, Gamma nails, and dynamic hip screws for fixation of intertrochanteric fractures of femur: A meta-analysis

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ARTICLE INFO

Article history:
Accepted 17 July 2014

Keywords:
Intertrochanteric fractures
Dynamic hip screw
Gamma nail
Proximal femoral nail antirotation
Meta-analysis

ABSTRACT

Background: Which surgical strategy is the best one for intertrochanteric fractures remains a controversial issue. Dynamic hip screw (DHS) and Gamma nail were commonly used but often associated with some complications, such as fixation failure and implant-related fractures. Meanwhile, proximal femoral nail anti-rotation (PFNA) fixation has recently been developed for minimally invasive surgery to reduce the complications rate. To facilitate the clinical decision-making, we conducted an updated meta-analysis to discuss the optimal treatment of intertrochanteric fractures aiming to determine which implant gives the lower rates of blood loss, complications (peri-implant fracture, fixation failure, infection, thromboembolic), reoperation, and mortality, as well as the minimal duration related to surgery (fluoroscopic exposure, surgery and hospital stay).

Patients and methods: Seven electronic databases were searched for randomized controlled trials (including OVID, Springer, Google Scholar, PubMed, Cochrane library, Embase, and Web of Science). Fourteen studies with 1983 patients were included. The modified Jadad Scale was used to assess the methodological quality of these studies. Risk of bias in the included studies was assessed using the Cochrane Risk of Bias tool. Comparison among the three groups was based on twelve indicators, including operative time, fluoroscopy time, operative blood loss, length of hospital stays, wound infection or hematoma, pneumonia, thromboembolic complications, fixation failure, operative fracture of femur, later fracture of femur, reoperation, and mortality.

Results: (1) PFNA group versus DHS group: PFNA was associated with less blood loss (mean difference (MD) = −253.86, 95% CI = −270.25 to 237.47; P < 0.00001) and lower rate of fixation failure (MD 0.20, 95% CI 0.07 to 0.59; P = 0.004), but led to more fluoroscopy time (MD 2.11, 95% CI 1.78 to 2.43; P < 0.00001). (2) PFNA group versus Gamma nail group: PFNA led to less blood loss (MD −55.30, 95% CI −60.07 to −50.53; P < 0.00001), shorter fluoroscopy time (MD −0.50, 95% CI −0.55 to −0.45; P < 0.00001) and length of hospital stay (MD −0.20, 95% CI −0.27 to −0.13; P < 0.00001); (3) DHS group versus Gamma nail group: DHS was associated with lower rate of operative fracture of femur (MD 0.31, 95% CI 0.11 to 0.89; P = 0.03), later fracture of femur (MD 0.16, 95% CI 0.06 to 0.43; P < 0.0004), and reoperation (MD 0.49, 95% CI 0.27 to 0.88; P = 0.02), but caused more blood loss (MD 29.49, 95% CI 8.27 to 50.70; P = 0.006). In contrast, there was no difference regarding operative time, infection hematoma, pneumonia, thromboembolic events, and mortality.

Discussion: PFNA should be a priority choice for treatment of intertrochanteric fractures with minimal rate of fixation failure, less blood loss and shorter length of hospital stay. DHS has distinct advantages over Gamma nail with lower rate of plant-related complications and should be preferred device for intertrochanteric fractures. However, owing to the low quality evidence currently available, more high-quality RCTs are needed to confirm these findings.

Level of evidence: Level II.

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http://dx.doi.org/10.1016/j.otsr.2014.07.023
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1. Introduction

With a growing aging population, the incidence of intertrochanteric fractures is rising [1]. It has been estimated that intertrochanteric fractures occur in more than 200,000 people each year in the United States, with reported mortality rates ranging from 15% to 30% [2].

There is a considerable debate regarding which is the optimal implant for fixing intertrochanteric fractures. Options for treating intertrochanteric fractures include extramedullary fixation and intramedullary fixation. Dynamic hip screw (DHS), the most representative implant of extramedullary fixation, has been considered the gold standard for treatment of intertrochanteric fractures. However, DHS often fails to give good results in the unstable and reverse oblique fracture, which limits its clinical use [3,4]. Gamma nail has been widely used for many years because of its inspiring clinical results [5,6]. Long-term studies, however, revealed that Gamma nail might cause higher intra-operative and late complications that often require revision surgery [7,8]. PFNA was designed to minimize the risk of these implant-related complications, and preliminary results suggested that this goal might have been achieved [9,10]. PENA provides angular and rotational stability, which is especially important in osteoporotic bone, and allows early mobilization and weight bearing on the affected limb [11,12]. Biomechanical tests have shown its biomechanical superiority to sliding hip screw or Gamma nail [13].

Recently, a number of prospective randomized trials have been performed to compare the management of intertrochanteric fractures using these three fixation methods. However, these studies were limited in sample size and quality of methodology, and failed to draw a definitive conclusion on which fixation method is optimal for intertrochanteric fractures in reducing complications and improving prognosis. Thus, to provide a strong support for clinical decision, we conducted an updated meta-analysis to evaluate the efficacy of three interventions in treatment of intertrochanteric fractures through twelve evaluation criteria. The questions that drive the current study were the following: which implant gives the lower rates of blood loss, complications (peri-implant fracture, fixation failure, infection, thromboembolic), reoperation, and mortality, as well as the minimal duration related to surgery (fluoroscopic exposure, surgery and hospital stay).

2. Methods

2.1. Inclusion criteria

2.1.1. Search strategy

The electronic databases of PubMed (1974–9/2013), Embase (1974–9/2013), and Web of Science (1966–9/2013), Cochrane Library (Issue 6, 2013), Embase (1974–9/2013), Google Scholar (1974–9/2013), Springer (1989–9/2013), and OVID (1992–9/2013) were searched using a sensitive methodological filter for etiology studies. The key words including “intertrochanteric fractures”, “proximal femoral nail antirotation”, “dynamic hip screw”, and “Gamma nail” were used. Google Scholar and Medical matrix were also searched to investigate potentially relevant literature. In addition, the reference lists of included studies and all related review articles were checked for further trials, published or unpublished. Language and publication status date were not restricted, and gray literatures were also investigated, as well as ongoing trials.

2.2. Data collection and analysis

2.2.1. Selection of studies

The inclusion criteria are as follows:

- patients over 60 years old with stable or unstable peritrochanteric fractures (peritrochanteric or intertrochanteric), excluding the pathological fractures;
- interventions including, DHS Gamma nail, or PFNA fixation;
- prospective, randomized controlled trials.

Duplicates or multiple publications of the same study, case reports, and animal studies were excluded from this review.

Twelve indicators assessed the outcomes:

- operative time;
- fluoroscopy time;
- operative blood loss;
- length of hospital stays (days);
- wound infection or hematoma;
- pneumonia;
- thromboembolic complications;
- fixation failure;
- operative fracture of femur;
- later fracture of femur;
- re-operation;
- mortality.

Two authors independently undertook the screening of studies. An initial screening of titles and abstracts was performed to remove those that were obviously outside the scope of the review. When the title or abstract could not be rejected with certainty, the full text article was obtained for further evaluation.

2.2.2. Data extraction and management

Data were extracted for all studies that met the inclusion criteria. For each study, two review authors independently completed data extraction forms that were tailored to the requirements of this review. All disagreements were resolved by discussion between the two review authors. If consensus could not be made, a third review author would be asked to complete the data extraction form and discuss the paper with the other two authors until the consensus was reached. If any data were missing from the trial reports, the review authors would attempt to obtain the data by contacting the authors. Any disagreement was resolved by discussion.

2.2.3. Assessment of risk of bias in included studies

Two reviewers assessed each study according to the modified Jadad Scale independently [14]. In this scale, the maximum quality score is seven points. The points are given according to the following rules: two points for appropriate methods of randomization, two for appropriate methods of blinding, two for appropriate methods of allocation concealment, and one for all enrolled patients participate in the study except for those who quit with reason. Low quality studies were rated score zero to three points and high quality four to seven points.

2.2.4. Data synthesis

This study used the Review Manager 5.1 software for meta-analysis (Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration). When there were dichotomous variables, risk ratios (RR) were calculated for each study. When the data were continuous and the standardized mean difference (SMD) or the mean difference (MD) was used, 95% confidence intervals were determined for all effect sizes. Heterogeneity was analyzed using Chi² tests before meta-analysis ($P = 0.05$). If there was no heterogeneity ($P > 0.05$, I² < 50%), a fixed effect model was used, otherwise ($P < 0.05$) a random effect model was used. Sensitivity analysis was carried out by removing relevant research to observe whether the homogeneity and the results changed significantly. If it did, this was used to find the reason of heterogeneity for further analysis.

We then judged the results for stability and strength. If the heterogeneity was too large to analyze, the descriptive analysis was presented.

3. Results
3.1. Description of studies

The literature search yielded 123 studies, including 52 duplicates or duplicate publications which were eliminated at first. 11 studies clearly did not match our inclusion criteria by title and abstract and were excluded then. No data was obtained from gray literature investigation as well from ongoing trials (we had no answer from the authors despite they were contacted). For the remaining 60 papers, the full articles were retrieved and assessed according to our inclusion criteria. 46 of these did not meet the inclusion criteria. Therefore, 14 prospective randomized controlled trials were included in this review. The list of studies excluded and reasons for exclusion are shown in Fig. 1. The assessment of study quality was present in Table 1. The characteristics of included studies are shown in Table 2.

3.2. Effects of interventions
3.2.1. Operative time (minutes)

Three studies reported the comparison of operative time between PFNA group and DHS group. The heterogeneity test showed a statistical heterogeneity among these studies ($I^2 = 99\%, P = 0.00001$) and random-effects model was adopted. No statistical difference was found between PFNA group and DHS group in terms of operative time (MD $-14.95$, CI $-44.50$ to $16.50$; $P = 0.37$). Similarly, pooled results showed that there was no statistical difference whether between DHS group and Gamma nails group (MD $0.16$, 95% CI $-0.24$ to $0.57$; $P = 0.42$) or between PFNA group and Gamma nails group (MD $-4.50$, 95% CI $-5.23$ to $-3.77$; $P < 0.00001$).

3.2.2. Fluoroscopy time

Comparison of fluoroscopy time between PFNA group and DHS group was available in two studies. Data pooled by a fixed-effects model confirmed that fluoroscopy time with PFNA was greater than with DHS (MD $2.11$, 95% CI $1.78$ to $2.43$; $P < 0.00001$) (Fig. 1). Only one study involved the comparison of fluoroscopy time between PFNA group and Gamma nail group. Pooled result indicated that fluoroscopy time with PFNA was less than with Gamma nail (MD $-0.50$, 95% CI $-0.55$ to $-0.45$; $P < 0.00001$). No data were eligible to compare DHS with Gamma nail in terms of fluoroscopy time.

3.2.3. Operative blood loss

Four studies investigated the difference of operative blood loss between PFNA group and DHS group. Data pooled by a fixed-effects model demonstrated that operative blood loss with PFNA was less than with DHS (MD $-25.89$, 95% CI $-27.02$ to $-23.72$; $P < 0.00001$) (Fig. 2). Analogously, pooled results of one study indicated that blood loss with PFNA was less than with Gamma nail (MD $-55.30$, 95% CI $-60.07$ to $-50.53$; $P < 0.00001$). Expectedly, pooled results of four studies revealed that operative blood loss with DHS was greater than with Gamma nail (MD $29.49$, 95% CI $8.27$ to $50.70$; $P = 0.006$) (Fig. 3).
Table 1
Quality assessment according to the modified Jadad Scale.

<table>
<thead>
<tr>
<th>Study [reference]</th>
<th>Random sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding</th>
<th>Withdrawals or dropouts (%)</th>
<th>Quality score</th>
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</tr>
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<td>Closed envelope</td>
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<td>Unclear</td>
<td>2</td>
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<td>Unclear</td>
<td>Unclear</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Yaozeng et al. [19]</td>
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<td>Sealed envelope</td>
<td>Unclear</td>
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<td>5</td>
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<td>Blind-envelope</td>
<td>Unclear</td>
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<td>4</td>
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<td>3</td>
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<td>Unclear</td>
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</table>

Table 2
Characteristics of included studies.

<table>
<thead>
<tr>
<th>Study [reference]</th>
<th>Age</th>
<th>No. of fractures in each group</th>
<th>Outcomes</th>
<th>Target population</th>
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<td></td>
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<td>DHS</td>
<td>Gamma nail</td>
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<td>81.2</td>
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<td>79</td>
<td>48</td>
<td>47</td>
</tr>
<tr>
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<td>81.0</td>
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<td>49</td>
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<td>75.4±1.0</td>
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<td>70</td>
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<td>42</td>
<td>39</td>
</tr>
<tr>
<td>Garg et al. [21]</td>
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<td>64.3</td>
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<td>113</td>
</tr>
<tr>
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<td>80.86</td>
<td>85</td>
<td>50</td>
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<td>79.2±2.9</td>
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<td>60</td>
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<td>83.1</td>
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<td>72–90</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>Xu et al. [27]</td>
<td>78.5±7.9</td>
<td>77.9±7.8</td>
<td>55</td>
<td>55</td>
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</tbody>
</table>

3.2.4. Length of hospital stay (days)

Only one study reported the comparison of length of hospital stay between PFNA group and DHS group. Data pooled by a fixed-effects model indicated that there was no statistical difference between the two groups (MD –0.40, 95% CI –1.03 to 0.23; P=0.21). Analogously, pooled results also showed that there was no statistical difference between DHS group and Gamma nail group (MD 0.16, 95% CI –0.24 to 0.57; P=0.42). However, we found PFNA significantly shortened the length of hospital stay compared with Gamma nail (MD –0.20, 95% CI –0.27 to –0.13; P<0.00001).

3.2.5. Wound infection or hematoma

Comparison of wound infection or hematoma between PFNA group and DHS group were documented in two studies. Data pooled by a random-effects model showed no statistical difference between the two groups (MD 0.26, 95% CI 0.01 to 0.50; P=0.37). Analogously, pooled results indicated that there was no difference whether between DHS group and Gamma nail group (MD 0.90, 95% CI 0.55 to 1.48; P=0.68) or between PFNA group and Gamma nail group (MD 1.07, 95% CI 0.36 to 3.15; P=0.91) regarding the rate of wound infection or hematoma.

Fig. 2. Forest plot diagram showing fluorescopic time when using PFNA or DHS.

Fig. 3. Forest plot diagram showing operative blood loss when using PFNA or DHS.
3.2.6. Pneumonia

Only one study provided the comparison of pneumonia rate between PFNA group and DHS group. Data pooled by a fixed-effects model showed no statistical difference between the two groups (MD 0.41, 95% CI 0.08 to 2.20; P=0.30). Similarly, pooled results showed that there was no difference whether between DHS group and Gamma nail group (MD 1.41, 95% CI 0.62 to 3.22; P=0.42) or between PFNA group and Gamma nail group (MD 1.35, 95% CI 0.35 to 5.27; P=0.66) with respect to pneumonia rate.

3.2.7. Thromboembolic complications

Eight studies reported the comparison of thromboembolic complications between DHS group and Gamma nail group. We pooled data by a fixed-effects model which demonstrated that there was no statistical difference in thromboembolic complications between the two groups (MD 0.73, 95% CI 0.50 to 1.07; P=0.11). No data were eligible to compare PFNA with DHS or PFNA with Gamma nail concerning the thromboembolic complications.

3.2.8. Fixation failure

To compare the fixation failure rate between PFNA group and DHS group, we conducted subgroup analysis which confirmed that fixation failure rate with PFNA was lower than with DHS (MD 0.20, 95% CI 0.07 to 0.59; P=0.004) (Fig. 4). However, pooled results showed no statistical difference whether between DHS group and Gamma nail group (MD 0.87, 95% CI 0.55 to 1.37; P=0.35) or between PFNA group and Gamma nail group (MD 2.23, 95% CI 0.53 to 9.32; P=0.27) with respect to fixation failure rate.

3.2.9. Operative fracture of femur

Only one study reported the comparison of operative femur fracture rate between PFNA group and DHS group. Data pooled by a fixed-effects model indicated that there was no statistical difference between the two groups (MD 5.61, 95% CI 0.26 to 11.62; P=0.27). However, pooled results of six studies showed that operative femur fracture rate with DHS was lower than with Gamma nail (MD 0.31, 95% CI 0.11 to 0.89; P=0.03) (Fig. 5). No data were eligible to compare PFNA with Gamma nail in operative femur fracture.

3.2.10. Later fracture of femur

Only one study investigated the difference of later femur fracture rate between PFNA group and DHS group. We pooled data by a fixed-effects model, which showed no statistical difference between the two groups (MD 3.30, 95% CI 0.13 to 82.78; P=0.47). Analogously, pooled results indicated that there was no difference between PFNA group and Gamma nail group (MD 3.29, 95% CI 0.33 to 32.41; P=0.31). However, pooled results of eight studies showed that later femur fracture rate with DHS were lower than with Gamma nail (MD 0.16, 95% CI 0.06 to 0.43; P=0.0004) (Fig. 6).

3.2.11. Reoperation

Only one study provided the comparison data of reoperation rate between PFNA group and DHS group. Pooled data indicated that there was no difference between the two groups (MD 0.06, 95% CI 0.00 to 1.12; P=0.06). However, pooled data of seven studies (1144 patients) showed that reoperation rate with DHS was less than with Gamma nail (MD 0.49, 95% CI 0.27 to 0.88; P=0.02) (Fig. 7). No data were eligible to compare reoperation rates with PFNA versus Gamma (Fig. 8).

3.2.12. Mortality

Only one study reported the comparison of mortality rate between PFNA group and DHS group. Data pooled by a fixed effects-model showed no statistical difference between the two groups (MD 1.26, 95% CI 0.26 to 6.04; P=0.77). Similarly, pooled results of seven studies confirmed that there was no difference between DHS and Gamma nail on the mortality rate (MD 0.97, 95% CI 0.72 to 1.30; P=0.84). No data were eligible to compare PFNA with Gamma nail in mortality.

4. Discussion

The optimal management of intertrochanteric fractures is still controversial. DHS and Gamma nail were most commonly used for fixing intertrochanteric fractures in the last decade [29]. However, PFNA, the latest developed device, is considered as a perfect device for intertrochanteric fracture with a lower incidence of complications [9,10]. Previous randomized controlled trials and meta-analyses failed to draw a unanimous conclusion. To facilitate a clinical decision, we conducted an updated meta-analysis to determine the optimal treatment of intertrochanteric fractures. Our meta-analysis suggests that PFNA can benefit intertrochanteric fractures with less blood loss and lower rate of fixation failure in comparison with DHS and Gamma nail; while DHS has advantages of lower rate of operative fracture of femur, later fracture of femur, and reoperation in comparison with Gamma nail.

The following limitations of this meta-analysis should be acknowledged. Firstly, despite a comprehensive search without any restriction, not all related randomized trials are included mainly because of publication bias or selection bias. Strict searches in the library and included bibliographies were conducted to reduce these biases. Secondly, many trials in our study included both stable and unstable fractures, and we were unable to obtain adequate information from the included studies to make any distinction in outcome for unstable versus stable intertrochanteric fractures. This may cause an over- or under-estimation of the true results. Therefore, we will consider the potential for presenting a summary of the evidence based on fracture type in our next meta-analysis. Thirdly, many trials herein involve different generations of Gamma nails, and the newer-generation implant is associated with decreased risk of implant-related fractures, which may affect the overall therapeutically effect of Gamma nail. Hence, we will conduct a subgroup analysis in terms of different generations of Gamma nails in our next meta-analysis. Lastly, we failed to assess the heterogeneity of populations regarding age level of autonomy and gender between studies. To compensate for this deficiency, we will assess the heterogeneity of these two factors in our next meta-analysis.

In the current study, we found no significant difference in several parameters (length of surgery, pneumonia, thromboembolic complications, and wound infection or hematoma) among PFNA, DHS, and Gamma nail. Our findings revealed that PFNA significantly reduced the length of hospital stay compared with Gamma nail, which implied that PFNA is superior to Gamma nail in terms of postoperative recovery.

In regard to blood loss, pooled results showed that fracture fixation with DHS led to more blood loss than with PFNA or Gamma nail. And this finding was supported by other meta-analyses [30,31]. Shen et al. [30] compared PFNA with DHS for treatment of intertrochanteric fractures, and they concluded that PFNA could benefit intertrochanteric fractures patients with less blood loss and fewer complications. This may be because DHS placement requires a relatively large exposure and significant soft tissue stripping, which cause serious bleeding [32]. However, Giraud et al. [33] reported a different finding that using the DHS was associated with less blood loss and at a lower cost in comparison with proximal femoral nail. Noteworthy, in order to avoid the surgical trauma of DHS, the Gotfried percutaneous compression plate (PCCP, Orthofix McKinney, Texas, USA) was developed for fixing intertrochanteric fractures with a minimally invasive method [34]. This device is mainly indicated for intertrochanteric fractures with intact lateral walls (AO type 31.A1, 31.A2, B2.1). And its theoretical advantages
Fig. 4. Forest plot diagram showing operative blood loss when using Gamma nail or DHS.

Fig. 5. Forest plot diagram showing the fixation failure rate when using PFNA or DHS.

Fig. 6. Forest plot diagram showing the operative femur fracture odds ratios when using DHS or Gamma nail.

Fig. 7. Forest plot diagram showing rates of later femur fracture when using DHS or Gamma nail.
are the provision of rotational stability, by using two screws in the femoral neck, and a reduction in the lateral cortical damage [35].

Ma et al. [36] performed a meta-analysis comparing PCCP with DHS for treatment of intertrochanteric fractures, and reported that PCCP allowed significantly shorter operative time, reduced blood and transfusion, as well as diminished incidence of cardiovascular events.

As many studies indicate, although an attractive biomechanical concept, Gamma nail has been associated with a significantly increased risk of intra-operative and later fracture around or below the implant [7,8,16]. In our findings, Gamma nail Indeed resulted in a higher risk of intra-operative and later fracture compared with DHS. This is also consistent with the results of many relevant systematic reviews [8,14,37]. These complications were attributed largely to the original design features of Gamma nail, leading to the redesign of newer-generation implants. Inspiringly, with newer designs and an improved understanding of the Gamma nail technique, risks of femoral shaft fractures significantly decreased [38,39].

In addition, another enhancer of Gamma nail was Bocchi, Bertone, Caniggia, Maniscalco (BCM™) (Lima™, Villanova, Italy) nail. It was designed to combine the advantages of the nail and its intrinsic stability with those of the screw-plate device (cephalic screw positioning, intra-operative impaction of up to 10 mm) without having the drawbacks of the Gamma nail (smaller nail diameter, opportunity to change with a plate) and of the screw-plate (post-operative impaction within the fracture site). In 1999, a series of 56 intertrochanteric fracture patients from Siena (Italy) had been reported benefitting from the insertion of this innovative fixation device [40]. Foulonne et al. [41] performed a case-control study on BCM™ nail versus DHS to fix pertrochanteric fractures. They found that BCM™ nail was associated with lower incidence of secondary displacement, higher healing rate, and better functional recovery. In addition, no intraoperative implant-related fractures were observed in the BCM™ subgroup of patients.

There were no significant differences in intra-operative and later femoral shaft fracture between PFNA and DHS, and this important finding was supported by another meta-analysis [31]. PFNA was designed to minimize the risk of these implant-related complications, and preliminary results suggested that this goal might have been achieved [9,10]. The inserted PFNA blade achieves an excellent fit via bone compaction and requires less bone removal than a screw does, which provides angular and rotational stability and is very beneficial for unstable intertrochanteric fractures or patients with osteoporosis [11,42]. And these advantages ensure the patient’s early mobilization and weight bearing on the affected limb [11,12].

No significant difference was found in fixation failure (cutting-out or non-union) between Gamma nail and PFNA or DHS. However, similar to the previous study, a significant lower risk of fixation failure was found in PFNA group in comparison with DHS [31]. Relative to DHS, PFNA is an intramedullary device with a helical blade rather than with a screw; this allows a better purchase in the femoral head to limit cut-outs due to varus deviation and rotation. In terms of reoperation, present results show that PFNA had no evidence of superiority to DHS. However, we found DHS was associated with a lower risk of reoperation than Gamma nail, which was contrary to the previous meta-analysis [43,44].

In conclusion, PFNA should be a priority choice for treatment of intertrochanteric fractures with minimal rate of fixation failure, less blood loss and shorter length of hospital stay. While DHS has distinct advantages over Gamma nail with lower rate of plant-related complications and should be preferred device for intertrochanteric fractures. However, owing to the low quality evidence currently available, more high-quality RCTs are needed to confirm the findings from this meta-analysis, and the effects of long-term period also need further study to improve clinical decision-making.

Disclosure of interest
The authors declare that they have no conflicts of interest concerning this article.

Source of funding: The funding of this work was supported by Yongchuan Hospital Chongqing Medical University. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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